

**Site Master File
of
L-Ornithine-L-Aspartate**

Jing Jing Pharmaceutical Co., Ltd

2025.07.07

1. General information on the manufacturer

1.1 Contact information on the manufacturer

1.1.1 Company name, registered address

Company name: Jingjing Pharmaceutical Co., Ltd.

Registered address: No. 88, Jingyi Road, Dacaozhuang Industrial Park, Ningjin County, Xingtai City, Hebei Province

1.1.2 The name and address of the company's production plant, as well as the building and production workshop in the factory

The names of buildings and production workshops in our company's factory area are shown in Table 1

Table 1: Names of buildings and production workshops in the factory

No	building name	department or workshop
No1	201	Workshop 201
No3	203	Workshop 203
No5	205	Workshop 205
No6	Boiler Room	Workshop 203
No4	storehouse	storehouse
No5	solvent area	Workshop 206
No6	office building	The third and fourth floors are laboratories
No7	office building	Company office building

1.1.3 Business contact information (including 24-hour contact numbers in the event of product defects or recalls)

project	Name	position	Tel	landline
contact	Jumin Niu	quality manager	86-13483182401	86-319-5566781
24 hours contact	Xiuli Liu	Customer	13831108726	86-311-83079373

1.1.4 Production address: No. 88, Jingyi Road, Dacaozhuang Industrial Park, Ningjin County, Xingtai City, Hebei Province.

1.1.5 The latitude and longitude coordinates of the factory are: Longitude: 114.999062 Latitude:

37.528435

1.2 Authorized pharmaceutical manufacturing activities of the site

1.2.1 Our company's existing production range is: sterile APIs, pharmaceutical excipients, and APIs. See Annex 1 for its valid production license text

1.2.2 Brief description of manufacture, import, export, distribution and other activities as authorised by the relevant Competent Authorities including foreign authorities with authorized dosage forms/activities, respectively; where not covered by the manufacturing authorization

At present, our company has obtained 11 registration approvals from the State Food and Drug Administration, 6 of which are APIs and 5 of which are pharmaceutical excipients. And passed GMP certification on February 13, 2018, the varieties are: sterile API (arginine, anhydrous sodium carbonate, N(2)-L-alanine-L-glutamine). Long-term production of sterile raw materials arginine, anhydrous sodium carbonate and alanyl glutamine (formerly known as: N (2)-L-alanine-L-glutamine). Staged production: APIs: Alanylglutamine, Ornithine Aspartate (exported from Korea)

Our company exports varieties: arginine, anhydrous sodium carbonate and alanyl glutamine, aspartate ornithine.

The company is not currently involved in drug import, distribution and other activities.

1.2.3 Types of products currently produced: The types of products currently produced by our company are included in Annex 1. Annex 2: None

1.2.4 In the past 5 years, our company's provincial-level (including commissioned by the provincial bureau) and above drug production quality management standards and registered production site inspections are shown in the following table.

No	Inspection agency	Inspection time
1	Hebei Provincial Drug Administration	December 22, 2017 to December 25, 2017
2	Hebei Provincial Drug Administration	October 17, 2019
3	Japan PMDA	December 10, 2019 to December 13, 2019
4	Hebei Provincial Drug Administration	July 13, 2020 to July 14, 2020
5	Hebei Provincial Drug Administration	30 March 2022 to 2 April 2022

GMP certificate see Appendix 3

1.3 Any other manufacturing activities carried out on the site

Other production activities carried out by our company: none.

2. Quality management**2.1 The quality management system of the manufacturer****2.1.1 Briefly describe the operation of the company's quality management system and the referenced standards**

The company's quality management system has established a complete quality management system document in accordance with the 2010 version of GMP, covering all processes and factors affecting product quality. Including quality management, organization and personnel, plant and facilities, equipment, materials and products, confirmation and verification, document management, production management, quality control and quality assurance, commissioned production and commissioned inspection, self-inspection, etc. A complete organizational structure has been established, and the functions of each department and the responsibilities of personnel at all levels have been formulated.

The Quality Department performs the responsibilities of quality assurance and quality control, and consists of quality assurance and quality control. The quality assurance system work section includes document management, material management, production process control and hygiene monitoring, verification management, change management, deviation management, corrective and preventive measures, product quality review and analysis, quality feedback, recall, commissioned inspection, risk management, Self-inspection and training, computerized systems, quality statistics, analysis and external work.

Quality control is responsible for the daily sampling, quality inspection and control of our company's raw and auxiliary materials, packaging materials, finished products, intermediate products, process water (purified water, water for injection), responsible for the management of raw and auxiliary materials, product retention samples, and product accelerated test inspections , Continuous stability inspection and sample inspection in product quality review activities.

The operation of the company's quality system refers to the requirements of relevant laws and regulations on pharmaceuticals, such as the "Drug Administration Law", "Good Manufacturing Practice for Pharmaceuticals" and "Administrative Measures for Drug Registration", to ensure that the operation

of the system meets the requirements of laws and regulations.

2.1.2 Quality system related responsibilities including senior management

In order to strictly implement the relevant national laws and regulations, quality standards and contract requirements for product application, safety and other characteristics. The company specially formulated the post responsibilities of the general manager, the production management person in charge, the quality management person in charge, and the quality authorized person, and formulated the functions of the quality department.

2.1.2.1 General Manager

- (1) Preside over the overall management of the company. Organizing the implementation of board resolutions. Propose management policies and work plans for each stage.
- (2) To draw up a plan for the establishment of the company's management organization.
- (3) To formulate the basic system of the company.
- (4) Formulate specific regulations of the company.
- (5) Convening and presiding over the general manager's office meeting, inspecting, supervising and coordinating the work progress of each department, listening to the work summary and report of each department, and making decisions or guiding opinions.
- (6) Preside over the company's team building and standardize internal management.
- (7) Responsible for cadre training, and organize the human resources department to formulate cadre promotion, training and promotion plans.
- (8) According to the annual and monthly assessment plan formulated by each department, the general manager's office meeting was held to discuss, revise and issue a formal assessment plan. According to the annual and monthly assessment plan, the company's assessment agency will formulate an assessment distribution plan after assessing the performance of each department's responsibilities and objectives.
- (9) Responsible for the construction of the company's corporate culture, and propose to the board of directors corporate renovation, development plans and extra-budgetary spending plans.
- (10) Review and issue documents issued in the name of the company.
- (11) Responsible for handling company emergencies.
- (12) To formulate the assessment objectives and remuneration mechanism of the competent

department at each stage.

(13) Formulate the annual financial budget and submit it to the board of directors. After discussion and revision, it will be decomposed and implemented.

(14) Responsible for the company's quality management.

(15) Responsible for the company's production safety management.

2.1.2.2 Production management manager

(1) Ensure that the products are produced and stored in accordance with the approved process regulations to ensure product quality.

(2) Ensure strict implementation of various operating procedures related to production operations.

(3) Ensure that batch production records and batch packaging records are reviewed by designated personnel and sent to the quality department.

(4) Ensure that the plant and equipment are maintained to keep them in good operating condition.

(5) Ensure that all necessary verification work is completed.

(6) Ensure that production-related personnel have undergone necessary pre-job training and continuing training, and adjust the training content according to actual needs.

(7) Complete the following work together with the person in charge of quality management:

① Review and approve documents such as process regulations and operating procedures of products.

② Supervise the sanitation of the factory area.

③ Ensure that key equipment is confirmed.

④ Ensure that the production process verification is completed.

⑤ Determine and monitor the storage conditions of materials and products.

⑥ Keep records.

⑦ Supervise the implementation of GMP.

⑧ Monitor the factors that affect product quality.

2.1.2.3 Head of Quality Management

(1) Ensure that raw and auxiliary materials, packaging materials, intermediate products, products to be packaged and finished products meet the registered and approved requirements and quality standards.

- (2) Ensure that batch records are reviewed prior to product release.
- (3) Ensure that all necessary inspections are completed and approve quality standards, sampling methods, inspection methods and other quality management operating procedures.
- (4) Review and approve all quality-related changes.
- (5) Ensure that all major deviations and out-of-standard inspection results have been investigated and dealt with in a timely manner.
- (6) Approve and supervise the entrusted inspection.
- (7) Supervise the maintenance of plant and equipment to keep them in good operating condition.
- (8) Ensure that all necessary validation or verification work is completed, and review and approve the validation verification scheme and report.
- (9) Make sure to complete the self-test.
- (10) Evaluate and approve material suppliers.
- (11) Ensure that all complaints related to product quality have been investigated and dealt with promptly and correctly.
- (12) Ensure the completion of the product's continuous stability inspection plan and provide data for stability inspection.
- (13) Ensure the completion of product quality review analysis.
- (14) Ensure that all relevant personnel of the enterprise have undergone necessary pre-job training and continuing training, and adjust the training content according to actual needs.
- (15) Review the product's process regulations, operating procedures and other documents.
- (16) Supervise the sanitation of the factory area.
- (17) Ensure that critical equipment is identified.
- (18) Ensure that the production process verification is completed
- (19) Approve and supervise commissioned production.
- (20) Determine and monitor storage conditions for materials and products.
- (21) Keep records.
- (22) Supervise the implementation of each department's compliance with the "Good Manufacturing Practice for Drugs".
- (23) Monitor the factors that affect product quality

.2.1.2.3 quality authorized person

Implement the laws and regulations on drug management, organize and standardize the quality management of drug production in enterprises. Organize the establishment and improvement of the quality management system of the pharmaceutical production of the enterprise, and monitor the system to ensure its effective operation.

Be responsible for the following quality management activities and exercise the right to make decisions:

approval for the release of the finished product;

Approval of quality management documents;

Process validation and approval of key process parameters;

Approval of internal control quality standards for materials and finished products;

Approval of non-conforming product handling;

Approval of product recall;

Participate in activities that have a key impact on product quality. For example, the selection of key material suppliers, the selection of key production equipment, the selection of key personnel in production quality departments, and other work related to drug quality, and exercise the right of veto

(4) In the process of drug production quality management, the quality authorized person should take the initiative to communicate and coordinate with the drug supervision and management department.

2.1.3 Status of factory quality system certification and accreditation

Workshop	Certificate name	Production and Certification Scope	Date of issue	Certificate No	Validity period	Accredited unit
201 Workshop	GMP certificate	Sterile API (Arginine, Anhydrous Sodium Carbonate N(2-L-Alanine-L-Glutamine))	February 13, 2018	HE20180011	February 12, 2023	Hebei Food and Drug Administration

2.2 Release procedure of finished products

2.2.1 Describe in detail the qualification requirements of the authorized person responsible for the batch confirmation and release process

The quality authorized person shall have at least a bachelor's degree in pharmacy or related majors (or intermediate professional technical title or licensed pharmacist qualification), have at least five years of practical experience in drug production and quality management, and have been engaged in drug production process control and quality inspection.

The quality authorized person shall have the necessary professional theoretical knowledge and have undergone training related to product release before he can perform his duties independently.

2.2.2 Outline batch confirmation and release procedures

The company's release management procedures are compatible with the drug production quality management. For the finished product applying for release, the production workshop shall first review the production and packaging process records related to the product. After the audit is correct, fill in the audit result on the "Batch Record Audit Release Form" and sign it and submit it together with the batch production record to the quality assurance specialist for audit.

The quality assurance specialist will review the batch production records and batch packaging records without error, sign the "Batch Record Review Release Form" and submit it to the quality archives.

After the quality control has completed the inspection, the quality control file administrator will organize the inspection records and submit them to the quality control manager after preliminary review. The quality control manager shall review the batch inspection records, sign the Batch Record Review Release Form after review and submit it to the archives.

After completing the audit, the quality authorized person should fill in the "Finished Product Audit Release Form", and finally decide the release of the product.

2.2.3 Responsibilities of quality authorized person/Product Releasers in Pending Inspection and Release and Marketing Authorization Conformance Assessment

The exercise of decision-making power, approval of finished product release, and finished product review are as follows:

- (1) Review whether the production process meets the requirements of production license and registration approval;
- (2) Check whether various batch records are complete;
- (3) Check whether the identification (name, code, batch number) of all production and inspection

records are consistent;

- (4) Whether the site clearance and production preparations meet the requirements;
- (5) Whether the production process is operated according to the approved SOP;
- (6) Whether the corresponding cleaning and cleaning operations have been carried out;
- (7) Whether the cleaning or sterilization of the equipment and packaging materials used is recorded in the production records;
- (8) Whether the production of each process is completed within the specified time limit;
- (9) Whether the sampling and online control results meet the requirements;
- (10) Whether the batch number and validity period of the certificate, labels, etc. used are correct, and whether the material balance of each process meets the regulations;
- (11) Whether the label amount is balanced;
- (12) Whether the batch production meets the specified limit or product, and whether the reason for the deviation has been recognized;
- (13) Whether the inspection results of the Quality Control Department are in compliance with the current quality standards;
- (14) Whether each record is complete and verified by investigation;
- (15) Whether the production environment meets the specified requirements.

2.2.4 the arrangements between authorized persons/qualified persons when several authorized persons/qualified persons are involved;

The quality authorized person can delegate part or all of the quality management responsibilities to the qualified persons , but the authorized person shall be responsible for the qualified persons drug quality management behavior of the authorized personnel. The responsibilities of the delegated parties shall be clearly defined in writing. When qualified persons perform their duties, their corresponding quality management activities are documented.

Quality authorized person: Niu Jumin, who has obtained the qualification of quality authorized person after training, and filed with Hebei Food and Drug Administration on May 25, 2015.

2.2.5 Our company does not apply Process Analytical Technology (PAT) and real-time or parametric release of products.

2.3 Management of suppliers and contractors

2.3.1 a brief summary of the establishment/knowledge of supply chain and the external audit

programme

The company has established the "Material Supplier Quality Audit Standard Management Procedure", which stipulates the requirements and working procedures for supplier level confirmation, supplier selection, supplier audit, and supplier file management. The safety level of materials is determined according to factors such as product quality risk, and is divided into critical materials and non-critical materials. Suppliers of critical materials are designated as A-level suppliers, and suppliers of non-critical materials are designated as B-level suppliers. The audit method of suppliers is to conduct on-site audits of raw material suppliers among A-level suppliers every two years, and conduct on-site audits of other A-level suppliers every four years. Documentation audits of B-level suppliers are conducted every four years. An annual assessment of all material suppliers is conducted annually to determine whether they can continue to be qualified suppliers.

2.3.2 Briefly describe the qualification confirmation system for contractors, API manufacturers and other key material suppliers

According to the company's "Material Supplier Quality Audit Standard Management Procedures" document, the preliminary selection of suppliers is carried out by means of questionnaires. The quality department organizes the evaluation according to the "Supplier Basic Information Questionnaire" and related materials. The Public Support Department is responsible for requesting small samples and inspection reports from qualified units, which will be inspected by quality control. Suppliers who are confirmed to meet the requirements initiate quality audits. Audit content: including verifying the authenticity of the supplier's qualification documents and inspection reports, and comprehensively evaluating its quality management system. After the evaluation work is completed, it will be reviewed by the supplier audit team, reported to the quality person in charge for approval, and opinions will be given. Approved suppliers will issue the "Qualified Supplier Directory" to the Quality Department, Public Support Department and Production Department.

Create supplier profiles. Check the validity of the qualification documents in the supplier file on a quarterly basis, and update the information that is not within the validity period.

2.3.3 Entrusted production, entrusted inspection and other project entrustment

Our company currently has no varieties for commissioned production.

2.3.4 Our company has no contract to manufacture enterprises and laboratories. Appendix 4 : none.

2.3.5 Briefly describe the responsibilities of the entrusting party and the consignee in product

release

NA

2.4 Quality risk management

2.4.1 brief description of quality risk management (QRM) methodologies used by the manufacturer

Enterprise quality risk management methods include FMEA assessment methods, hazard analysis and critical control points, brainstorming, etc.

According to risk issues, set up a quality risk management team. Team leader: the manager of the quality department; members: the person in charge of the relevant department and the relevant technical personnel of the enterprise. When necessary, external professionals can be invited to join the risk management team, such as professional technical personnel, experts from external units, etc.

Evaluation methods are divided into regular evaluation and change evaluation. Routine assessment: refers to a comprehensive assessment of product characteristics, raw material procurement, production process control, storage, transportation, use and other links in accordance with GMP regulations to identify potential quality risks. Change assessment: Changes are made to raw and auxiliary materials, packaging materials, quality standards, inspection methods, operating procedures, workshops, facilities, equipment, instruments, and production processes. The quality management minister designates a special person to be responsible for evaluating changes.

Evaluation scope: evaluation of raw and auxiliary materials; evaluation of plant facilities; evaluation of personnel; evaluation of production process; evaluation of equipment; evaluation of management system; evaluation of quality standards of intermediate products and finished products; evaluation of verification evaluation; evaluation of analytical methods and inspection processes ; Evaluation of air purification system and environmental monitoring; Evaluation of water system and monitoring; Evaluation of process gas system and monitoring.

2.4.2 The scope and focus of quality risk management, including quality risk management activities carried out at the company level, as well as risk management activities carried out within the company.

The scope of the company's GMP quality risk management: first, risk management for establishing quality management; second, quality risk management for workshops, equipment, and facilities; third, quality risk management for material management; fourth, quality risk management for

production management; The fifth is the quality risk management of laboratory control and stability research; the sixth is the quality risk management of continuous improvement.

The key point is to carry out risk assessment on the characteristics of the product itself, procurement of raw and auxiliary materials, production process control, storage, transportation, use and all activities that affect product quality in accordance with GMP requirements.

3. Personnel

3.1 Organization chart of enterprise quality management, production and quality control and their responsible persons, including senior management and authorized persons, etc. See Appendix 5

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3.2 Number of employees engaged in quality management, production, quality control, storage and distribution of pharmaceutical products

project	Number of employees (person)
Quality Management	15
Quality Control	20
Production	142
store	6
distribution	12

4. Premises and equipment

4.1 Premises

4.1.1 Briefly describe the production plant

The layout of our company's factory area is divided into production area, power supply area, storage area, inspection area, office area and other areas. The factory area is 66,600 square meters, and the factory buildings include workshop 201, workshop 203, workshop 205, warehouse, office building (including laboratory) and so on.

4.1.2 Briefly describe the size of the production area

The production line of ornithine aspartate is workshop 205. The varieties currently produced in workshop 205 are alanylglutamine and ornithine aspartate. The production capacity of each variety is shown in the table below.

name	production capacity/T	Production line name

Ornithine Aspartate	35T/month	Workshop 205
Alanyl Glutamine	28T/month	Workshop 205

Appendix 6 : Layouts of production areas including material and personnel flows, general flow charts of manufacturing processes of each product type (dosage form)

4.1.3 Warehouse floor plan, see Appendix 7

4.1.4 Our company currently has no special storage conditions.

4.2 **Brief description of heating, ventilation and air-conditioning (HVAC) systems**

The air-conditioning purification system in the clean area of workshop 205 has three air-conditioning units: AHU-2 (air supply in the batching area), AHU-3 (air supply in the laundry area), and AHU-4 (air supply in the crystallization, separation washing, drying, and sub-packaging area). The air-conditioning purification system (HVAC) performs three-stage filtration on the air with primary efficiency (initial effect model G4 bag type), medium efficiency (F8 bag type), and high efficiency, and the clean area environment meets the requirements of Class D cleanliness.

Air treatment process: The air conditioning purification system filters the air in three stages: primary, medium and high efficiency. It consists of a new air return section, a bag-type primary effect section, a surface cooling water retaining section, a fan section, a flow equalization section, a steam heating section, a steam humidification section, a medium-efficiency filter section, and an air outlet section. The clean air filtered by the tertiary filter is efficiently sent to each clean (room) area by the air duct. Mainly adopts the top air supply and the lower side return air (some rooms use the side supply and lower return or lower row).

Air conditioner design parameters

level	205 Workshop air conditioning system
	Class D
temperature. C	18 ~26
humidity%	45-65
Number of air changes/h	>15
Total air volume m ³ /h	14000
Total return air volume m ³ /h	—
Return air utilization %	—
Cooling capacity KW	125

Heating capacity KW	85
Humidification capacity kg/h	45
differential pressure	The static pressure difference between adjacent clean rooms of different cleanliness levels should be $\geq 10\text{pa}$. The static pressure difference between different clean rooms of the same level should be $\geq 5\text{Pa}$. Static pressure difference between clean room and non-clean room $\geq 10\text{pa}$
Air volume	The difference between the measured air volume and the design air volume in the clean room is within $\pm 15\%$ of the design air volume

4.3 Brief description of water systems

Overview of purified water system: It is mainly composed of pretreatment unit, pH adjustment device, primary reverse osmosis pre-destroyer, intermediate water tank, secondary reverse osmosis deep desalination device, EDI device and purified water distribution system.

The purified water distribution system is designed with a circulating pipeline, and the water point is designed with a U-bend. The material of the inner cylinder and the head of the storage tank is 316L, and it is equipped with a sterilizing respirator. A 360-degree rotating spray ball is set for cleaning in the tank, and the material is 316L stainless steel. The material of the circulation pipeline is 316L stainless steel. Set up sampling ports for total water supply, total return water, and sampling ports at the bottom of the storage tank; pasteurization is used for system sterilization and sterilization. The installation of the purified water pipeline shall maintain a certain inclination, and the whole system has no blind pipes and dead ends. Comply with GMP requirements. The water quality meets the requirements of Part II of the 2020 edition of the Chinese Pharmacopoeia.

Schematic drawings of water systems See Appendix 7

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

Compressed nitrogen: The air is pressurized by the compressor, and the condensed water and oil stains are removed by the high-efficiency degreaser, and then it enters the refrigerating machine to remove most of the water. After being filtered by a precision filter, it enters the catalytic purifier to remove oil mist and harmful gases. Air is introduced into the adsorption separation system for oxygen and nitrogen separation. Nitrogen flows from the upper valve through the nitrogen storage tank, through

the precision filter and the nitrogen storage tank. It is transported to the batching post in the 205 workshop and filtered to the point of use by a 0.45um PTFE filter element, a 0.22 um PTFE filter element in the clean room, and a D-level clean area terminal filter element.

4.5 Equipment

4.5.1 Listing of major production and control laboratory equipment with critical pieces of equipment identified should be provided in Appendix 8.

4.5.2 Cleaning and sanitation

Established equipment cleaning operation documents or cleaning and disinfection operation documents. Prescribes the cleaning method used for equipment in direct contact with medicines: rinsing or wiping with purified water as a cleaning agent, and prescribes how the equipment should be cleaned.

Situation description for cleaning validation:

The company has established the "Cleaning Verification Standard Management Procedure". It specifies the preconditions for cleaning validation, the selection of product targets for validation and validation methods, sampling methods, analytical methods, acceptance criteria, and validation periods.

When the cleaning procedures and cleaning methods are significantly modified; the products produced are changed; when the equipment shape is significantly changed, the cleaning verification plan shall be revised and the production line equipment cleaning verification shall be carried out. Revalidation is performed every 3 years when there are no changes to procedures, products, or equipment.

4.5.3 Good manufacturing practices critical computerized systems

Our company has drafted "Computer System Supplier Quality Audit Standard Management Procedure", "Computer System Data Standard Management Procedure", "Computer System Emergency Standard Management Procedure" and "Computerized System Personnel Authority Standard Management Procedure". Established a list of computerized systems, formulated three-level authorization management for computers, and clarified the content of computerized system data audit, data backup and computerized system verification management.

5. Documentation

5.1 According to the requirements of GMP (revised in 2010), formulate a document management system. The content covers the entire management scope of the company's existing departments and

workshops, strengthens the standardized management of operations in each department, and makes various management work have rules to follow.

Our company's file system is classified according to the function of file use, and is divided into standard procedures, technical standards and records. The standard procedures are further divided into management procedures (SMP) and operational procedures (SOP). Technical standards include finished products, intermediate product quality standards, raw and auxiliary material quality standards, packaging material quality standards, process regulations, verification programs, etc.).

Records include batch production records, batch inspection records, sales records, verification reports, self-inspection reports, material ledgers, etc. The paper version of the approved documents shall be archived as the original, and the records shall be managed together as an attachment to the standard procedure document or technical standard document.

5.2 Documents and records are kept within the production facility.

6. Production

6.1.1 Type of products

Drug Name	dosage form	registration number
Alanyl Glutamine	API	Y20200000065
L-Ornithine L-Aspartate	API	--

- The factory does not manufacture an investigational medicinal product (IMP) dosage form.

6. 1.2 Handling of Toxic or Hazardous Substances

The company has established the Hazardous Chemicals Management System, which regulates the procurement, storage and use of hazardous chemicals. The packaging of hazardous chemicals is required to be accompanied by a chemical safety data sheet that is exactly the same as that of the hazardous chemicals and affixed with labels. Post and hang corresponding warning signs in the storage and use places of hazardous chemicals. Hazardous chemicals are stored in special sites or warehouses, and the potential safety hazards of hazardous chemicals are regularly checked. The use of hazardous chemicals shall be managed by a special person, and a special account shall be established for registration. Establish corresponding emergency plans and organize emergency drills on a regular basis. Manage hazardous waste in accordance with the "Requirements for Hazardous Waste Generating Units to Establish a Ledger" and fill in relevant records. Hazardous waste is handed over to a qualified third

party for disposal.

6.1.3 Description of the special equipment or stage to manufacture the product

The batching tank, crystallizing tank, centrifuge, double-cone rotary vacuum dryer and packing machine in workshop 205 are shared equipment. Common species are L-Aspartate L-Ornithine, Alanyl Glutamine, D-calcium pantothenate. The above varieties are staged production.

6.1.4 Cases without Process Analytical Technology (PAT) applications

6.2 Process validation

The company has formulated the "Process Validation Management Procedure". The document stipulates: After completing the verification and calibration of plant facilities, production equipment, instrumentation, inspection facilities and equipment and inspection methods, and after the verification and implementation personnel have been trained. According to the approved process verification plan, the verification shall be carried out in accordance with the production process regulations and post operation documents. All records are true and accurate. All sampling inspections are carried out in strict accordance with approved procedures. Process validation is revalidated every 3 years. When the standard production process related to product quality is changed, which may affect product quality, re-verification is required.

6.2.2 Principles of Rework or Rework

♦ Principles of rework

(1) Intermediate products, products to be packaged, finished products and returns that do not meet the quality standards can be reworked.

(2) Rework is allowed only after it does not affect the quality of the product, meets the quality standards of raw materials, and is based on the predetermined and approved operating procedures and the relevant risks are fully assessed.

(3) Rework of intermediate products, products to be packaged, finished products and returns due to various reasons. If the quality still does not meet the quality standard after rework, it can be reworked again, but the total number of rework cannot exceed 3 times.

♦ Principle of reprocessing

The process, method, procedure, procedure, quantity and proportion of raw material reprocessing require additional verification and testing. Products obtained after reprocessing need to be considered

for additional related item inspections and stability studies.

6.3 Material management and warehousing

6.3.1 Handling of starting materials, packaging materials, semi-finished products and finished products, including sampling, pending inspection, release and storage

The company has drafted "Standard Management Procedures for Material Warehousing" and "Standard Management Procedures for Material Review and Release". The warehouse administrator conducts a preliminary inspection of the materials according to the "Material Preliminary Inspection Record", and the preliminary inspection contents include: suppliers, accompanying documents, packaging, etc. After passing the initial inspection, the materials are placed in the specified area. According to the management of the products to be inspected, use the yellow fence and the yellow identification plate of the area to be inspected to distinguish, and fill in the "Inspection Request Form", "Material Location Card", and "Material Storage Ledger". Submit to quality control 2 and take samples for testing. Quality control 2 is inspected according to the quality standards of each material. After passing the inspection, the quality assurance will issue the "Material Review Release Form" and the inspection report to the warehouse administrator. Quality Control 2 also issues a green "Qualification Certificate". Warehouse administrators distinguish qualified raw and auxiliary materials with green line fences, and affix green "Qualification Certificates" one by one. The material is transferred to a qualified state..

The company has drafted "Sampling Standard Management Procedure" and "Finished Product Standard Management Procedure". Product sampling for quality assurance. Quality control for finished product inspection. The workshop submits the "Material Temporary Storage Slip" to the warehouse manager, and the finished product is temporarily stored in the warehouse. The status of the finished product is pending inspection. After passing the quality control inspection, the workshop submits the finished product receipt. After the warehouse receives the "Finished Product Review Release Form" issued by the Quality Department, the finished product will be converted into a qualified state.

Quality Assurance After sampling the intermediate product, it is inspected. The intermediate products that pass the inspection are transferred to the next process for use. If it needs to be stored in the warehouse, the workshop shall go through the temporary storage procedures and store the intermediate products in the warehouse.

6.3.2 Arrangements for the handling of rejected materials and products

The company has drafted the "Standard Management Procedures for Disposal of Unqualified Products", which stipulates the handling procedures for unqualified materials (raw and auxiliary materials, packaging materials, etc.) and unqualified products.

When the raw materials and packaging materials arrive, the warehouse administrator will conduct an initial inspection. If the initial inspection fails, it will be rejected on the spot after being approved by the quality department. Those that cannot be rejected will be marked with a "unqualified" sign. The unqualified materials that appear during the incoming inspection process will be returned by the public support department after the warehouse receives the unqualified inspection report. Due to improper storage conditions or unforeseen factors (such as power failure, water pipe leakage, etc.), the quality of the inventory materials is unqualified, and the relevant procedures shall be followed. The quality department and the production department decide whether to rework or destroy the materials that are contaminated during the production process according to the degree of contamination and the reasons.

Unqualified intermediate products produced in the production process shall be reported to the person in charge of quality step by step, and corrective measures shall be proposed, which shall be implemented after the approval of the person in charge of quality, so as to reduce the risk to an acceptable level. Find out the reason for the non-conforming product, if it can be reprocessed, reprocess it, or with the approval of the person in charge of quality, destroy it according to relevant regulations.

For unqualified products that have not left the factory, find out the reasons for the unqualified products, and propose corresponding corrective measures, and report to the quality person in charge for approval, give treatment advice, and reprocess or destroy them.

Unqualified products caused during storage and transportation will be re-sampled and tested by quality control and quality assurance. If the inspection is qualified and there is no quality problem, the packaging will be replaced by the production department according to relevant procedures and can be sold again.

The substandard products that have entered the market shall be recalled in time according to the "Standard Management Procedures for Product Recall".

7. Quality control

The total area of the quality control area is 816m², and the inspection area is equipped with

various special inspection equipment.

The third floor of the laboratory is equipped with sample separation room, gas phase room, physical and chemical room, liquid phase room, high temperature room, instrument room, standard solution room, balance room, and infrared instrument room. It can be used for the inspection of physical and chemical items such as identification, pH, electrical conductivity, loss on drying, moisture, residue on ignition, light transmittance, content, related substances, and residual solvents.

The fourth floor of the laboratory is equipped with a microbial limit inspection room, a sterility inspection room, a positive detection room, an insoluble particle inspection room, a bacterial endotoxin inspection room, and a culture room. It is used for the inspection of microbial items such as microbial limit, sterility inspection, insoluble particles, and bacterial endotoxin.

8. Distribution, complaints, product defects and recalls

8.1 Distribution (to the part under the responsibility of the manufacturer)

8.1.1 Types (wholesale licence holders, manufacturing licence holders, etc) and

locations (EU/EEA, USA, etc.) of the companies to which the products are shipped from the site;

Our company holds a business license and a production license, and is a modern pharmaceutical enterprise integrating drug research and development, production and sales.

8.1.2 Description of the system used to verify that each customer / recipient is legally entitled to receive medicinal products from the manufacturer;

According to the management regulations of the sales department, all customers are required to verify whether they have legal receiving qualifications before cooperation, and require customers to provide business licenses. If it is a manufacturer, it should also provide a production license (stamped with the company's official seal).

8.1.3 Brief description of the system to ensure appropriate environmental conditions during transit, e.g. temperature monitoring/ control;

Controls required for the product in transit: by confirming the mode of transportation to ensure that no quality defects occur during transit. Products should be handled with care during transportation, loading and unloading, and should be stacked in strict accordance with the outer packaging diagrams, signs, and requirements or take effective protective measures to ensure product safety. After loading, it should be bundled firmly, and the gasket should be added to prevent the package from being damaged

due to product impact. Quality or quantity problems during transportation are the responsibility of the transporter.

The sales department selects the appropriate means of transport and signs a transport contract with the transport unit. The warehouse confirms the goods according to the requirements of the "Finished Product Delivery Notice", and the quality assurance personnel can only deliver the goods after signing. The carrier driver issues a receipt, and the finished product can be shipped out of the warehouse.

8.1.4 Product distribution management and methods to ensure its traceability

When the finished product is sold and shipped, the "Product Shipping Record" must be filled out item by item for each batch to ensure the traceability of the sale of the finished product. So that the products that have been sold can be recalled in a timely and effective manner when necessary.

8.1.5 Measures to prevent the flow of products into illegal supply chains

Customers are required to provide a business license before cooperation, and if it is a production enterprise, a production license is also required. Only after verifying that it is qualified to purchase can we cooperate with it.

8.2 Complaints, product defects and recalls

Our company has drafted the "Customer Feedback Standard Management Procedure" document, which stipulates the feedback handling process. After receiving the feedback, the customer service will inform the Quality Assurance. The Quality Assurance will fill in the "Customer Feedback Processing Flow Sheet", formulate an investigation plan, and reply the investigation results and treatment measures to the customer.

Our company has formulated the "Product Recall Standard Management Procedure", which can be divided into three levels according to the potential safety hazards and the severity of the hazards.

Relevant departments should report to the Quality Department in a timely manner when a recall is required. Under the unified organization of the person in charge of quality, determine the name, batch number, specification, quantity and sales quantity of the recalled product according to the batch records, warehousing records, warehousing records, product delivery records and other documents of the product, and fill in the "Product Recall Notice" one". Report to the recall team, and execute the recall procedure after the team leader signs and approves. quality assurance Fill out the Recall Plan Form.

After the recall is completed, the quality department summarizes and evaluates the recall effect, and fills in the "Recall Effect Evaluation Form".

The Quality Department evaluates the effectiveness of the product recall management system annually. The Quality Department organizes a simulated recall exercise every year to ensure that all products in the sales batch are recalled.

9. **Self-inspections**

The company has drafted the "GMP Self-inspection Standard Management Procedure" in accordance with the requirements of the "Good Manufacturing Practice for Drugs". This document specifies the organization, methods, frequency, basic procedures, evaluation standards, specific implementation requirements, and improvement measures of our company's self-inspection. Self-inspection frequency: organize self-inspection at least every six months, and self-inspection methods are divided into comprehensive self-inspection, follow-up inspection, and special inspection.

The inspection scope in the self-inspection plan is formulated in accordance with the "Good Manufacturing Practice for Drugs" and related appendices. It includes all activities of pharmaceutical manufacturers that may affect product quality and specifications: institutions and personnel, plant and facilities, equipment, materials and products, validation and verification, document management, production management, quality control and quality assurance, Commissioned production and commissioned inspection, Product Shipments and Recalls, Complaints and adverse reactions, rectification of previous self-inspection records and implementation of measures.

The quality assurance organization convened an inspection team meeting to formulate a "self-inspection plan". Determine the specific inspection time, inspection content and inspectors of each department. The inspectors conduct on-site inspections according to the division of labor, and require the inspectors to make a complete record of the inspection items during the self-inspection process. After the inspection, the quality assurance is responsible for organizing the final inspection meeting, and the self-inspection team will conduct a systematic analysis of the evaluation situation. For the defect items, form the "Self-inspection Defect Item Summary Table". Deficiencies found in self-inspections are notified to departments, and corrective and preventive actions are required. The quality assurance is responsible for filling out the Rectification Notice.

After receiving the Rectification Notice, each inspected department shall analyze and rectify

according to the process of deviation analysis, risk assessment, corrective and preventive measures and change management procedures, and propose improvement measures. When the scheduled completion date of the rectification measures has arrived, the quality assurance should appoint a special person to confirm the implementation of the rectification plan according to the "Reformation Plan Tracking Form", and to track and inspect the rectification situation, make an evaluation, and attach the supporting materials to the report.

After the self-inspection and rectification of all departments of the company are completed, the "Self-inspection Report" is completed.

The relevant attachments are as follows:

Annex 1: Drug Production License

Annex 2: None

Annex 3: GMP Certificate

Annex 4: None

Appendix 5: Company Organization Chart

Annex 6: General floor plan of the factory area, floor plan of the production area and flow chart

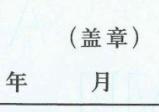
Attachment 7: Warehouse floor plan, schematic diagram of water system

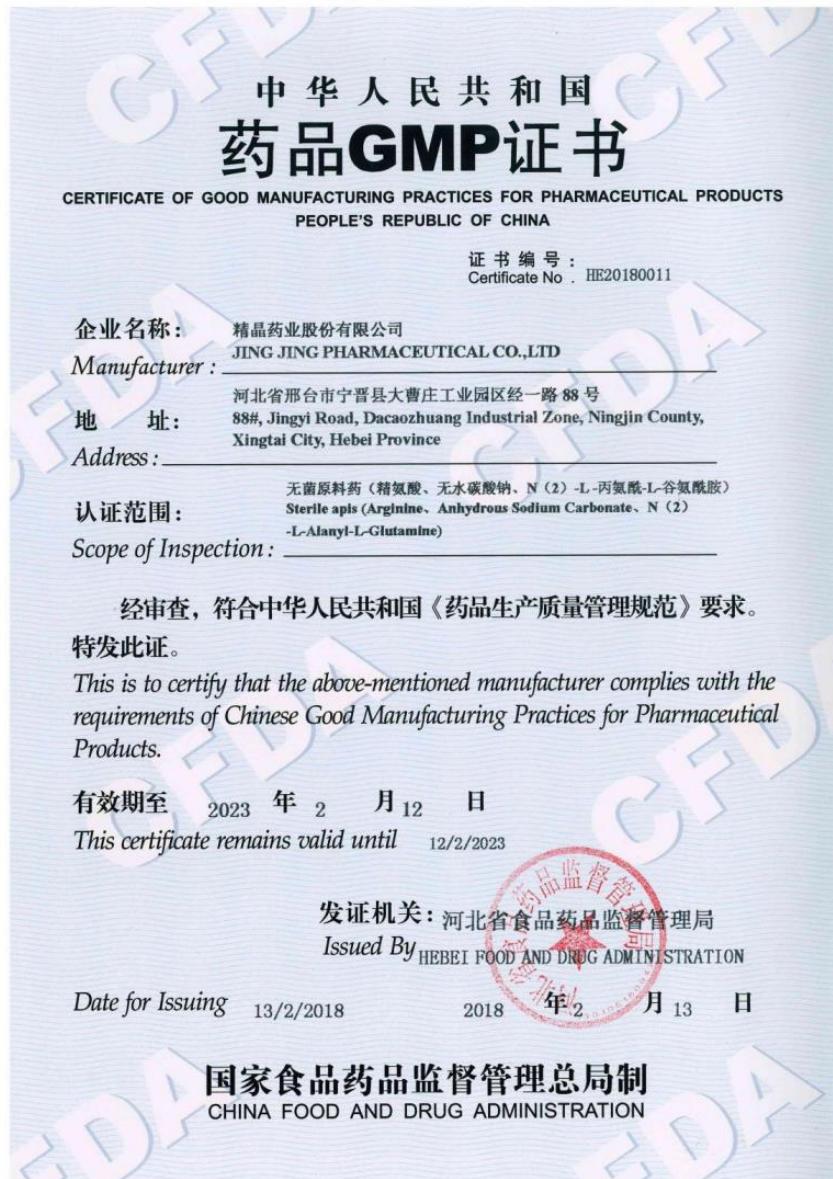
Annex 8: List of main instruments and equipment for production and inspection



一、车间和生产线情况:			
生产地址	车间	生产线	范围
河北省邢台市宁晋县大曹庄工业园区经一路 88 号	201 车间	201 生产线	无菌原料药（门冬氨酸鸟氨酸）
	201 车间	201 生产线	无菌原料药（精氨酸）
	201 车间	201 生产线	无菌原料药（无水碳酸钠）
	201 车间	201 生产线	无菌原料药（丙氨酸、谷氨酰胺 ^{(曾用名 N (2)-L-丙氨酸-L-谷氨酰胺)} ）
	201 车间	201 生产线	无菌原料药（盐酸精氨酸）
	201 车间	201 生产线	无菌原料药（精氨酸酶皮二酸）
	202 车间、201 车间	202、201 生产线	无菌原料药（阿维巴坦钠）
	107 车间、205 车间	107、205 生产线	原料药（丙氨酸谷酰胺）
	205 车间	205 生产线	原料药（泛酸钙）
	205 车间	205 生产线	原料药（门冬氨酸鸟氨酸）
205 车间	205 生产线	原料药（无水葡萄糖）	
205 车间	205 生产线	原料药（精氨酸）	

二、委托或受托情况:					
类型	企业名称	生产/注册地址	药品名称	药品批准文号	委托有效期

变更记录		
事项: ①增加生产范围:原料药(门冬氨酸钾), 对应生产地址:河北省邢台市宁晋县大曹庄工业园区经一路 88 号, 车间: 107 车间、205 车间, 生产线: 107、205 生产线, 仅限注册申报使用。②增加生产范围:原料药(门冬氨酸镁), 对应生产地址:河北省邢台市宁晋县大曹庄工业园区经一路 88 号, 车间: 107 车间、205 车间, 生产线: 107、205 生产线, 仅限注册申报使用。	 2024 年 9 月 25 日	
事项: 增加生产地址和生产范围, 河北省邢台市宁晋县大曹庄工业园区经一路 88 号:原料药(阿维巴坦钠中间体 A8), 车间: 205 车间, 生产线: A8 合成线, 通过药品 GMP 符合性检查后方可上市销售。	 2024 年 3 月 4 日	
事项: 生产地址和生产范围, 河北省邢台市宁晋县大曹庄工业园区经一路 88 号:原料药(泛酸钙), 车间: 206 车间, 生产线: 206 生产线, 仅供出口。	 2024 年 6 月 12 日	
事项:	 年 月 日	

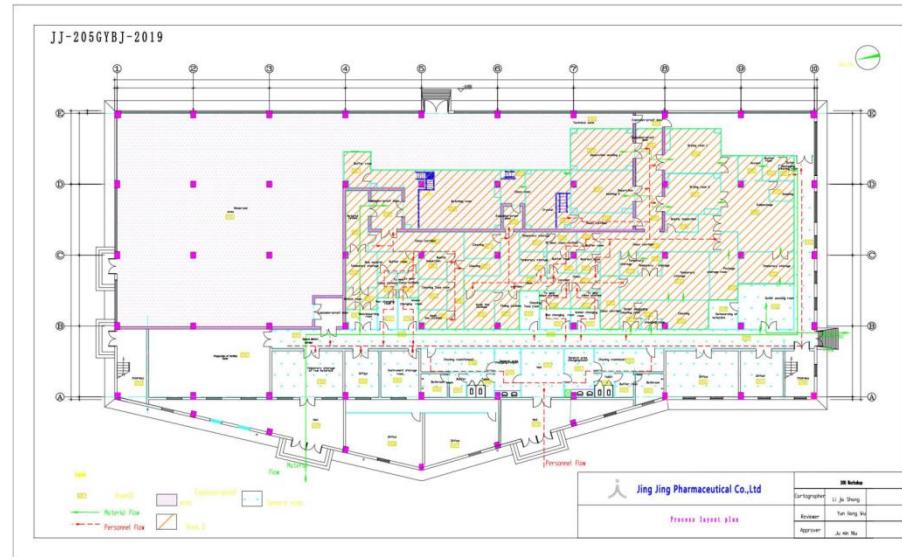
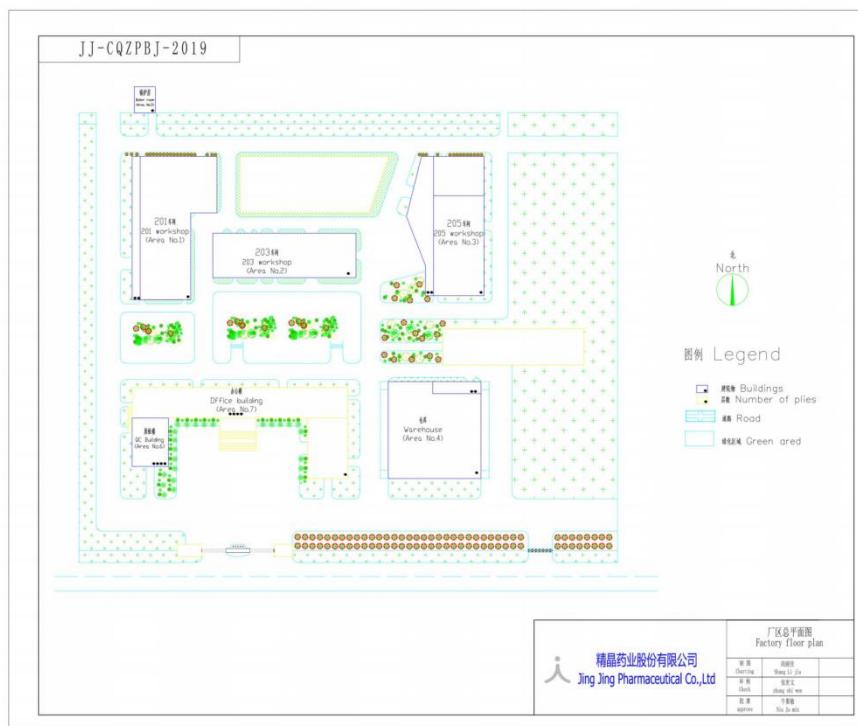


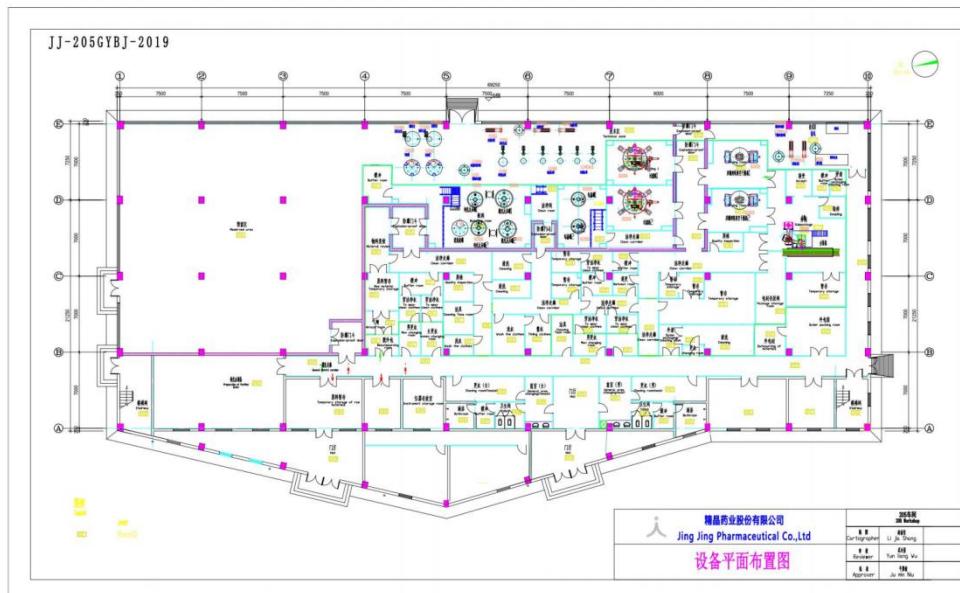
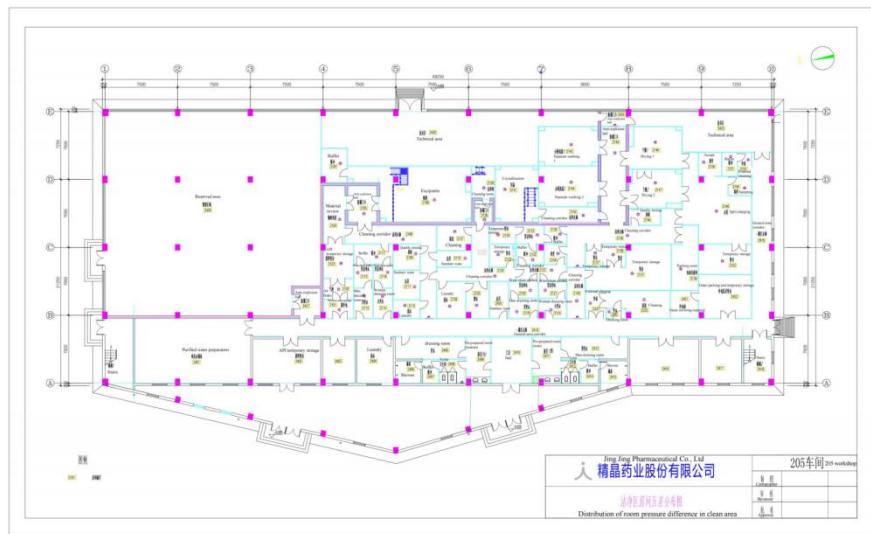


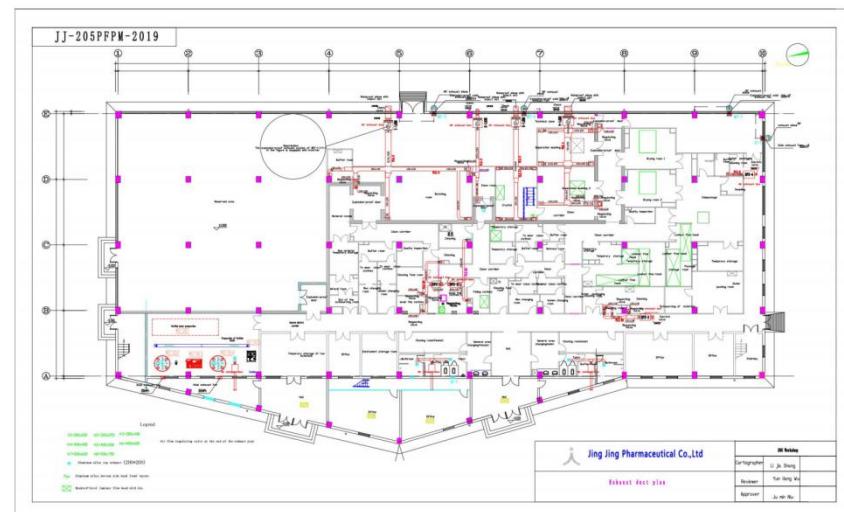
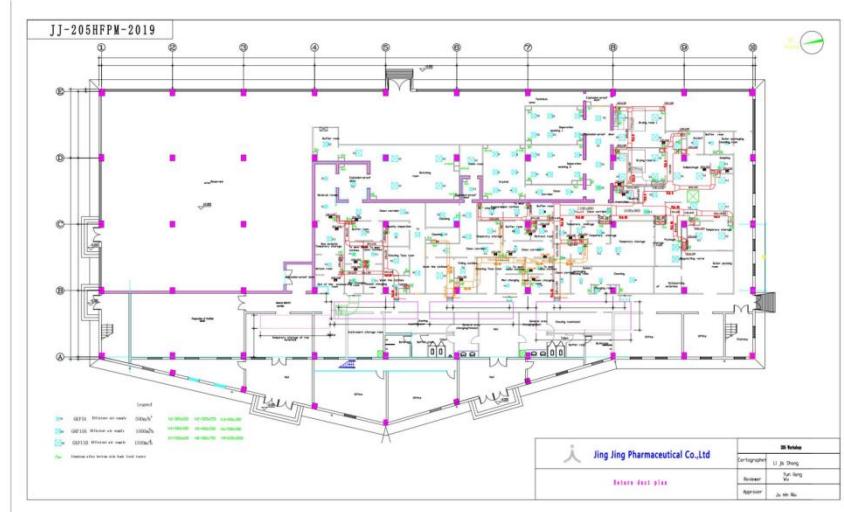
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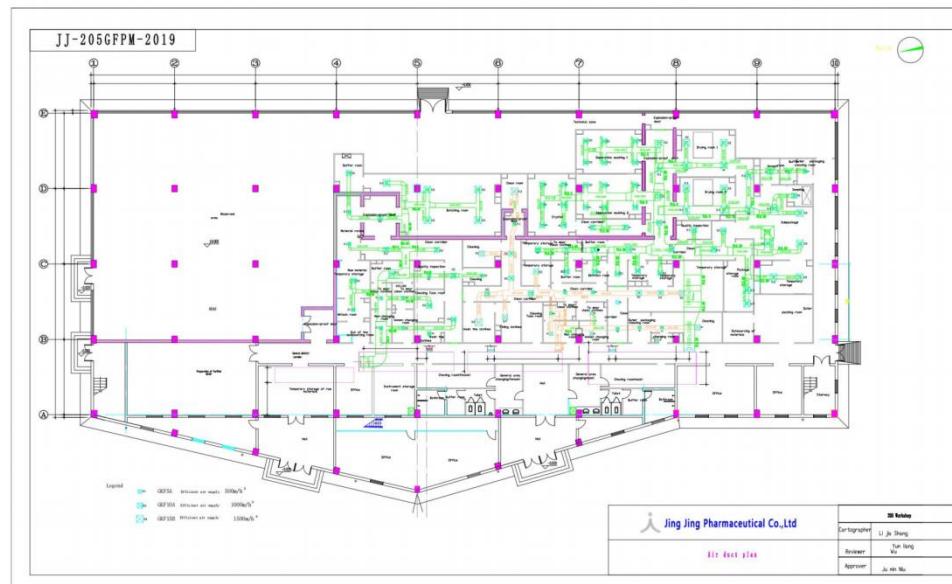
Annex 6: General floor plan, floor plan and flow diagram of the production area

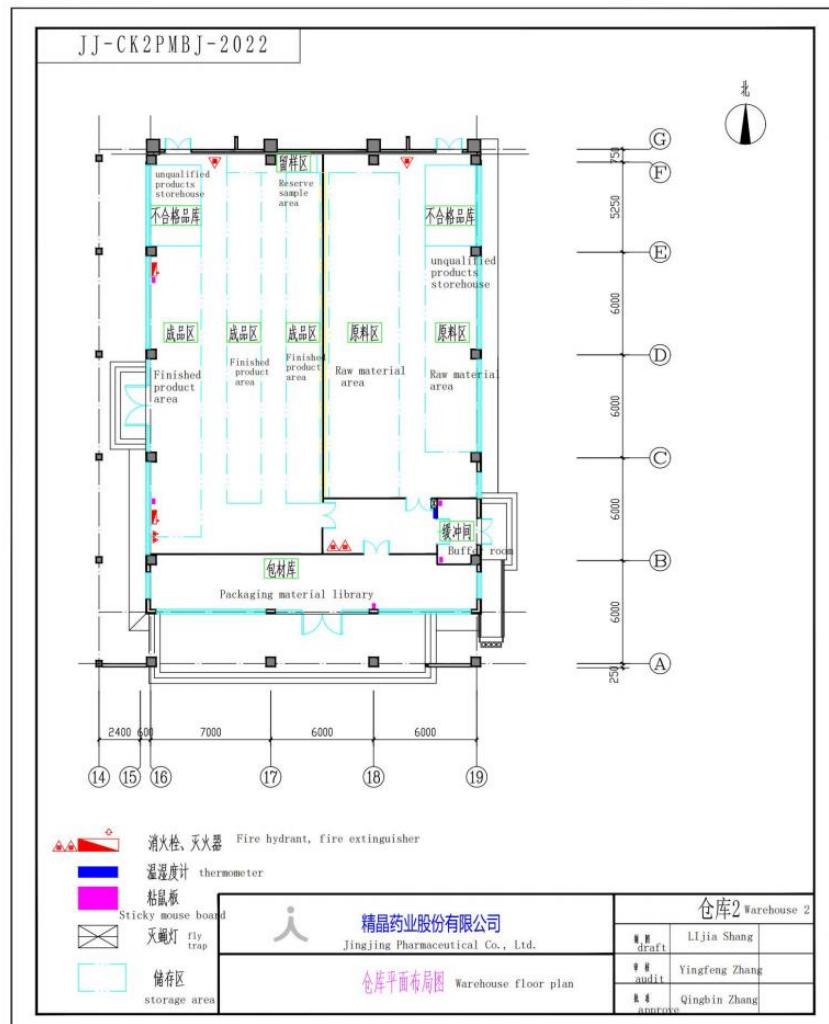
- 6.1 General layout of the factory
- 6.2 Floor plan of 205 workshop flow of people and logistics
- 6.3 Distribution of pressure difference in clean room of workshop 205
- 6.4205 Layout plan of workshop equipment
- 6.5 Plan of 205 workshop return air duct
- 6.6 205 workshop exhaust duct plan
- 6.7 Plan of 205 workshop air supply duct

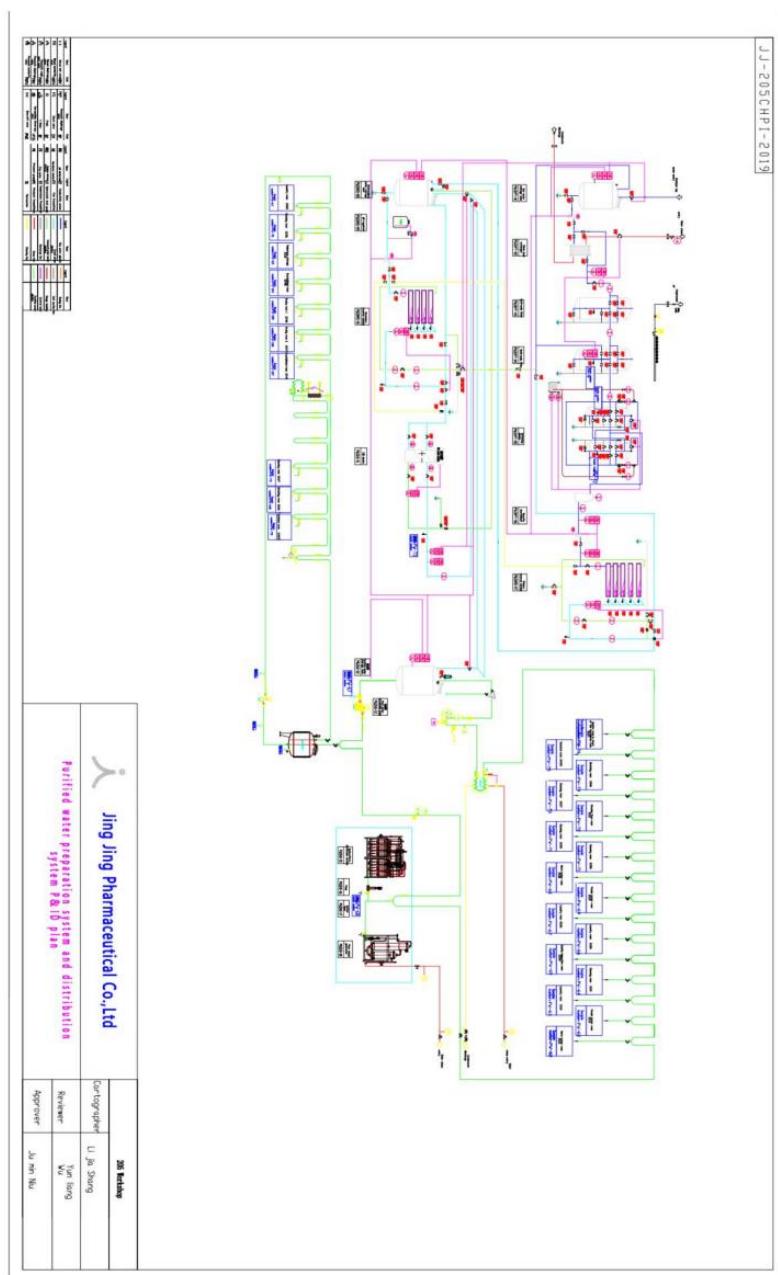












List of Ornithine Aspartate Production Equipment

No	Equipment name	Equipment material	Equipment Model/Specification	Manufacturer
1	transformation tank	316L	2000L	Wenzhou Jingzhan Light Industry Machinery Co., Ltd.
2	transformation tank	316L	2000L	Wenzhou Jingzhan Light Industry Machinery Co., Ltd.
3	Decolorization tank	316L	3000L	Wenzhou Jingzhan Light Industry Machinery Co., Ltd.
4	Decolorization tank	316L	3000L	Wenzhou Jingzhan Light Industry Machinery Co., Ltd.
5	plate and frame filter	316L	Q=5m³/h	Haining Yongsheng Membrane Filtration Equipment Manufacturing Co., Ltd.
6	Precision filter	316L	Three cores; 20 inches; 226 sockets	Shanghai Geely Fluid Equipment Co., Ltd.
7	Precision filter	316L	Three cores; 20 inches; 226 sockets	Shanghai Geely Fluid Equipment Co., Ltd.
8	Precision filter	316L	One core; 20 inches; 226 sockets	Shanghai Jinke Filter Equipment Co., Ltd.
9	Precision filter	316L	One core; 20 inches; 226 sockets	Shanghai Jinke Filter Equipment Co., Ltd.

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10	Crystallizing tank	316L	3000L	Wenzhou Jingzhan Light Industry Machinery Co., Ltd.
11	Crystallizing tank	316L	3000L	Wenzhou Jingzhan Light Industry Machinery Co., Ltd.
12	centrifuge	316L	LD=1500	Jiangsu Saideli Pharmaceutical Machinery Manufacturing Co., Ltd.
13	filter	316L	F=2m²	Wenzhou Yaguang Technology Industry Co., Ltd.
14	Double Cone Rotary Vacuum Dryer	316L	1600L	Wuxi Hongsheng Pharmaceutical Equipment Co., Ltd.
15	Double Cone Rotary Vacuum Dryer	316L	1600L	Wuxi Hongsheng Pharmaceutical Equipment Co., Ltd.
16	Dispenser	complex	---	Aoxing Pharmaceutical Equipment (Shijiazhuang) Co., Ltd.
17	Purified water system	---	2t/h	Shandong Huifang Jingying Medical Equipment Co., Ltd.

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Ornithine Aspartate Instrument and Equipment Registration Ledger

No	Testing instruments and equipment names	Specifications	Measuring range	Accuracy	Manufacturer's name
001	Electronic balance	ME104TE	0.1mg~120g	±0.1mg	METTLER TOLEDO Instruments (Shanghai) Co., Ltd.
002	Electronic balance	XSE105DU	0.01mg~41g	±0.01mg	METTLER TOLEDO Instruments (Shanghai) Co., Ltd.
003	automatic polarimeter	SGWzz-2	±45° (Optical rotation) ±120°Z (sugar content)	Level 0.02	Shanghai Shenguang Instrument Co., Ltd.
004	pH计	FE28	pH0.00~14.00	Level 0.01	METTLER TOLEDO Instruments Ltd.
005	Infrared Spectrophotometer	iS5	400~4000 cm ⁻¹	2cm ⁻¹	Thermo Fisher Scientific (China) Co., Ltd.
006	Electric blast drying oven	101-1A	room temperature~+10 °C -250°C	±1°C	Tianjin Taisite Instrument Co., Ltd.
007	Electric heating constant temperature drying oven	WHLL-65BE	room temperature~+5 °C -300°C	<±1°C	Tianjin Taisite Instrument Co., Ltd.
008	Box type resistance furnace	SXz-8-10D	0~1000°C	0.2%FS±1°C	Longkou Electric Furnace Factory
009	Clarity detector	YB-II	1000~4000LX		Tianjin Tianguang Optical Instrument Co., Ltd.
010	UV-visible spectrophotometer	UV-2600	185~900nm	±0.3nm	Shimadzu Instruments (Suzhou) Co., Ltd.
011	Gas Chromatograph	7890B	-----	-----	Agilent Technologies, Inc.
012	automatic potentiometric titrator	ET18	0~2000μV	Level 0.01	METTLER TOLEDO Instruments (Shanghai) Co., Ltd.
013	Karl Fischer moisture meter	ET08	-----	-----	METTLER TOLEDO Instruments (Shanghai) Co., Ltd.

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