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1. General Provisions

Article 1 This practice is established according to "Drug Administration Law of PRC" and "Implementation Regulations of the PRC Drug Administration Law" in order to regulate drug production quality control.

Article 2 Pharmaceutical companies should establish a drug quality management system. The system should cover all factors that affect drug quality, including all of organized and planned activities that ensure the quality of medicines meet its intended use.

Article 3 This practice, as a part of quality management system, acts as the basic requirements for drug production management and quality control with the aim of minimizing contamination, cross-contamination and confusion, error and other risks in the process of drug production to ensure Pharmaceutical companies can constantly produce drugs meeting its intended use and registration requirements.

Article 4 Enterprises should strictly enforce the practice; adhere to the honest and trustworthy, and to prohibit any false, deceptive behavior.

2. Quality Management

2.1 General rules

Article 5 Enterprises should establish a quality target that meets pharmaceutical quality management requirements, applying all of requirements on safety, efficacy and quality control related with drug registration to whole process of drug production, control and product release, storage and shipment to ensure that production of pharmaceuticals meet their intended use and registration requirements.

Article 6 Top management personnel should ensure implementation of established quality objectives; staff of different levels, suppliers and distributors should work together and assume their responsibilities.

Article 7 Enterprises should be equipped with adequate, qualified staff, facilities, facilities and equipment to provide necessary conditions for achievement of quality objectives.

2.2 Quality assurance

Article 8 Quality assurance is part of the quality management system. Enterprises must establish a quality assurance system, while building a complete documentation system to ensure effective operation of the system.

Article 9 Quality assurance system should ensure that:

1. design and development of drugs reflects requirements of this practice;
2. production management and quality control activities are consistent with requirements of this Code;
3. management responsibilities are clearly defined;
4. raw materials and packaging materials purchased and used are correct;
5. effective control of intermediate products;
6. implementation of validation and verification;
7. perform production, analysis, analyze and review strictly in accordance with procedures;
8. each batch can only be released with approval of qualified person;
9. appropriate measures for drug quality assurance are available in process of storage, shipment and subsequent operation ;
10. periodic analysis and evaluation of validity and applicability of quality assurance system in accordance with self-analysis operating procedures

Article 10: The basic requirements for Pharmaceutical production and quality management:

(a) To develop production process, and perform systematic review to certify it can sustainably and stably manufacture qualified products
(b) Production technology and major changes need to be validated;
(c) Equipped with necessary resources, including at least the following:

1. Personnel with appropriate qualifications and qualified by training;
2. Adequate premises and facility;
3. Proper equipment and maintenance support;
4. Right raw materials, packaging materials and labels;
5. Approved procedures and operation procedures;
6. Appropriate storage conditions.

(d) Accurate and understandable language should be used to develop operation procedures;
(e) The operators are trained to operate in accordance with proper operating procedures;
(f) Production process should be documented; deviations should be investigated and recorded;
(g) Batch records and shipping records should allow traceability of complete history of batch products, and should be kept properly for easy reference;
(h) Reduce quality risk in process of drug shipment;
(i) Establishment of drug recall system should ensure any batch can be recalled after distribution;
(j) Investigate complaints and quality defects and take measures to prevent recurrence of similar quality defects.

2.3 Quality control

Article11: Quality control, including related organization, documentation system, and sampling, and analysis to ensure materials or products complete their necessary analysis prior to release and to confirm quality meet requirements.

Article 12: The basic requirements of quality control:
(a) QC shall be equipped with appropriate facilities, equipment, instruments and trained personnel for effective and reliable completion of all related quality control activities;
(b) Operating procedures should be available for sampling, analysis, test of raw materials, packaging materials, intermediate products, packaging and finished products as well as stability analysis of the product, and if necessary, carry out environmental monitoring to ensure compliance with the requirements of this practice;
(c) Authorized personnel should sample raw materials, packaging materials, intermediate products, packaging and finished products in accordance with required method;
(d) Analysis methods should be validated or confirmed;
(e) Sampling, analysis, and check should be recorded, and deviations should be investigated and recorded
(f) Materials, intermediate products, packaging and finished products must be checked and analyzed according to quality standards and should be recorded;

(g) Packaging materials and final product should have sufficient retained samples for necessary analysis or check except the final finished packaging container that is too large, retained samples for finished product should be packaged the same as final packaging.

2.4 Quality Risk Management

Article 13 Quality risk management, a kind of prospective and retrospective method, is a systematic process to evaluate, control, communication, review the quality risk.

Article 14 Quality risks should be evaluated on basis of scientific knowledge and experience to ensure product quality.

Article 15: The methods, measures, forms and documents formed in the process of quality risk management process should be appropriate to the level of existing risk.

3. Organization and personnel

3.1 General rules

Article 16 Enterprises should establish a management structure appropriate to drug manufacturing and organizational structure chart.
Enterprises should establish an independent quality control department to perform quality assurance and quality control responsibilities. Quality assurance department and quality control departments can be established separately within quality management department.

Article 17 Quality control department should be involved in all quality related activities, and responsible for reviewing all documents relevant to this practice. Quality management personnel shall not delegate responsibilities to other departments.

Article 18 Enterprises should be equipped with adequate and suitably qualified (including education, training and practical experience) management and operations staff; responsibilities of each department and each position should be clearly defined. Responsibilities cannot be missed, and overlapped responsibilities should be clarified. Responsibilities of each person should not be overburden.
All personnel should be clear about and understand their responsibilities, familiar with requirements related to their duties and receive proper traiing, including pre-service training and continuing training.

Article 19: Normally responsibilities should not be delegated to others. The responsibilities which are in definite need of delegation can be delegated to the qualified and designated personnel.

3.2 Key personnel

Article 20 Key personnel should be full-time staff in the enterprise, at least including responsible person, person in charge of production management, quality management and qualified person.
Person responsible for quality control and production management shall not serve each other. Person responsible for quality management and quality qualified can serve each other. Operating procedures should be developed to ensure qualified personnel perform their duties independently, free from interference from business leaders and other personnel.

Article 21 Owners of enterprises
The responsible person for enterprise, as the primary responsible person for the enterprise, should cover overall responsibility for daily management of enterprises. The

responsible persons shall be responsible for providing necessary resources, rational planning, organization and coordination to ensure independent performance of responsibilities of quality management department in order to ensure realization of business objectives and production of pharmaceuticals in accordance with the regulatory requirements.

Article 22 Person in charge of production management
Qualifications:
Person in charge of production management should at least have a degree in pharmacy (or intermediate professional titles or Licensed Pharmacist) with at least three years' engagement in drug production and quality management experience, including at least one year of medicine production management experience, and have been trained on professional knowledge relating to manufactured product.
Main responsibilities:
1. To ensure drugs are manufactured and stored in accordance with approved process procedures to ensure drug quality;
2. To ensure strict implementation of all operation procedures related to the operation and production;
3. To ensure batch production and packaging records have been reviewed and sent to quality management department;
4. To ensure implementation of facilities and equipment maintenance for good running condition;
5. To ensure completion of all necessary validation;
6. To ensure personnel related to production receive necessary pre-service training and continuing training, and adjust training contents basing on actual needs.

Article 23 Personal in charge of quality management
Qualifications: person in charge of quality management should have at least a degree in pharmacy or related (or intermediate professional titles or Licensed Pharmacist) with at least five years' experience in pharmaceutical production and quality management, including at least one year in medicine Quality management, and have received professional knowledge training relating to manufactured products.
Main responsibilities
1. To ensure raw materials, packaging materials, intermediate products, packaging and finished products meet requirements and quality standards approval in registration;
2. To ensure completion of batch record review before product release;
3. To ensure completion of all necessary analysis;
4. Approve operation procedures about quality standards, sampling methods, analysis methods and other quality management;
5. Review and approve all quality-related changes;
6. To ensure all significant deviations and OOS of analysis results have been timely investigated and handled;
7. Approve and monitor contractual(entrusted) analysis;

8. Supervision of facilities and equipment maintenance to ensure it keeps in good running condition;
9. To ensure completion of necessary qualification or validation, review and approval of qualification or validation protocols and reports;
10. To ensure complete self-analysis;
11. Assessment and approval of materials suppliers;
12. Ensure all quality-related complaints have been investigated, and timely and correctly treated;
13. To ensure completion of quality continual stability study, and provide stability study data;
14. To ensure completion of quality review;
15. To ensure quality control and quality assurance personnel have received necessary pre-service training and continuing training, and training need to be adjusted according to actual needs.

Article 24 Person in charge of production management and quality management normally share following responsibilities:
(a) Review and approve products process procedures, operation procedures and other documents;
(b) To supervise facilities hygiene status;
(c) Ensure key equipment has been qualified;
(d) Ensure completion of production process validation;
(e) Ensure all related employees have received necessary pre-service training and continuing training, and training need to be adjusted basing on actual need;
(f) Approve and supervise contractual production;
(g) Identify and monitor the storage conditions of materials and products;
(h) Record-keeping;
(i)Monitoring implementation of the practice;
(j) Monitoring factors that affect product quality.

Article 25 Qualified people
Qualifications:
The qualified person should have at least bachelor degree in pharmacy or related (or intermediate professional titles or Licensed Pharmacist) with at least five years' practices in pharmaceutical production and quality management, and have engaged in pharmaceutical production process control and quality analysis.
The qualified person shall have necessary professional knowledge, and shall only perform responsibilities after receive training related to product release.
(B) Main responsibilities:
1. Involving in establishment of the enterprise quality system, internal self-check and external quality audit, validation, and reports of adverse drug reaction, product recalls and other quality management activities;

2. Assume responsibilities of product release to ensure production and analysis for each batch released are in line with relevant laws and regulations, drug registration requirements and quality standards;
3. The qualified person should present product release review record in accordance with the second article mentioned above before product release and should incorporate it in the batch record.

3.3 Training

Article 26 Enterprise shall designate specific department or person responsible for training management; training or plan reviewed or approved by person in charge of production management and quality management should be available. Training records should be preserved.

Article 27: All personnel related with pharmaceutical production and quality should be trained, and training should be appropriate to the requirements for corresponding position. In addition to theory and practice training of this practice, responsibilities and skills training about related positions and laws and regulation should be available. And actual result of training should be evaluated.

Article 28 Operator engaged in high-risk operation areas (such as: production area for high activity, highly toxic, infectious, and sensitizing materials) should receive specialized training.

3.4 Personnel hygiene

Article 29 All personnel should receive training on hygiene requirements; enterprises should establish personal hygiene rules to minimize risk of contamination caused by person.

Article 30 Personal hygiene practice should include health, hygiene habits and dressing. Person in production areas and quality control should have proper understanding of personal hygiene practice. Enterprises should take measures to ensure implementation of personnel Hygienic Practice.

Article 31 Enterprises should manage personnel health and establish health files. Production personnel in direct contact with drugs shall receive health checks before induction and later health check should be performed at least once a year.

Article 32 Enterprises should take appropriate measures to keep person wound surface, infectious diseases or other diseases that may contaminate drug from being engaged in drug production.

Article 33 Visitors and untrained personnel shall not have access to production and quality control areas. When there is need for access, instruction on personal hygiene, dressing and other matters should be given.

Article 34: Any person entering the production area shall change clothes in accordance with provisions. Materials, style and dressing way of clothes should be appropriate to work engaged and air cleanliness level.

Article 35 Personnel entering the clean production areas shall not wear make-up accessories.

Article 36 There should be no smoking and eating, storage of food, beverages, cigarettes and drugs for personal use and other non-production items in production and storage area.

Article 37 Operators should not directly touch drugs, and packaging materials and equipment surface that will be contact with drug with bare hands.

4. Facility and utilities

4.1 General provisions

Article 38 Facilities sites, design, layout, construction, renovation and maintenance must comply with requirements of pharmaceutical production to minimize contamination, cross contamination, confusion and errors and to facilitate cleaning, operation and maintenance.

Article 39: The sites for facilities should be selected by taking protective measures for facilities and production into consideration. Facilities should be located in an environment able to minimize risk of contamination on materials and product.

Article 40 Enterprises should have a clean production environment; factory floors, roads and transportation should not cause contamination to production of drugs; overall layout of production, administrative, living and support areas should be reasonable and not impede each other; facilities, personnel and materials flow within the facilities should be reasonable.

Article 41 Facilities should be properly maintained and maintenance activities will not adversely affect drug quality. Facilities should be cleaned and sanitized according to detailed written operating procedures.

Article 42 Facilities should be equipped with proper lighting, temperature, humidity and ventilation to ensure quality of product produced and stored as well as performance of related equipment will not be directly or indirectly affected.

Article 43 Facilities and utilities should be designed and installed to prevent entrance of insects or other animals. Necessary measures should be taken to prevent use of rodenticides, pesticides and smoke agent will not cause contamination on equipment, materials, and products.

Article 44 Appropriate measures should be taken to prevent access of unauthorized personnel. Production, storage and quality control areas should not be used as access for staff that not belongs to this area.

Article 45 Facilities, utilities, fixed pipeline as-built drawings after completion of construction or reconstruction should be reserved.

4.2 Production area

Article 46 Facilities, production utilities and equipment should be designed and used as required for drug properties, process flow and level of cleanliness in order to reduce risk of contamination and cross-contamination and also meet following requirements :

(a) Feasibility of multi-drug facilities, production utilities and equipment should be evaluated by taking drug properties, process and intended use into consideration, and related evaluation report should be available.
(b) Drugs with special properties, such as highly sensitizing drugs (e.g. penicillin) or biological products (such as BCG or other use of medicines prepared from microbial activity), must be produced with dedicated and independent facilities, production utilities and equipment. Operation area of penicillin with a large amount of dust should maintain a relatively negative pressure. The exhaust discharged into outdoors should be purified to meet requirements and air vents should be away from other air purification system inlet;
(c) Production of β-lactam structure and sex hormone contraceptive drugs must use dedicated utilities (such as a independent air purification systems) and equipment and should be strictly separated from production areas for other drugs;
(d) Certain hormones, cytotoxic class, highly active chemicals should be produced with dedicated utilities (such as a separate air purification systems) and equipment; special protective measures, if needed, should be validated. Drugs mentioned above can share same utilities and equipment through divided production.
(e) The exhaust fan of air purification system mentioned in above b, c, and d should be purified.
(f) Drug production facilities should not be used to produce non-medicinal products that may adversely affect drug quality.

Article 47 Production areas and storage areas should be equipped with sufficient space to ensure orderly storage of equipment, materials, intermediate products, packaging and finished products and to avoid confusion of different products or materials, cross contamination, and omission and error caused by production or quality control operations.

Article 48 Air purification systems should be installed according to drug variety, operation requirement as well as external environment in order that production area can be ventilated properly, temperature and humidity are controlled, and air is purified and filtered to ensure production environment for drug meet requirement.

Pressures difference between clean areas and non-clean areas clean areas, among clean areas of different levels should not be less than 10 psi. When necessary, pressure difference should be maintained among areas with the same level of cleanliness but different functions (operating room).

Areas where liquid and solid preparations, cavity medication (including rectal application), topical pharmaceutical skin preparations and other non-sterile

preparations as well as final processing of packaging materials with direct contact with drug are exposed should be designed in accordance with requirements for D-level in Annex. Company can establish control on microorganism according to product specification and properties.

Article 49 Inner surfaces of clean area (walls, floors, ceiling) should be smooth, with tight interface, free from cracks and fall-off particles to avoid dust and permit effective cleaning and if necessary, sanitization.

Article 50 Various channels, lighting, air outlets and inlets and other public utilities should be designed and installed to facilitate cleaning. And maintenance should be performed from outside.

Article 51 Drainage facilities should be appropriate to installation installed to avoid back-flow. Open drain should be avoided, and be as shallow as possible to facilitate cleaning and sanitization.

Article 52 Raw materials and excipients for preparation should be weighed in preparation room specially designed.

Article 53: Operation rooms that generate dust (operation rooms such as sampling, weighing, mixing, and packaging of dried material or product) should maintain relatively negative pressure or take special measures to prevent spread of dust, cross-contamination and to facilitate cleaning.

Article 54 Facilities or areas used for dug packaging should be properly designed to avoid confusion or cross-contamination. Isolation measures should be taken when there are several packaging lines in the same area.

Article 55 Production areas should be equipped with appropriate lighting; lighting in visual check area shall meet requirements.

Article 56: In-process control can be located within production area when in-process control operation will not adversely affect product quality.

4.3 Warehousing area

Article 57 Storage areas should be equipped with sufficient space to ensure orderly storage of quarantined, accepted, rejected, return or recalled raw materials and excipients, packaging materials, intermediate products, packaging and finished products and other materials and products.

Article 58 Storage areas should be designed and constructed to ensure good storage conditions and equipped with ventilation and lighting utilities. Storage area should be able to meet storage conditions for materials or products (such as temperature and

humidity, protection from light) and requirements for safe storage. The storage area needs to be analyzed and monitored.

Article 59 Highly reactive materials or products and printed packaging materials should be stored in a secure area.

Article 60 Reception, distribution and shipping areas should be able to protect materials, products from being impacted by outside weather (such as rain, snow). Layout and utilities of receiving area should be able to ensure outer packages for materials and product can be cleaned before warehousing.

Article 61: If an independent area is used to store quarantine materials, this area should be labeled clearly and only restricted to authorized personnel.
Rejected, returned or recalled materials or products should be quarantined.
If other means are adopted to replace physical separation, this method should be of equivalent security.

Article 62: Usually there should be separate material sampling area. Air cleanliness level in sampling area should be consistent with production requirements. If sampling is performed in other area or by other means, contamination or cross contamination should be avoided.

4.4 Quality Control Area

Article 63 Quality control laboratory should normally be separated from production areas. Biological analysis, microbiological and radioisotope laboratory should also be separated from each other.

Article 64 Laboratory should be designed to meet its intended use and to avoid confusion and cross-contamination. And there should be enough area for sample disposal, storage of retained samples and samples for stability study as well as record keeping.

Article 65: When necessary, specialized equipment room should be set to keep sensitive equipment from static electricity, vibration, humidity or other external disturbances.

Article 66 Laboratory used to treat biological or radioactive samples and other special items should be consistent with relevant national requirements.

Article 67 Experimental animal rooms should be strictly separated from other areas; its design and construction shall comply with relevant regulations and equipped with separate air-handling facilities and dedicated channels for animals.

4.5 Auxiliary area

Article 68 Location and design of lounge should not adversely affect production area, storage area and quality control area.

Article 69 Changing rooms and rest rooms should permit easy access for people and be suitable for the number of users. Rest room should not be directly connected with production and storage area.

Article 70: The maintenance area should be as far away from production area as possible. Spare parts and parts for maintenance use in clean area should be stored in dedicated rooms or tool cabinet.

5. Equipment

5.1 General rules

Article 71 Design, selection, installation, alteration and maintenance of equipment must comply with its intended use to minimize risk of contamination, cross-contamination, confusion and errors and to facilitate operation, cleaning, maintenance, and if necessary, disinfection or sterilization.

Article 72 Operation procedures for equipment use, cleaning, maintenance and repair should be established and operation record should be maintained.

Article 73 Equipment purchasing, installation, qualification documentation should be established and kept.

5.2 Design and installation

Article 74: The production equipment should not adversely affect drug quality. The equipment surface in direct contact with drug should be smooth, clean, easy to clean or disinfect, corrosion-proof, and shall not have chemical reaction with drug, absorb drug or release materials into drug.

Article 75 There should be weighing, measuring tools, instruments and meters with appropriate range and precision.

Article 76 Cleaning and washing equipment should be appropriate and should not be the source of contamination.

Article 77 Lubricants, cooling agents used for equipment shall not cause contamination to drug or containers. The use of lubricants of food grade or equivalent grade should be encouraged.

Article 78 Standard operation procedure should be established for purchasing, analysis, storage, maintenance, distribution and scrap of production molds. And these molds should be kept by designated staff and recorded.

5.3 Maintenance and repair

Article 79 Equipment maintenance and repair shall not affect product quality.

Article 80 Preventive maintenance plan and operating procedures for equipment should be established, and equipment maintenance and repair should be recorded.

Article 81 Equipment should be re-qualified after renovation or major maintenance and can only be used in production after being proved to meet requirement.

5.4 Use and cleaning

Article 82 There should be clear operation procedures for main production and analysis equipment.

Article 83 Equipment should be used within identified parameters.

Article 84: Production equipment should be cleaned in accordance with detailed operation procedures.

Production equipment cleaning SOP should specify the followings: specific and complete cleaning methods, cleaning equipment or tools, cleaning agents name and method of preparation, method to remove previous batch identification, method to protect cleaned equipment from being contaminated, maximum reservation time for cleaned equipment, method to inspect cleaning status of equipment before use. The operators are able to clean all kinds of equipment in a reproducible and efficient way.

If equipment needs to be assembled, sequence and method of equipment assembly should be specified; if equipment needs to be sanitized or sterilized, specific sanitization or sterilizing method should be determined; the maximum time that allows equipment to stay before cleaning after completion of production should be stipulated.

Article 85: Cleaned production equipment should be stored in clean and dry conditions.

Article 86 There should be log for equipment and instruments used for drug manufacturing or analysis to record items including use, cleaning, maintenance and repair as well as date, time, drug name manufactured and analyzed, specifications and batch number.

Article 87: The status of production equipment should be clearly marked to identify equipment codes and product information (such as name, specification, batch number); production equipment not used in production should be clearly identified with cleaning status.

Article 88: Rejected equipment, if possible, should be moved out of production and quality control areas, and its status should be clearly identified before moving-out.

Article 89 Main fixed pipes should be marked with product information and flow direction.

5.5 Calibrations

Article 90 Weighing, measuring, instruments, recording and control equipment and instrumentation should periodically be calibrated and tested in accordance with operation procedure and calibration plan. And calibration and analysis should be recorded. The calibration range should cover use range for actual production and analysis.

Article 91 Key weighing and measuring tools, instruments, recording and control equipment used in production and test should be calibrated to obtain accurate and reliable data.

Article 92 Calibration standards should be used for calibration and calibration standard should comply with national regulations. The name, number, calibration expiry date and Certification No. of qualified calibration should be specified in calibration record and record should be traceable.

Article 93 Weighing and measuring apparatus, instruments, and equipment used for recording and control should be clearly identified with calibration expiry date.

Article 94 Weighing and measuring instruments, equipment used for control and record without calibration, or out of validity, out of alignment should not be used.

Article 95 Automated or electronic equipment used in production process, packaging, warehousing should be calibrated and checked regularly in accordance with operational procedures to ensure proper running. Calibration and analysis should be recorded.

5.6 Water for drug manufacturing

Article 96 Pharmaceutical water should be suitable for their purposes and meet "Pharmacopoeia of PRC" and related requirements. Drinking water should be used as pharmaceutical water at the least.

Article 97 Water treatment equipment and distribution system should be designed, installed, run and maintained to ensure quality of pharmaceutical water meets established standards. Operation of water treatment equipment shall not exceed its designed capacity.

Article 98: Materials of water tanks and distribution loops for purified water, injection water should be non-toxic, corrosion resistant; tank vents should be installed with hydrophobic sterilizing filter without fiber fall-off; pipes should be designed and installed to avoid died corner and died leg.

Article 99: Breeding of microorganisms should be prevented in preparation, storage and distribution of PW and WFI. Purified water can be circular, heat cycle above 70 ℃ can be used for WFI.

Article 100 Pharmacy water and raw water quality should be regularly monitored and correspondingly recorded.

Article 101 Pipelines for PW and WFI should be cleaned and sanitized in accordance with SOP. When microbial contamination of pharmaceutical water reaches alert limits or corrective limit, it should be handled in accordance with operating procedures.

6. Materials and products

6.1 General rules

Article 102: Raw materials and excipients used for drug manufacturing and packaging materials in direct contact with drug should meet related quality standards. The ink used directly on drug should meet food grade standards.
Imported raw materials and excipients shall comply with relevant state regulations on importation.

Article 103 Materials and products operating procedures should be established to ensure correct reception, storage, distribution, use, delivery to avoid contamination, cross contamination, confusions and errors.
Materials and products should be processed in accordance with operation procedures or process instructions and be recorded.

Article 104: There should be quality evaluation for materials suppliers' selection and change; material purchasing can only starts with approval of quality management department.

Article 105 Transportation for materials and products should ensure to satisfy quality requirement. And transportation condition should be qualified for materials and products that demand special requirement on delivery.

Article 106 There should be operation procedure for reception of packaging materials and printing packaging materials of raw materials and excipients and that in direct contact with drug. All the materials and products received should be analyzed to ensure they are consistent with requirements on purchasing orders. And these suppliers have been qualified by quality management department.

Outer packages of materials should be attached with labels identified with regulated information and should be cleaned when necessary. The issues of damaged outer packages or other issues that may affect materials quality should be reported to quality management department and then should be investigated and recorded.

Each reception should be recorded with following information:
(A) Name of the material indicated on delivery note and container
(B) Name and (or) code of the materials used within the enterprise;
(C) Date of receipt;
(D) Name of suppliers and manufacturers (if different);
(E) Batch number identified by Supplier and manufacturer (if different);
(F)Total number of materials or products received and packaging containers;
(G) Batch number or serial number designated by company after reception;

(H) Related description (such as packaging conditions).

Article 107 Materials received and final products after production should be managed as quarantine conditions until they are released.

Article 108 Materials and products should be stored and transferred by bathes in accordance with their properties and should be distributed and delivered in compliance with principle of consumption of the materials or products that were received or will be expired first.

Article 109 Appropriate operation procedures should be available for computerized warehouse management to prevent mixing and error caused by system failure, shutdown or other special cases.
It is not compulsory to mark materials, products and other related information fully identified by computerized warehousing management system in written readable form.

6.2 Raw materials and excipients

Article 110 Corresponding operation procedures should be developed to take appropriate measures such as checking or analysis to confirm that each package of raw materials and excipients are correct.

Article 111: If materials of many batches are received at a time, these materials should be sampled, analyzed and released by batches.

Article 112 Raw materials in warehousing areas should be at least properly identified with following information:
A. Materials name and internal code specified;
B. Batch number specified during reception;
C. Material quality status (for example, qualified, rejected, sampled);
D. Expiry or reanalysis period.

Article 113: Only raw materials and excipients within expiry or reanalysis date and released with approval of quality management department can be used.

Article 114 Raw materials and excipients should be stored in accordance with the expiry or reanalysis period. During storage period, if special circumstances those adverse effects on the quality are found, reanalysis should be performed.

Article 115 Designated people should be assigned to perform preparation, precise weighing or measuring after materials check, and then perform correct identification.

Article 116: Any material, related weight or volume should be reviewed independently by others and the review should be recorded.

Article 117: All the excipients used for drug of the same batch should be stored together and properly identified.

6.3 Intermediate products and bulk products

Article 118: Intermediate products and bulk products should be stored in appropriate conditions.

Article 119: Intermediate products and bulk products should be clearly labeled with at least following information:
(a) Product name and internal product code;
(b) Product batch number;
(c) Quantity or weight (such as gross, net, etc.);
(d) Production processes (if necessary);
(e) Product quality status (if necessary, such as quarantine, qualified, rejected, sampled.)

6.4 Packaging materials

Article 120: The requirements for management and control of packaging materials and printed packaging materials in direct contact with drug should be same with those for raw materials and excipient.

Article 121 Packaging materials shall be distributed by specified person in accordance with operating procedures and measures should be taken to prevent mixing and error to ensure packaging materials for pharmaceutical production are correct.

Article 122 Operation procedures should be established to design, review, approve printing and packaging materials to ensure content of printed packaging materials comply with those approved by drug regulatory department. Specific file should be created to preserve the original sample of printing and packaging material with signature of approval.

Article 123: When there is a change for version of printing and packaging materials change, measures should be taken to ensure the version of printed packaging materials used for products is correct. Obsolete print templates should be recalled and destroyed.

Article 124 Printing and packaging materials should be properly stored in dedicated area with restriction to unauthorized personnel. Cutting labels or other printing and packaging materials in bulk pack should be stored and delivered in separate and sealed containers to avoid confusion.

Article 125 Printing and packaging materials should be kept specified person and distributed in accordance with operating procedures and the demand quantity.

Article 126: Any batch of packaging material or printed packaging material distributed should be identified with name and batch number of products.

Article 127 Expired or obsolete printed packaging materials should be destroyed and recorded.

6.5 Final products

Article 128 Finished goods should be stored in quarantine status prior to release.

Article 129 Storage condition of finished goods shall meet the requirements for that approved by drug registration.

6.6 Materials and products which need special management

Article 130 Narcotic drugs, psychotropic substances, toxic drugs for medical use (including ingredients), radioactive drugs, drug precursor chemicals, flammable, explosive and other dangerous goods should be accepted, stored, managed as required by national regulations.

6.7 Other

Article 131: Each packaging container for rejected materials, intermediate products, bulk and finished products shall be identified clearly and kept properly in quarantine area.

Article 132: The disposal of rejected materials, intermediate products, bulk packaging and finished products should be approved by person in charge of quality management, and the disposal should be recorded.

Article 133: The recall of products should be approved in advance, and related quality risk should be fully assessed to decide the necessity of a recall. The recall process should be performed according to predetermined operating procedures and should be recorded. The expiry date for recalled products after treatment should be determined in accordance with date for the batch produced at the earliest.

Article 134 Drug products may not be reworked. Rejected intermediates for preparations, bulk packaging and finished products generally may not be reprocessed. The reprocessing can only be allowed on premise that operation procedures for reprocessing will not adversely affect product quality, comply with related quality standard, and is approved and its related risk have been fully evaluated. Reprocessing should be recorded.

Article 135: As for finished products produced from combined process of reworking, reprocessing or recovery, quality management department should consider the need for additional relevant analysis and stability study.

Article 136: Pharmaceutical returns operating procedures should be established by enterprises, and related records should include at least: product name, batch number, specifications, and quantity, and name and address of return company, return date and reasons, and advice for final disposition.
The same returned product with same batch number returned from different channels should be recorded, stored and treated separately,.

Article 137: Only there is evidence that quality of returns is not adversely affected by means of analysis, inspection and investigation, and evaluation has been performed by quality management department in accordance with operation procedure, the returns can be considered to be repackaged, re-shipped for distribution. The evaluation should consider at least following: drug property, required storage conditions, current status and history of drug, time interval between delivery and return and other factors. The returns that fail to meet requirements of storage and transportation should be destroyed under the supervision by quality management department. If there is doubt on quality of returns, returns can't be re-shipped.
If returns are recovered, products after recovery shall meet the established quality standards and Article 133's requirements.
There must be records for recovery process and results for returns.

7. Validation and qualification

Article 138: Enterprises shall specify validation or qualification activities to prove critical factors related to operations can be effectively controlled. The scope and depth for validation or qualification should be decided upon risk assessment.

Article 139: An enterprise‘s utilities, facilities, equipment and analysis instruments shall be qualified. Production, operating and analysis should be performed as required for production process, operation procedures and analysis method that have been already validated. The qualified status should be maintained continuously.

Article 140: Documents and records for qualification and validation should be established to provide evidence to meet following intended objectives:
(A) Design qualification should demonstrate that design of utilities, facilities and equipment meets its intended use and requirements of this practice;
(B) Install qualification should demonstrate construction and installation of facilities, utilities and equipment meet design standards;
(C) Operational Qualification should demonstrate that plant, utilities, equipment operates in accordance with design standards;
(D) Performance qualification should demonstrate that plant, utilities, and equipment can continuously meet standards in normal operation procedures and process conditions. ;
(E) Process validation should demonstrate a manufacturing process can produce product that meet its established use and registration requirements with process parameters established by production process parameters.

Article 141: The suitability for routine production should be validated prior to using new recipe or production processes. Production process can always produce products that meet intended use and registration requirements by using required raw materials and equipment.

Article 142: When there is change for main factors affecting product quality, such as raw materials, prepackaging materials in direct contact with drug, production equipment, production environment (or facilities), production process, and analysis methods, qualification or validation shall be conducted.
When necessary, it should also be approved by drug regulatory authorities.

Article 143: Cleaning methods should be validated to confirm cleaning effects for efficient prevention of contamination and cross-contamination. Cleaning validation should thoroughly consider such factors as use status for equipment, detergents and disinfectants used, sampling methods and locations, and related sampling recovery rate, property and limits of residues, sensitivity of analysis methods for residues, and etc.

Article 144: Validation and qualification is not a one-time activity. After first qualification or validation, revalidation or re-qualification should be taken based on retrospective analysis of product quality. Critical production processes and operating procedures should be periodically re-validated to ensure its ability to achieve desired results.

Article 145: Company should establish validation master plan to demonstrate critical information of qualification and validation in form of documentary.

Article 146L: It must be specified in VMP or other related documents that stability of utilities, facilities, equipment, analysis equipment, production processes, operating procedures and analysis methods can be continuously maintained.

Article 147 Qualification and validation protocols shall be established based on the object for qualification or validation and reviewed, approved. Qualification or validation protocols should have clear responsibilities.

Article 148: Qualification and validation should be implemented in accordance with pre-determined and approved protocol. After qualification or validation is finished, report should be issued, reviewed and approved. The results and conclusions of qualification or validation (including evaluation and recommendations) should be documented and archived.

Article 149: Process procedures and operation procedures should be confirmed according to validation results.

8. Document management

8.1 Principles

Article 150: Documents is an essential element of quality assurance systems. Enterprises must have correct written quality standards, production recipe and process procedures, operation procedures, records and so on.

Article 151: An enterprise shall establish operation procedures of document management for systematic design, development, review, approval and issuance of documents. Documents relevant to this specification shall be reviewed by quality management department.

Article 152: The contents of documents should be corresponding with related requirements for drug Production License and drugs registration, and be convenient for tracing history of each batch of product.

Article 153 Document drafting, revising, reviewing, approving, replacement or

withdraw, replication, storage and destroy should be managed in accordance with operating procedures, and related records for document distribution, withdraw, duplication, and destroy should be in place. .

Article 154: Document drafting, revision, review, approval should be signed by the appropriate staff s with date marked.

Article 155 Document should be identified with title, type, purpose, and document code and version number. Content should be precise, clear and easy to understand, and not be ambiguous.

Article 156 Document should be stored by classification in clear order for easy access.

Article 157: Any error should be avoided in duplication of original copies; copied files should be clearly visible.

Article 158 Documents should be periodically reviewed and revised, and be managed as required preventing misusage of older version. The documents distributed and used should be of approved current version, and the withdrawn or documents of old version should not be present on work site.

Article 159: Each activities related to this practice shall be recorded to ensure that production, quality control and quality assurance activities can be traced. Records should leave enough space for filling data. Records should be finished timely, true, legible, readable and uneasy to erase.

Article 160: Records, maps and graphs automatically printed from production and analysis equipment shall be used as far as possible, and information of product or the sample name, batch number and recording device should be identified. The operator should sign name and date.

Article 161: Records should keep clean and not be torn, and any alteration is forbidden. Any changes to record shall be signed with name and date, and original message is still clear and legible. If necessary, reasons for change should be described. If records need to be transcribed, original records shall not be destroyed and should be saved as attachment for transcribed records.

Article 162 Every batch drugs should have batch records, including batch production records, batch packaging records, batch analysis records, batch release and approval records and other records related to the product. Batch records should be managed by quality management department, and should be kept until one year after the expiration date.

Article 163: If data is recorded by electronic data processing systems, photography or other reliable methods, SOP for systems used should be in place; record accuracy should be reviewed.
If electronic data processing system is used, right of data input or alteration is only limited to authorized personnel. Any change and deletion should be recorded; a password or other means should be adopted to control system registry; critical data should be independently reviewed by others after its input.
There should be tapes, microfilms, paper copies or other methods for batch records kept in electronic methods as backup to ensure records are secures and data information is easily accessible in storage period.

8.2 Quality Standards

Article 164 Materials and finished products should have current approved quality standards; if necessary, intermediate or bulk products should also have quality standards.

Article 165 Quality standards for materials generally should include:
(A) Basic information for materials:
1. Materials name specified by company and materials code for internal use;
2. The basis of quality standards;
3. Approved suppliers;
4. The samples or drafts for printing and packaging materials..
(B) Reference for sampling, analysis methods, or related operating procedures;
(C) The limit requirements for qualitation and quantitate;
(D) Storage conditions and precautions;
(E) Expiry or reanalysis date.

Article 166: There should be quality standard for intermediates and bulk products purchased or for sale; if the intermediates' analysis results are used to evaluate quality of finished product, intermediates' quality standards corresponding to those for finished products should be established.

Article 167 Quality standards for finished products shall include:
(A) name and code of finished products;
(B) recipe code corresponding to products (if available);
(C) product specifications and packaging form;
(D) reference for sampling, analysis methods, or related operation procedures;
(E) limited requirements for qualitation and quantitate;
(F) storage conditions and precautions;
(G) expiry date

8.3 Process procedure

Article 168: Process procedures approved by company should be available for each production batch for each kind of drugs. Each kind of packaging form for drugs of different specifications should have its own packaging requirements. The process procedure should be established basing on process approved in registration.

Article 169: Any random alteration to process procedure should be forbidden. Change, if necessary, should be revised, reviewed and approved in accordance with relevant operation procedures.

Article 170 Preparation's process procedure should include at least:
(A) Production recipe:
1. The name and code of products;
2. Product dosage form, specifications and batch quantities;
3. The list of raw materials used (including material used in the production process, but does not appear in finished products) should clarify designated name, code, and use amount of each material; if amount of raw materials requires conversion, calculation method should also be explained.
(B) Production operating requirements:
1. Description of production site and equipment used (such as location and code of operating rooms, cleanliness level, necessary requirements for temperature and humidity, equipment model and code, etc.);
2. Reference of Methods or related operation procedures to prepare critical equipment (such as cleaning, assembling, calibration, sterilization, etc.);
3. A detailed description of production steps and process parameters (such as materials checking, pretreatment, sequence of charging materials, mixing time, temperature, etc.);
4. All in-process control methods and standards;
5. The expected final yield limit, when necessary, limit yield of intermediate goods, material balance calculations and limits should be described;
6. Storage requirements of bulk products including containers, labels and special storage conditions;
7. Precautions that need to be noted.
(C) The requirements for packaging operation:
1: Packaging form indicated with quantities, weights, or volumes of products in final package container;
2. Complete list of all packaging materials needed, including name, amount, specification, type, of packaging materials and code of each packaging material relevant to quality standard;
3. Real samples or duplicates for printing and packaging materials; printing location for batch number and expiry date should be marked
4. Precautions that need to be addressed, including checks of production area and equipment, check to verify packing line clearance has been completed before packaging operation starts, etc.

5. The instructions of packaging steps, including precaution for important ancillary operation and equipment, check of packing material before use
6. Detailed operations for process control including sampling methods and standards
7. The material balance calculation methods and limits for bulk products, printing and packaging materials,.

8.4 Batch production records

Article 171: Each lot shall have a relevant batch production record from which production history and quality for this batch can be traced.

Article 172 Batch production records should be based on the current approval process procedure to develop relevant content. Records should be designed to avoid error filling. The name, specifications and batch number of the products should be marked on every page of batch production records.

Article 173 Original blank batch records shall be reviewed and approved by production management leader and quality management leader. Batch production records for copying and distribution shall be controlled in accordance with operating procedures and recorded, each batch of products can only release an original blank copy of the batch production record.

Article 174: In the production process, each operation performed should be promptly recorded; at the end of operation, operator should confirm the production with signature of name and date.

Article 175 Batch production record should include:
(A) product name, specification, and batch number;
(B) starting and ending date and time for production and intermediate process;
(C) signature of person in charge of each production process;
(D) signature of the operator of production steps; if necessary, signature of reviewer for operation (such as weighing);
(E) each batch No. of raw materials and number actually weighed (including recovery charged or batch No. and quantity for reprocessed products);
(F) operations or activities related to production, process parameters and control range, as well as code of main production equipment used;
(G) records of process control results and operator's signature;
(H) yield obtained from different production processes and if necessary, material balance calculations;
(I) record about special problems or unusual events, including detailed description or investigation report for deviation from process procedure. The records should be approved with signature.

8.5 Batch Packaging Records

Article 176: Packages for each batch of the product or partial products should have batch packaging records from which packaging operations for this batch of product and quality-related issues can be traced.

Article 177 Batch packaging records should be established basing on information related to packaging in process procedure. Records should be designed to avoid filling errors. Names, specifications, packaging form and lot numbers of products being packaged should be marked on each page of batch packaging record.

Article 178 Batch packaging records should include batch number and quantity of the bulk product, batch number and planned quantity of finished products. Review, approval, copying and distribution requirements for original blank packaging batch record are the same as those for original blank batch production records.

Article 179: In packaging process, every operation performed should be promptly recorded, and at the end of operation, packaging operator should check it by signing name and date.

Article 180 Batch packaging records include:
(A) product name, specifications, packaging form, batch number, production date and expiry date;
(B) date and time of packaging operations;
(C) signature of person responsible for packaging operation ;
(D) signature of operator for each packaging process;
(E) name, batch number and quantity of actual use for each kind of packaging material;
(F) inspection record checked according to process procedures , including process control results;
(G) details of packaging operations, including code for equipment and packaging production line used;
(H) real samples of printing and packaging materials used and printed with batch number, expiry data and other printed content; duplicate printed with information mentioned above can be used for printing and packaging materials which are not easy to be filed according to batch packaging records;
(I) records on special problems or unusual events, including detailed description or investigation report on deviations from process specification with approved signature;
(J) Name, code, and quantity distributed, used, destroyed or returned to the warehouse, actual yield, and materials balance checks for all printing packaging materials and bulk products.

8.6 Operating procedures and records

Article 181: Operation procedures should include subject, code, version number, issue department, effective date, distribution department, and signature of people responsible

for preparation, review and approval, as well as indicated with date, title, text and change history.

Article 182 Plant, equipment, materials, documents and records should have a number (or code), and SOP of number assignment should be established to ensure that the number (or code) is unique.

Article 183 Corresponding operation procedures should be available for following activities, and process and results should be recorded:
(A) validation and qualification;
(B) equipment assembly and calibration;
(C) plant and equipment maintenance, cleaning and disinfection;
(D) personnel-related matters such as training, clothes change and hygiene;
(E) environmental monitoring;
(F) pest control;
(G) change control;
(H) deviation handling;
(I) complaints;
(J) drug Recall;
(K) returns

9. Production Management

9.1 Principle

Article 184: All drugs should be manufactured and packaged in accordance with approved process procedure and operating procedures and relevant records should be in place to ensure that drugs meet required quality standards and comply with requirements of pharmaceutical production licenses and registration.

Article 185: Operation procedures of dividing production batches should be developed, and division of production batches should be able to ensure uniformity of quality and features for the same batch.

Article 186: There should be operation procedure for creating production lot number and determining drug manufacturing date. Batch No assigned to each batch of drugs should be unique. Unless otherwise specified by regulatory requirements, production date cannot be late than the start date of final mixes before molding or filling (sealing) operation. The date of product packaging cannot be used as date for production.

Article 187: Product yield and material balance for each batch should be checked, to ensure material balance comply with set limits. If different, reasons must be identified, it can only be treated as normal products after no potential quality risk is confirmed.

Article 188: Production operation of drug of different varieties and specifications should not be performed in the same room at the same time, unless there is no possibility of confusion or cross-contamination.

Article 189: In each stage of production, products and materials should be protected from microbial and other contamination.

Article 190: In production process of drying materials or products, especially high activity, highly toxic or sensitizing materials or products, special action should be taken to prevent dust generation and diffusion.

Article 191: Containers for all materials, intermediate products or bulk products, and major equipment, necessary operating room used in production should be labeled or identified by other means with name, specifications and batch number for product or materials, and if necessary, should also be indicated with production process.

Article 192: Identification information on containers, equipment or facilities should be clear; identification format should be approved by related department of the Company. Also different color can be used to distinguish status of materials identified (e.g.,

quarantined, accepted, rejected or cleaning, etc.).

Article 193: The pipes and other connecting devices for products transportation from one area to another area should be checked to ensure connection is correct.

Article 194: At the end of each production, production field should be cleared to ensure that no materials, products and documents related with this production left on equipment and work site. Before next production starts, previous site clearance should be checked.

Article 195: Any deviation from process procedure or operating procedures should be avoided. The deviation, if occurred, should be treated in accordance with operating procedures about deviation treatment.

Article 196 Access of production plants should be only restricted to authorize personnel.

9.2 Prevent contamination and cross contamination in process of production

Article 197 Measures as much as possible should be taken to prevent contamination and cross-contamination in production process, such as:
(A) drugs of different varieties should be manufactured in separate areas;
(B) use of stage production;
(C) set up necessary air lock room and exhaust; pressure difference should be controlled in areas with different air cleanliness level;
(D) risk of contamination caused by untreated or inadequately treated air re-entering production area;
(E) operator should wear specific protective clothing in production areas easy to generate cross-contamination;
(F) equipment should be cleaned in accordance with cleaning and decontamination operation procedures which have been validated or have been proved to be efficient; if necessary, residues on device surface in direct contact with material should be analyzed;
(G) produce in a closed system;
(H) inlet of drying equipment should be equipped with air filters, exhaust air should be equipped with device to prevent backflow;
(I) use of tools that are fragile, easily scaling, easy to generate mold apparatus should be avoided in the process of production and cleaning; when screen is used, measures should be taken to prevent its fracture;
(J) preparation of liquid formulations, filtration, filling and sealing, sterilization and other processes should be completed within stipulated time;
(K) storage period and storage conditions should be specified for intermediates of ointment, cream, gel, and other semi-solid preparations and suppositories.
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Article 198: Measures taken to prevent contamination and cross-contamination should be regularly checked, and applicability and effectiveness of measures should be evaluated.

9.3 Production operations

Article 199: Inspection should be performed before start of production to ensure product, document or materials unrelated with this batch of production is not left on equipment and work site, and equipment is cleaned and in inactive status. Inspection results should be recorded.
Before operation, name, code, lot number and identifications of materials or intermediates should be checked to ensure materials or intermediates used in production are correct and meet requirements.

Article 200 Necessary process control and environmental monitoring should be performed and recorded.

Article 201: Production site must be cleared by production operator after each production stage is finished, and operator should fill in site-clearance record. Clearance records should include: operating room code, product name, batch number, production processes, date of clearance, inspection items and results, and signatures of clearance operator and reviewer. Clearance records should be incorporated into batch production records

9.4 Packaging operations

Article 202 Packaging operating procedures should establish actions to reduce contamination and cross-contamination, and risk of confusion or error.

Article 203 Before starting packaging, inspection should be performed to ensure that workplace, packaging lines, printing machine and other equipment are in clean or inactive state, and products, document or packaging materials unrelated with this batch of production is not left. Inspection results should be recorded.

Article 204: Before packaging operation, recipients should also check packaging materials are correct, and name, specification, quantity, and quality status of packaging materials used for bulk products are consistent with process procedure.

Article 205: Each packaging operation site or packaging production line should be identified with product name, size, lot number and quantities that are being packaged.

Article 206.Isolation or other prevent action should be taken to avoid contamination, cross contamination or confusion when there are several packaging lines packaging simultaneously.

Article 207 Packing containers shall be kept clean before use to ensure there is no glass debris, metal particles and other contaminants.

Article 208: Labeling shall be promptly performed after products sub-packaging and sealing. If labels are not applied timely, its operation should be performed in accordance with relevant operating procedures to avoid labels confusion or mislabeled.

Article 209: Information separately printed or online printed in packaging line (such as product lot number or expiry date) shall be analyzed to ensure it is correct and is recorded. If it is manually printed, analysis frequency should be increased.

Article 210: As for cutting-type labels or labels that are printed separately (out of packaging lines), special measures should be taken to prevent confusion.

Article 211 Function of electronic reading machines, label counters or other similar devices should be checked to ensure accurate running. Inspection should be recorded.

Article 212 Contents printed or molded on packaging materials should be clear, not easily faded and erased.

Article 213: During packaging process, process control checks of products should at least include following:
(A) packaging appearance;
(B) whether packages are complete;
(C) whether products and packaging materials are correct;
(D) whether printed information is correct;
(E) Whether On-line monitoring device runs properly.
Samples removed from the packaging line should not be returned to prevent products from confusion or contaminated.

Article 214: When there are abnormalities due to packaging processes and there is need for re-packaging of products, repackaging should be checked, investigated and approved by designated person. Re-packaging should be recorded in detail.

Article 215: In material balance checks, if significant differences for quantities are found for bulk products, printing and packaging materials and finished products, investigation should be performed and final products cannot be released before results are obtained.

Article 216: At the end of packaging, remaining packaging materials already printed with batch number should be accounted and destroyed by dedicated person and recorded. If there are packaging materials without printed batch number, these labels

should be returned to warehouse in accordance with operating procedures.

10. Quality control and quality assurance

10.1 Quality Control Laboratory Management Section

Article 217 Quality control laboratory personnel, facilities; and equipment should be appropriate to products nature and production scale.

Normally Enterprise should not contract the third party for analysis. But when there is indeed a need for contractual analysis, outsourcing analysis taken by external lab should be described in analysis report.

Article 218: Person responsible for Quality control should have sufficient qualifications and experience in managing one or more labs in the same enterprise.

Article 219: The analysis personnel in quality control laboratory should at least graduate from technical secondary school or high school education on related majors, receive training related to analysis operations engaged and pass training assessment.

Article 220: Quality control laboratories shall be equipped with Pharmacopoeia, standard map and other necessary reference books, reference substances or standard substance and other related standard substance.

Article 221 Documents of quality control laboratory shall conform to principles of Chapter VIII and meet following requirements:

(A) The quality control laboratory should have at least following detailed documents:

1. Quality standards;
2. Sampling operating procedures and records
3. Analysis operation Procedures and records (including analysis records or laboratory notebooks);
4. Analysis report or certificate;
5. Necessary operating procedures for environmental monitoring, recording and reporting;
6. Necessary validation reports and records of analysis methods;
7. Operational procedures and records for instrument calibration and equipment use, cleaning, maintenance.

(B) Analysis records of each batch of drug should include quality analysis records for intermediate products, bulk and finished products and all quality analysis information related to this batch of drug can be traced from these analysis records;

(C) Method easy for trend analysis should be adopted to save some data (such as analysis data, environmental monitoring data, and microbiological monitoring data for pharmaceutical water);

(D) In addition to information related with batch record, but also other raw data and records should be preserved for easy access.

Article 222: Sampling should at least meet following requirements:
(A) Quality control department's staff are entitled to enter production area and storage area for sampling and investigation;
(B) Perform sampling according to approved operating procedures, operation procedures should be specified in detail:
1. Person authorized for sampling;
2. Sampling methods;
3. Apparatus used;
4. Sample quantities;
5. Sample division method;
6. Type and status of container used to store samples;
7. Disposal and identification of remaining samples and samples after sampling;
8. Sampling precautions, including preventive measures taken to reduce all kinds of risks during sampling process, especially notes for sterile or hazardous materials sampling and prevention of contamination and cross-contamination in sampling process;
9. Storage conditions;
10. Cleaning and storage requirements for sampling apparatus
(C) Sampling methods should be scientific, reasonable to ensure its representativeness;
(D) Retained samples should be representative of products or materials of that batch being sampled, other samples can be taken to monitor the most critical steps in production process (such as beginning or end of production);
(E) Sample container should be labeled, indicating sample name, batch number, sampling date, package containers from which samples are taken, sampling operator and other information;
(F) Samples should be stored in accordance with storage requirements.

Article 223 Analysis of materials and products manufactured from different stages should at least meet following requirements:
(A) The enterprise shall ensure drugs are fully analyzed in accordance with the approved registration method;
(B) Analysis method should be validated in one of following cases:
1. The use of new analysis methods;
2. Analysis methods that need to be changed;
3. Analysis methods are not recorded in "Chinese Pharmacopoeia" and other statutory criteria;
4. Other analysis methods that need to be validated required by regulations.
(C) As for analysis method that does not require validation, enterprise should qualify analysis methods to ensure analysis data is accurate, and reliable;
(D) A written operating procedures should be available for analysis to specify analysis method, instruments and equipment, and content of Laboratory Procedures should be the same with analysis method qualified or validated;
(E) Analysis records should be traceable and reviewed to ensure results and records are

consistent. All calculations should be strictly checked;
(F) Analysis records shall at least include following:
1. Name, dosage form, specification, batch number or lot number supplied for product or material, and if necessary, name or source of supplier and manufacturer (if different);
2. Quality standards and analysis operation procedures on which analysis records are based
3. Model and code for analysis instruments or equipment used for analysis;
4. Preparation batch number of analysis solution and culture media used in analysis, resource and batch number of reference substance or standard substance;
5. Relevant information about animals used for analysis;
6. Analysis process, including preparation of reference substance solutions, each specific analysis operation, and necessary temperature and humidity;
7. Analysis results, including observations, calculations and map or graph, and reference of analysis report on which it is based;
8. Analysis date
9. Signature and date signed by inspector
10. Signature and date of reviewer for analysis and calculation
(G) All process control (including process control performed by production staff) shall be conducted in accordance with methods approved by quality management department, and analysis should be recorded;
(H) Quality of glass instrument, reagent, solution, referent substance and culture media for volume analysis in the lab should be analyzed;
(I) when necessary, laboratory animals used in analysis should be analyzed or quarantined before use . Feeding and management should comply with regulations related to laboratory animals. Animals should be identified and historical record of use should be maintained.

Article 224: Quality control laboratory should establish operational procedures of OOS investigation for analysis results. Any OOS of analysis results must be thoroughly investigated in accordance with operating procedures and recorded.

Article 225: Materials and products maintained by Enterprises as required, used for traceability and investigation of drug quality are considered as retained samples. Samples used for study of product stability are not regarded as retained samples. Retained samples should at least meet following requirements:

A. Retained samples should be managed as required by operation procedures;
B. Retained sample can represent materials or products of that batches being sampled;
C. Retained samples of finished products.
1. Each batch of drug shall have retained samples; if one batch of drugs is packaged into several packages, each time at least one package of marked final products with the minimum quantity should be retained.
2. The packaging form of retained samples should be the same with that for commercial drug on sale. And simulated commercial packaging can be adopted;

3. The number of retained samples for each batch of drugs should be adequate to ensure full analysis can be performed twice in accordance with quality standard approved for registration(excluding sterility analysis and progeny analysis, etc.);
4. As long as packaging integrity of retained samples is not adversely affected, retained samples should be analyzed visually at least once per year during preservation period. If unusual, a thorough investigation should be conducted and appropriate measures should be taken;
5. Observation of retained samples should be documented;
6. Retained samples should be stored at least one year after expiration date under conditions approved in registration;
7. If drug production is terminated or closed by enterprises, retained samples should be transferred to be kept by authorized units, and local drug regulatory departments should be informed of this transfer in order that they can obtain samples at any time when necessary.
(D) Retained samples for materials:
1: There should be samples retained for each batch of raw materials and packaging materials in direct contact with the pharmaceuticals used in production of preparation. As for drug packaging materials in direct contact (such as infusion bottle), if samples of final product are retained, additional retained samples are not necessary;
2. Quantity of retained samples for materials should at least be adequate to meet requirements for identification;
3. Except raw materials with poor stability, raw materials used for production of preparation (excluding solvents, gas or pharmaceutical water used in production process) and packaging materials in direct contact with the pharmaceuticals shall be retained for at least two years after product release. As for materials with a shorter validity, retentions time can be correspondingly shortened;
4. Retained Materials samples should be stored in accordance with conditions specified, when necessary, and if necessary, samples should be properly sealed and packaged.

Article 226: Management of Reagents, analysis solution, medium and analysis bacteria of should at least meet following requirements:

1. Reagents and culture media should be purchased from reliable suppliers, when necessary, suppliers should be evaluated;
2. Records for reception of reagents, analysis solution, and culture medium should be available, if necessary, container of the reagents, analysis solution; medium should be identified with reception date.
3. Reagents, analysis solution and medium should be prepared, stored and used in accordance with related regulations and use instruction. In special circumstances, identification or other analysis should be performed for reagents before reception or use.
4. Analysis solution and prepared medium should be marked with batch number, date of preparation and preparation operators. And preparation record (including sterilization) should be available.

Unstable reagents, analysis solution and medium should be marked with validity and special storage conditions. Standard solution, titrated solution should be also marked with the last date for standardized and correction factors, and standardization should be recorded;

5. Applicability of prepared medium should be checked and recorded. Use of Medium should be recorded;
6. All kinds of analysis organism needed for analysis should be in place. And operation procedures and related records should be established for storage, subculture, use and destroy.
7. Analysis organism should be identified properly at least with name, number, number of subculture, subculture date, subculture operator;
8. Analysis organism should be stored as stipulated, and storage method and duration should not adversely affect growth feature of analysis organism.

Article 227 Management of Standard and reference standard should meet at least following requirements:

1. Standard and reference standard should be stored and used as required;
2. Standard and reference standard should be properly identified with at least following information: name, batch number, date of preparation (if any), validity (if any), first open date, content or potency and storage conditions;
3. If company needs to prepare Standard or reference standard by itself, quality specification and operation procedure for preparation, identification, analysis, approval and storage should be established. Every batch of work standards or reference standards should be standardized against official standards or reference standards and validity should be specified. Potency or content of work standards or reference standard should be proved to maintain stable within validity through regular standardization. The process and result of standardization should be recorded.

10.2 Release of materials and products

Article 228 Operation procedures for approval and release of materials and products should be separately established to clarify criteria, responsibilities for approval and release with related records.

Article 229 Release of the material should at least meet following requirements:

1. Quality evaluation of material should at least include manufacturer's analysis reports, analysis results of material package integrity and tightness;
2. Materials quality evaluation should be concluded with clear results: approved for release, rejected or other decision;

Article 230 Release of the product should at least meet following requirements:
(A) Quality of each batch of drug should be assessed prior to release to ensure drug and its manufacturing meet requirements for registration and this practice, and following information should be checked:

1. The main production process and analysis method has been validated;
2. All necessary analysis and check have been finished taking actual production conditions and records into consideration;
3. All necessary production and quality control have been completed and signed by related managerial personnel;
4. Changes have been completed in accordance with relevant regulations, changes which needs approval from drug regulatory department have been approved;
5. All necessary sampling, analysis, review and audits for change or deviations have been finished;
6. All deviations related to this batch of products have been clearly described or explained, or fully investigated and then properly solved; when deviations relate to products of other batches, the issues should be solved together.

(B) Drug quality evaluation should be concluded with clear results: approved for release, rejected or other decisions;
(C) Each batch of drugs should be approved for release with signature of qualified person;
(D) Vaccine products, blood products, and In Vitro Diagnostic Reagents for blood screening and other biological products regulated by SFDA should obtain batch release qualification certificates prior to release.

10.3 Continued stability study

Article 231: Continual stability study intends to monitor quality of marketed drug to detect stability issues related to drug and production (e.g. variation of purity assay or dissolution rate) and to ensure drug can meet each quality specification when stored in identified conditions.

Article 232 Continued stability studies mainly focus on packaged products on sale, but also consider bulk products. For example, when bulk products need to be stored for a long time before being packaged or during transportation stage from manufacturing site to packaging sites, impact on stability of products after packaging should be evaluated. In addition, intermediates, if stored for a long time, should be undergone stability study.

Article 233 Continual stability study should be carried out with study protocol and concluded with reports. Equipment used for continual stability study (especially equipment or facilities used for stability study) shall be qualified and maintained in accordance with the requirements specified in Chapter Seven and Five.

Article 234 Period of Continued stability study should cover drug validity; study protocol should at least include the following:
(A) Number of batches studied for each specification and production batches;
(B) Related physical, chemical, microbiological and biological analysis methods; Specific Analysis methods for stability study can be adopted;
(C) Criteria of analysis method;

(D) Qualification criteria;
(E) Description of container closure systems;
(F) Analysis interval (analysis time point);
(G) Storage conditions (conditions for long-term stability study specified by “Chinese Pharmacopoeia" corresponding to storage conditions identified for drug should be adopted);
(H) Analysis items, if analysis items are fewer than items included in quality specification for final product, the reason should be explained.

Article 235 Batches studied and analysis frequency should be adequate to obtain sufficient data for trend analysis. Typically, at least one batch for drug of one kind of specification and primary package should be studied annually, except there was no production in that year.

Article 236: In some cases, additional batches should be studied for continued stability study, e.g., a major change or drug with significant deviation of the production and packaging should be included in the stability study. In addition, re-processing, rework or recycling of the batches should also be considered in the study, unless validation and stability study have been done.

Article 237: Key personnel, especially qualified person, should have a good understanding of results of continuing stability study. When continual stability study is not performed in company where bulk products and final products are manufactured, there should be a written agreement among all parties and results of ongoing stability study should be preserved for review by the drug regulatory authority.

Article 238: The results which fail to comply with quality specification or significant abnormal trends should be investigated. Company should consider the impact of any non-conformance results or significant abnormal trends already identified on the quality of marketed drug, and when necessary, should implement recall. Investigation results and corrective actions should be reported to local drug regulatory authority.

Article 239 Summary report should be prepared on basis of all data obtained including stage conclusions and then be recorded. Summary report should be reviewed regularly.

10.4 Change Control

Article 240: Enterprise shall establish a change control system to evaluate and manage all changes that affect product quality. Changes required approval from drug regulatory authority should be implemented with being approved.

Article 241: Operation procedures should be established to specify application, evaluation, review, approval and implementation of change for raw materials and excipients, packaging materials, quality specifications, analysis methods, operating

procedures, facilities, facilities, equipment, instruments, production process and computer software. Quality management department shall designate a person responsible for change control.

Article 242: Potential impact of changes on product quality should be evaluated. Companies can classify changes basing on nature, scope, potential impact on product quality (such as major, minor changes). Validations, additional analysis and stability study for changes should be determined with scientific evidence.

Article 243: Changes related to product quality, after raised by application department, shall be subject to assessment, then implementation plan should be established and implementation responsibilities should be classified, and ultimately changes should be reviewed for approval by quality management department. Changes implementation should be full recorded.

Article 244 When there is a change for raw materials and excipients, packaging materials in direct contact with drug, production process, main production equipment and other factors that affect the drug quality, quality of initial three batches of drug should be evaluated after implementation of change. If the change may affect the validity of medicines, quality assessment should also include stability study of the drugs produced after implementation of change.

Article 245: Relevant change documents should be ensured to be revised during the implementation of change.

Article 246 Quality control department should be responsible for maintaining all of change documents and records.

10.5 Deviation treatment

Article 247 Department head should ensure all people properly implement production process, quality specifications, analysis methods and operation procedures to prevent occurrence of deviation.

Article 248: Enterprise shall establish operation procedures of deviation treatment to specify deviation reports, records, investigation, treatment and corrective action taken. And related record should be done.

Article 249: Potential impact of any deviation on product quality should be evaluated Companies can classify deviations basing on nature, scope, potential impact on product quality (such as major, minor deviations). As for evaluation of major deviations, additional analysis for product and impact on product validity should be considered.

Where necessary, stability study should be performed for products relating to major deviations.

Article 250: Any cases deviated from the production process, material balance limits, quality specifications, analysis methods; operating rules should be recorded and immediately reported to the manager and quality management departments with clear description. Major deviation should be thoroughly investigated by quality management department together with other departments. Deviation investigation report shall be reviewed and signed by person designated by quality management department. Enterprises should also take preventive measures to effectively prevent recurrence of similar deviations.

Article 251: Quality management department should be responsible for classification and preservation of documents and records related to deviations investigation and treatment.

10.6 Corrective and preventive measures

Article 252: Enterprises should establish corrective action and preventive action system to investigate complaints, recalls, deviations, self or external analysis results, process performance and quality monitoring trends and then to take corrective and preventive measures. The depth and method of investigation should be compatible with the level of risk. Corrective and preventive action system should be able to facilitate understanding of product and process and improvement of products and processes.

Article 253: Enterprises should establish operation procedures for implementation of corrective and preventive action, at least including:
(A) Analyze complaints, recalls, deviations, or external and self-analysis results, process performance and quality monitoring trends and quality data from other sources to determine existing and potential quality problems. When necessary, appropriate statistical methods should be used;
(B) Investigate causes related to products, processes and quality assurance systems;
(C) Determine necessary corrective and preventive measures taken to prevent recurrence of the issues;
(D) Assess the reasonableness, effectiveness and adequacy of corrective and preventive measures;
(E) Changes occurred in process of implementing corrective and preventive measures should all be recorded;
(F) Ensure that relevant information has been passed to qualified person and person directly responsible for prevention of reoccurrence of the same issues;
(G) Ensure relevant information and corrective and preventive measures have been reviewed by senior management.

Article 254: Implementation of corrective and preventive measures should be documented and preserved by quality management department.

10.7 Evaluation and approval of suppliers

Article 255: Quality management department should perform quality evaluation on all suppliers of materials used in production and carry out on-site audits on quality system of main materials suppliers (especially manufactures) and exercise the power of veto on non-compliance suppliers.
Main materials should be decided upon quality risk of the drug manufactured, quantity of materials used, level of impact of materials on drug quality and other factors.
Legal representative, the responsible persons and other department personnel shall not disrupt or interfere with independent quality assessment performed by quality management department.

Article 256: Operation procedures to evaluate and approve suppliers should be established to clarify supplier qualification, principle of selection, quality assessment methods, assessment criteria, and procedures to approve material suppliers.
If quality assessment needs to be performed with on-site quality audit approach, audit items, period, composition and qualification of auditors should be clarified. If production of a small trial lot is necessary, production batches, production process, product quality specification, and stability study plan should be clarified.

Article 257: Quality management department shall designate a person responsible for quality assessment of material suppliers, on-site quality audit, and distribution of the approved list of qualified suppliers. The designated staff should be qualified with knowledge of relevant laws regulations and expertise with adequate practical experience in on-site quality audits.

Article 258: When carrying out on-site quality audit, auditors should verify the authenticity of supplier qualification documents and analysis report and verify if suppliers is qualified with analysis capabilities. Personnel organizations, facilities and equipment, materials management, production process flow and production management, equipment, instrument, and document management in quality control laboratory should be checked in order to perform a full assessment on its quality assurance system. On-site quality audit should be reported.

Article 259: When necessary, a small trial lot should be produced by using samples supplied by main materials suppliers and stability study should be conducted on the drug from trial lot.

Article 260: The assessment of materials suppliers carried out by Quality management department should at least include following: proof documents of supplier qualification, quality specifications, analysis reports, analysis data and reports of material samples provided by company. As for on-site quality audit and trial production of small quantities of samples, on-site quality audit reports, small scale product quality analysis report and stability study report should also be included.

Article 261: When material suppliers are changed, quality assessment should be conducted on new suppliers; when main material suppliers are changed, related validation and stability study should be performed on products.

Article 262: Quality management department shall send approved list of qualified suppliers to materials management department, and the list at least includes material name, specifications, quality specifications, manufacturer name and address, dealer (if any) name, etc. and these information should be timely updated.

Article 263: Quality management department should sign quality agreement with major material suppliers in which responsibility assumed by both parties should be clarified.

Article 264: Quality management department should perform periodic evaluation or on-site quality audit on materials suppliers and review and analysis on material quality analysis result, quality complaints and disposal records of rejected materials.
When there are quality issues or there is change for production conditions, process, quality specification, analysis methods, and key factors that may affect the quality, related on-site quality audit should be performed as soon as possible.

Article 265: Enterprises should create quality file for each material supplier which should include proof documents of the supplier qualification, quality agreements, quality specifications, sample analysis data and reports, supplier's analysis report, on-site quality audit reports, product stability study reports, regular quality review and analysis reports, and etc.

10.8 Product quality review and analysis

Article 266: Product quality review and analysis for all drug manufactured should be performed annually in accordance with operation procedures to check process stability, suitability of current quality specification for raw materials, excipients and final products and to timely detect adverse trends to determine improvement method for product and process. Consideration should be given to historical data from past retrospective analysis. Self-analysis should also be performed on effectiveness of quality review and analysis.
When there is a reasonable scientific basis, products can be reviewed and analyzed by classification basing on dosage form, such as solid dosage forms, liquid formulations and sterile preparations.
There should be report for review and analysis;
Enterprises should at least perform review and analysis for following cases:
(A)All changes for raw materials used in products, especially raw materials from a new supplier;
(B) Analysis results of critical in-process control points and final product;
(C) All batches which fail to meet quality specifications and related investigation;
(D) All significant deviations and related investigations, efficiency of corrective

actions preventive measures taken;
(E) All changes related to analysis methods or production processes;
(F) Any changes for drug registration already approved;
(G) Stability study results and any adverse trends;
(H) All returns complaints, recalls and investigations due to quality issues,;
(I) implementation and effects of corrective actions related to product process or equipment
(J) Work done for drugs newly approved and with change after on sale in accordance with the registration requirements;
(K) Qualification status of related equipment and facilities, such as HVAC, water system, compressed air, etc.;
(L) Fulfillment of technical contracts for contractual production or analysis .

Article 267: The results of review analysis should be evaluated to provide advice and reason on necessity of taking corrective and preventive measures or re-qualification or re-validation. Corrective actions should be taken in a timely and effective way.

Article 268 There should be written technical agreement between two parties for contractual drug production to specify responsibilities of each side for product review analysis to ensure quality review is timely performed and meet requirement.

10.9 Complaints and adverse reaction reports

Article 269: Reporting and monitoring system for adverse drug reaction should be established. And specific organization should be set up and managed by designated person.

Article 270 Take initiatives in collecting adverse drug reactions. There should be detailed record, evaluation, investigation and treatment, and timely measures to control possible risks for adverse reactions which should be reported to drug regulatory authority in accordance with requirements.

Article271: Operating procedures should be established to specify procedures that should be followed for registration of complaints, evaluation, investigation and handling as well as measures taken for complaints due to possible quality defects, including consideration of whether it is necessary to recall drugs from the market.

Article272 There should be specific and adequate support staff responsible for investigation and handling of quality complaints, and all complaints and investigation information should be notified to qualified person.

Article273: All complaints should be registered and reviewed. There should be detailed description and investigations for complaints related to quality defects.

Article274 Defects are found or suspected to exist for certain batch of drugs, drugs of other batches should be considered for review to identify whether they are affected.

Article275: Complaints investigating and handling should be recorded and identified with investigation information of products for related batches.

Article276 Review analysis of complaint records should be regularly performed in order to identify issues that should be aware of, probably reoccurred, and possibly caused repeated recall from the market to take corresponding measures.

Article277: When there is production failure, drugs deterioration or other significant quality problems occurred in company, appropriate measures should be taken; when necessary, the issues should be reported to local drug regulatory authority.

11. Contractual production and analysis

11.1 Principle

Article 278: In order to ensure quality of contractual products and accuracy and reliability of contractual analysis, entrusting party and the other party must sign written contracts commission to define responsibilities of each party, contractual production and analysis, and other technical issues.

Article 279: All activities of contractual production or analysis, including changes on technical or other aspects to be made, shall meet relevant requirements for drug manufacturing license and registration.

11.2 The Company

Article 280: The Company should check if contractor is capable of fulfillment of contractual work by assessment of contractor and on-site evaluation of conditions, technical level, and quality management and ensure contractor can comply with requirement of this practice.

Article 281 The company should provide contractor with all necessary information to enable them to implement operation in accordance with requirements for drug registration and other law and regulations.
The company should make all kinds of issues related to products or operation fully understood by the contractors, including possible damage to contractor's environment, facility, equipment, personnel, other materials or products caused by contractual product or operation.

Article 282: The Company should monitor whole process of contractual production or analysis.

Article 283 The Company should ensure materials and products meet corresponding quality specifications.

11.3 The Contractor

Article 284: The contractor should be equipped with adequate facilities, equipment, knowledge and experience and personnel to meet requirements for contractual production and analysis.

Article 285: The contractor should ensure materials; intermediates and bulk products provided to the Company meet their intended use.

Article 286: The contractors should not be involved in activities that adversely affect quality of products contracted for production or analysis.

11.4 Contract

Article 287: The contract signed between the Company and the contractor should specify responsibilities of each Party for product production and control in detail. And the technical terms in the contract should be prepared by managerial staff equipped with knowledge of pharmaceutical technology and analysis, and familiar with this practice. All work for contractual production and analysis should comply with related requirements for drug manufacturing license and drug registration and should be agreed by both parties.

Article 288: The procedures which should be followed by qualified person to approve each batch of drug for release should be defined in the contract to ensure each batch of drug is manufactured and analyzed in accordance with requirements for drug registration.

Article 289: Which side responsible for purchasing, analysis, release, production and quality control (including in-process control) and which side responsible for sampling and analysis should be defined.
In the case of contract analysis, whether the contractor performs sampling in facility of the Company or not should be specified in the contract.

Article 290 Contract should specify that the contractor have easy access to refer or analyze production, analysis and shipment records and samples kept by the Company at any time; when there are complaints of suspected quality defects or product recalls, the contractor should have easy access to all records related to evaluation of product quality.

Article 291: It should clearly state in the contract that the Company can perform check or on-site quality audit on the contractor.

Article 292 It should clearly state in the contract that the contractor is obliged to analysis carried out by drug regulatory authority.

12. Chapter12 Product shipment and recall

12.1 Principle

Article 293: Enterprise should establish a product recall system. If necessary, any batch of product with safety hazards can be quickly and effectively recalled from the market.

Article 294: Products returned and recalled due to quality issues should be destroyed as stipulated except the products with evidence the quality of returns is not adversely affected.

12.2 Delivery and transportation

Article 295: Shipment for each batch of products should be recorded. Sales for each batch of products can be traced and all of products distributed can be recalled when necessary. Shipping records shall include: product name, specification, batch number, quantity, consignees and address, contact information, shipping date, transportation and so on.

Article 296：One container can only contain products with at most two batch numbers which should be clearly identified on the outside, and the record for blended packing should be established.

Article 297: Shipping records should be kept at least one year after the expiration date.

12.3 Recall

Article 298: Operational procedures should be established to ensure effectiveness of the recall.

Article 299 Company should designate a person responsible for organizing and coordinating the recall and also be equipped with an adequate number of personnel. Person responsible for product recall should be independent of sales and marketing departments; when the person responsible for recall is not undertaken by qualified person, handling of the recall should be reported timely to qualified person.

Article 300: Recall should be able to start at any time, and quickly implemented.

Article 301: when product should be recalled from the market due to potential safety hazard, it shall immediately be reported to local drug regulatory authority.

Article 302: Person in charge of product recalls should be able to quickly access to the drugs shipment record.

Article 303: The recalled products should be identified and stored separately and properly, waiting final disposal decision.

Article 304: The recall process should be recorded, and concluded with a final report. The number of products shipped, the number recalled and the balance amount shall be stated in the report.

Article 305: The effectiveness of product recall system should be evaluated on a regular basis.

13. Self-check

13.1 Principle

Article 306: The internal self-analysis should be periodically conducted by quality management department to monitor implementation of this practice, evaluate compliance of company with this practice, and then to propose necessary corrective and preventive actions.

13.2 Self-analysis

Article 307: The self-analysis should be regularly performed on organization, personnel, utilities and facilities, equipment, materials and products, validation and verification, document management, production management, quality control and quality assurance, contractual manufacturing and analysis, product shipment and recall and other items as planned.

Article 308: The Company can designate personnel responsible for independent, systematic and comprehensive self-analysis, but external persons or experts can also be assigned for independent quality audit.

Article 309: Self-analysis should be documented. The self-analysis should be concluded with a self-analysis report including at least all cases observed, evaluation of findings and proposed corrective and preventive measures. Self-analysis results should be reported to top management personnel.

14. Supplementary Provisions

Article 310: This practice establishes basic requirements for pharmaceutical production and quality control and special demand for sterile drugs, biological products, blood products or production of drugs. This practice is created in form of Annex by SFDA.

Article 311: Enterprise can meet requirement of this practice by adopting validation as an alternative.

Article 312: Following terms (sorted by pinyin) included in this practice means:

(1) Packaging:
All necessary steps for bulk product to be packaged into a finished product, including

sub-packaging, labeling and so on. However, aseptic filling in the production of sterile products and filling packaging of final sterile products are not regarded as packaging.

(2) Packaging materials:
Packaging materials used for drug packages, including packaging materials and containers and printed packaging materials in direct contract with drug, but does not including packaging materials for delivery use
.

(3) Operation procedure:
Universal documents approved to guide the operation of equipment, maintenance and cleaning, validation, environmental control, sampling and analysis and other activities related to drugs manufacturing, also known as standard operating procedures.

(4) Products
Include intermediate products, bulk and finished products.

(5) The product life cycle:
All stages from initial research and development, listing until the delisting of the products.

(6) Products:
Products with all production steps and final packaging finished.

(7) Rework:
Subjecting a batch of intermediates or part of or all of bulk products that does not conform to quality standards manufactured from one production process to one or more processing steps that are different from the established manufacturing process in order to meet predetermined quality standards..

(8) Bulk products to be packaged:
Products waiting for packaging but all the other manufacturing processes already finished

(9) Quarantine status
The status of raw materials and excipients, intermediates, bulk products, or final products isolated physically or by other effective means pending a decision on their subsequent approval or rejection before allowed for charging in production or distribution on the market.

(10) Released
Refers to series of operations related to internal transfer of materials, intermediate products, bulk products, documentation, production molds in the production process

(11) Reanalysis
Re-analysis date specified by the Company to ensure raw materials, packaging materials meet their intended use after a period of storage

(12) Shipment
Refers to series of operations Company send the products to dealer or user, including order picking and transportation.

(13) Reprocess
Introducing a batch of intermediates or bulk products, part or all of final products that does not conform to standards or specifications from one production process back into the process for reprocessing in order to meet established quality specifications;

(14) Release
Quality evaluation of a batch of Materials or products pending on their decision for subsequent approval for use, distribution into the market or other actions.

(15) Senior Management
The highest level within the enterprise with right in control of enterprises, and with power and duty in mobilization of resources

(16) Process procedures
A or a set of documents prepared for manufacture of a certain number of final products including the production formulation, manufacturing and packaging operations requirements, quantity for raw materials and packaging materials, process parameters and conditions, processing instructions (including in-process control), notes and so on.

(17) Supplier
Refers to provider for materials, equipment, instrument, reagents, and service, such as manufacturers, distributors and so on.

(18) Recovery:
Blending of part or all of one or several batches of products manufactured previously that conform to related quality specifications into other batch.

(19) Computerized system
Integrated system used in reporting or automatic control, including data entry, electronic processing and information output.

(20) Cross-contamination
Cross contamination among different raw materials, excipients and products.

(21) Calibration

Range of activities to compare the measurement, recording, control equipment or system indication (especially the alleged volume) or physical value represented by material measuring with their corresponding reference value under specified conditions

(22) Stage production
Refers to concentration of production of a product in a period of time in the same production areas, thorough cleaning of shared production areas, facilities, equipment, industrial equipment, then change to produce another product

(23) Clean area
Rooms (areas) in which the number of dust particles and microorganisms should be controlled and building structure, equipment and use of which should be able to reduce the introduction, generation and retention of contaminants in this area

(24) Warning limit:
The critical parameters of the system beyond the normal range, but did not achieve the correction limit and need to be alerted and the implementation of corrective measures

(25) Correction limits:
The critical parameters of the system beyond the acceptable standard, need investigation and implementation of corrective measures

(26) The analysis results out of specification:
All situations when analysis results exceed the statutory standard and standard established by the enterprise

(27) Batch (or Lot)
A specific quantity of raw material and excipients, packaging materials and final products produced in a process or series of processes so that it is expected to be homogeneous within specified limits. In order to complete some production operations, one batch need to be divided to several sub-batches which will be finally blended into one homogeneous batch. In the case of continuous production, a batch may correspond to a defined fraction of the production. The batch size can be defined either by a fixed quantity or by the amount produced in a fixed time interval.
For example: homogeneous products of oral or topical solid, semi-solid preparations produced with the same mixing equipment from one mixingop used before the production of a mixed group of; oral or topical liquid preparation to filling (closed) by a final mix before The liquid produced by a group of homogeneous products.

(28) Lot number
A unique combination of numbers, letters, and/or symbols that identifies a batch (or lot)

(29) Batch record:
All of documents and records used to record production, quality analysis and release review for each batch of product and from which all relevant historical information related quality of final products can be traced.

(30) Air lock room:
separation room with two or more than two doors set between two or among several rooms (such as among rooms with different levels of cleanliness). The air lock room aims at controlling air flow during people or materials moving in and out. Air lock rooms are classified into personnel and materials air lock rooms.

(31) Enterprise
Refers to pharmaceutical companies unless otherwise specified in this practice.

(32) Qualification
A series of activities to demonstrate utilities, facilities, equipment run properly and can achieve desired results.

(33) Return
Activities of returning drugs to enterprise

(34) Documentation
Documents referred to in this specification includes quality standards, process procedures, operating procedures, records and reports, etc.

(35) Materials
Refers to the raw materials, excipients and packaging materials
For example: raw materials in chemical preparation refers to API; raw material in biological products refer to raw ingredient; raw materials in traditional Chinese medicine preparation refer to herbs, Chinese Herbal Medicine and herbal extracts purchased; raw material for API refers to other materials used in manufacturing of API except packing materials

(36) Material balance
Comparison of actual output or consumption and sum of consumption collected to theoretical yield or consumption, considering scope of deviation allowed.

(37) Contamination
Adverse impact of undesired introduction of impurities of a chemical or microbiological nature, or of foreign matter, into or onto a raw material, intermediate, or bulk products, final products during production, sampling, packaging or repackaging, storage or transport and other operations.

(38) Validation

A series of activities that demonstrate any operation procedure (or method), production process or system can achieve expected results.

(39) Printed packaging materials
Refers to packaging materials of specific style and texts, such as printed foil, labels, brochures, boxes and so on.

(40) Raw materials and excipients:
Any material used in drug manufacture except packaging materials

(41) Intermediate products:
Products with part of the processing steps finished but still requiring further processing to become bulk products to be packaged.

(42) In-process control
Also refers to process control, checks performed during production in order to monitor and, if appropriate, to adjust the process and/or to ensure that products conforms to its specifications. Monitoring of environment or equipment can be regarded as part of in-process control

Article 313: This practice shall come into force from March 1, 2011. The specific measures and implementation procedures should be specified in accordance with Article IX in "Drug Administration Law of the People's Republic".