Order of the China Food and Drug Administration

The Administrative Measures for the Registration of In-vitro Diagnosis Reagents, as deliberated and adopted at the executive meeting of the China Food and Drug Administration (CFDA) on June 27, 2014, are hereby issued, and come into force on October 1, 2014.

Director: Zhang Yong

July 30, 2014

Administrative Measures for the Registration of In-vitro Diagnosis Reagents

Chapter 1 General Provisions

Article 1 The Measures are formulated in accordance with the *Regulations on Supervision and Administration of Medical Devices* in order to regulate the registration and filing administration of in-vitro diagnosis reagents, and ensure the safety and effectiveness of in-vitro diagnosis reagents.

Article 2 Where any in-vitro diagnosis reagent is sold or used within the territory of the People's Republic of China, registration shall be applied for or filing shall be handled in accordance with the provisions of the Measures.

Article 3 The in-vitro diagnosis reagents mentioned in the Measures refer to the in-vitro diagnosis reagents administered as medical devices, including the reagents, reagent kits, calibrators, quality controls, etc. for in-vitro inspection of human body specimens in the course of disease prediction, prevention, diagnosis, treatment monitoring, prognosis observation and health status evaluation, which can be used independently or in combination with instruments, devices, equipment or systems.

In-vitro diagnosis reagents administrated as drugs and used in blood screening and radionuclide-labeled in-vitro diagnosis reagents do not fall into the administration scope of the Measures.

Article 4 Registration of in-vitro diagnosis reagents refers to the process in which the food and drug supervision and management departments implement a systematic evaluation on the studies conducted on the safety and effectiveness of the in-vitro diagnosis reagents to be launched to the market by the registration applicant and the results, and determine whether to approve such application, in accordance with legal procedures and the application of the registration applicant.

Filing of in-vitro diagnosis reagents refers to the process in which the filing applicant submits relevant data to the food and drug supervision and management departments, and the food and drug supervision and management departments keep such filing data submitted on file for reference.

Article 5 The registration and filing of in-vitro diagnosis reagents shall comply with the principles of openness, fairness and impartiality.

Article 6 Class I in-vitro diagnosis reagent shall be subject to administration by filing, while Class II and III in-vitro diagnosis reagent shall be subject to administration by registration.

As for the filing of domestic Class I in-vitro diagnosis reagent, the filing applicant shall submit relevant filing data to the food and drug supervision and management department at city level in places where districts are set.

Domestic Class II in-vitro diagnosis reagents shall be examined by provincial (autonomous regional, central-government-directly-administered municipal) food and drug supervision and management departments, and medical device registration certificates shall be issued after approval.

Domestic Class III in-vitro diagnosis reagents shall be examined by the China Food and Drug Administration, and medical device registration certificates shall be issued after approval.

As for the filing of imported Class I, the filing applicant shall submit relevant filing data to the China Food and Drug Administration.

Imported Class III in-vitro diagnosis reagents shall be examined by the China Food and Drug Administration, and medical device registration certificates shall be issued after approval.

The registration and filing of in-vitro diagnosis reagents manufactured in Taiwan, Hong Kong or Macao shall be carried out with reference to the relevant provisions for imported in-vitro diagnosis reagents.

Article 7 Where in-vitro diagnosis reagent applicants or filing applicants launch the product onto the market in their own name, they shall be legally liable thereto.

Article 8 Food and drug supervision and management departments shall promptly announce the information related to registration and filing of in-vitro diagnosis reagents according to the laws. The applicant may have access to approval progress and results, and the approval results may be made available to the public.

Article 9 The State encourages research and innovation of in-vitro diagnosis reagents, and implements special approval for innovative in-vitro diagnosis reagents in order to facilitate the promotion and application of new technology of in-vitro diagnosis reagents, and to promote the development of the medical device industry.

Chapter 2 Basic Requirements

Article 10 In-vitro diagnosis reagent registration applicant and filing applicant shall establish a quality management system related to product development and production, and maintain efficient operation thereof.

To apply for registration of a domestic in-vitro diagnosis reagent approved in accordance with the special approval procedures for innovative medical devices, if the sample is produced by other enterprise upon entrustment, the applicant shall entrust a medical device manufacturer with the corresponding scope of production; to apply for registration of a domestic in-vitro diagnosis reagent which is not approved in

accordance with the special approval procedures for innovative medical devices, the sample shall not be produced by any other enterprise by entrustment.

Article 11 The personnel responsible for registration or filing of in-vitro diagnosis reagents shall have the corresponding professional knowledge, and should be familiar with laws, regulations, rules and technical requirements related to the administration of medical device registration or filing.

Article 12 The product development of in-vitro diagnosis reagents includes selection & preparation of main raw materials, determination of product production technology, formulation of product technical requirements, product stability study, determination of positive cut-off value or reference range, as well as product analysis performance evaluation, clinical evaluation and other related work.

The applicant or filing applicant may refer to relevant technical guidelines for product development, and may also adopt different experimental methods or technical means, but shall explain the reasonableness thereof.

Article 13 When applying for registration or handling filing formalities, the applicant or filing applicant shall comply with the requirements on safety and effectiveness of in-vitro diagnosis reagents, and guarantee standardized process of development, as well as authenticity, integrity and traceability of data.

Article 14 The data submitted for application for registration or filing shall be made in Chinese. In case of any translation pursuant to foreign language materials, the original text shall be provided together with such translation. Any reference to documentary data not published to the public shall be furnished with supporting documents stating the data owner is licensed.

The applicant or filing applicant is liable to authenticity of the foresaid data.

Article 15 The imported in-vitro diagnosis reagents in application for registration or filing shall have been approved for marketing in the place where the applicant or filing applicant is registered or in the country (region) where the production site is located.

If the product is not administered as a medical device in the place where the applicant or filing applicant is registered or in the country (region) where the production site is located, the applicant or filing applicant is required to provide relevant supporting documents, including supporting documents proving that the place of registration or the country (region) where production site is located allows the foresaid marketing of such product.

Article 16 Overseas applicant or filing applicant shall establish its representative office within the territory of China or designate an enterprise within the territory of China as its agent to coordinate with such overseas applicant or filing applicant to carry out relevant work.

The agent shall assume the following responsibilities in addition to registration or filing of in-vitro diagnosis reagents:

(I) Keep contact with corresponding food and drug supervision and management departments, overseas applicant or filing applicant;

(II) Deliver relevant regulations and technical requirements to the applicant or filing applicant faithfully and accurately;

(III) Collect the information on adverse events of in-vitro diagnosis reagents after marketing and give feedbacks to the overseas applicant or filing applicant, and report to corresponding food and drug supervision and management departments;

(IV) Coordinate product recall work of in-vitro diagnosis reagents after marketing, and report to corresponding food and drug supervision and management departments;

(V) Assume other joint and several liabilities otherwise involved in product quality and after-sales services.

Chapter 3 Product Classification and Naming

Article 17 In-vitro diagnosis reagents are classified into Class I, II and III products with to product risk classification ranging from low to high.

(I) Class I products

1. Microbial media (not applicable to microorganism identification and drug sensitivity test);

2. Products for sample processing, e.g. hemolytic agent, diluents, staining solution, etc.

(II) Class II products,

Unless defined expressly as Class I and III, others are all Class II products, mainly including:

1. Reagent used for protein detection;

2. Reagent used for hydrocarbon detection;

3. Reagent used for hormone detection;

4. Reagent used for enzyme detection;

5. Reagent used for ester detection;

6. Reagent used for vitamin detection;

7. Reagent used for inorganic ion detection;

8. Reagent used for detection of drugs and drug metabolites;

9. Reagent used for autoantibody detection;

10. Reagent used for microorganism identification and drug sensitivity test;

11. Reagent used for detection of other physiological, biochemical or immune function indicators;

(III) Class III products

1. Reagent related to pathogenic pathogen antigen, antibody, nucleic acid and otherwise detection;

2. Reagent related to blood type, tissue matching;

3. Reagent related to human gene detection;

4. Reagent related to hereditary diseases;

5. Reagent related to detection of narcotics, psychotropic drugs, and toxic drugs for medical use;

6. Reagent related to detection of therapeutic drug target;

7. Reagent related to detection of tumor marker;

8. Reagent related to allergy (allergen).

Article 18 If Class II products listed in Article 17 are used for tumor diagnosis, adjunctive diagnosis and therapeutic process monitoring, or used for hereditary disease diagnosis, adjunctive diagnosis, etc., they shall be registered and administered as Class III products. When a reagent is used for detection of drugs and drug metabolites, if the drugs fall into the scope of narcotics, psychotropic drugs or toxic drugs for medical use, the reagent shall be registered and administered as a Class III product.

Article 19 Calibrators and quality controls may apply for registration in combination with the matching in-vitro diagnosis reagents or separately.

Calibrators and quality controls used in conjunction with Class I in-vitro diagnosis reagents shall be registered as Class II products; when calibrators and quality controls used in conjunction with Class II and III in-vitro diagnosis reagents apply for registration separately, they shall be registered according to the same class as the reagents; for calibrators and quality controls, they shall be registered by the higher class therein.

Article 20 The CFDA is responsible for preparation and adjustment of the product classification catalogue of in-vitro diagnosis reagents.

As for in-vitro diagnosis reagents newly developed which has not been listed in the classification catalogue of in-vitro diagnosis reagents, the applicant may directly apply for registration of Class III in-vitro diagnosis reagents, or may judge product class pursuant to classification rules, apply for classification confirmation to the CFDA, and then apply for product registration or handle product filing.

In case of direct application for registration of Class III in-vitro diagnosis reagents, the CFDA will determine the classification according to risk degrees. Where a domestic in-vitro diagnosis reagent is determined as Class II, the CFDA will transfer the application data to the provincial (autonomous regional, central-government-directly-administered municipal) food and drug supervision and management department in the place where the applicant is located for evaluation and approval; where a domestic in-vitro diagnosis reagent is determined as Class I, the CFDA will transfer the application data to the food and drug supervision and management departments for filing at city level in places where districts are set and the applicant is located.

Article 21 The naming of in-vitro diagnosis reagents shall comply with the following principles:

The product name of in-vitro diagnosis reagents shall generally be composed of three parts: the first part is the name of substance tested; the second part is the purpose, e.g.

serum diagnosis, determination of reagent kit, quality controls, etc.; the third part is the method or principle, e.g. ELISA, colloidal gold method, etc., which shall be listed in the brackets.

If the substance tested has many components or other special circumstance, the indication name related to the product or other substituted name may be adopted.

Class I in-vitro diagnosis products, calibrators and quality controls may be named according to their intended uses.

Chapter 4 Product Technical Requirements and Registration Testing

Article 22 On the premise of stable raw material quality and production technology, the applicant or filing applicant shall propose product technical requirements according to product development, clinical evaluation and other results in accordance with national standards, industry standards and relevant literature.

Product technical requirements mainly include performance indicators and test methods of finished product of in-vitro diagnosis reagents, in which performance indicators refer to functionality and safety indicators objectively judged for finished product, as well as other indicators related to quality control.

The product technical requirements of Class III in-vitro diagnosis reagents shall define main raw materials, production technology and semi-finished product requirements in form of appendices.

The product technical requirements of Class I in-vitro diagnosis reagents shall be submitted by the filing applicant to the food and drug supervision and management departments when handling filing, and those of Class II and III in-vitro diagnosis reagents will be verified and approved by the food and drug supervision and management departments when approving registration.

In-vitro diagnosis reagents marketed in China shall comply with the product technical requirements that have been registered and verified or filed.

Article 23 As for application for registration of Class II and III in-vitro diagnosis reagents, registration testing shall be conducted; for Class III products, registration testing on samples from 3 consecutive production batches shall be conducted. Medical device testing institutions shall test relevant products in accordance with the product technical requirements.

The production of samples for registration testing shall comply with the relevant requirements of the medical device quality management system, and only when the samples prove qualified in registration testing can clinical trial be implemented or registration be applied for.

To handle filing of Class I in-vitro diagnosis reagents, the filing applicant may submit reports on product self-inspection.

Article 24 To apply for registration testing, the applicant shall provide the testing institutions with all relevant technical data required for registration testing, samples for registration testing, product technical requirements and standards or references.

The samples for registration testing of domestic applicants shall be sampled by the food and drug supervision and management departments.

Article 25 For products with national standards and references available, the national standards and references shall be used for registration testing. The National Institutes for Food and Drug Control is responsible for organizing the preparation and calibration of national standards and references.

Article 26 Medical device testing institutions shall be qualified for medical device testing, conduct testing within their scope of business, and pre-evaluate the product technical requirements submitted by the applicant. The pre-evaluation opinions shall be issued to the applicant together with the registration testing reports.

The testing of products that have not been included in the scope of business of medical device testing institutions shall be conducted by capable testing institutions designated by the departments approving the registration of such products.

Article 27 If the same registration application includes different packaging specifications, it is allowed to conduct registration testing only on one packaging specification of the product.

Chapter 5 Clinical Evaluation

Article 28 Clinical evaluation of in-vitro diagnosis reagents refers to the process in which the applicant or filing applicant confirms whether the product meets the operating requirements or intended uses based on clinical literature data, clinical empirical data, clinical trials and other information.

Article 29 Clinical evaluation data refers to the documents formed in the clinical evaluation conducted by the applicant or filing applicant.

Clinical trial on in-vitro diagnosis reagents (including trials for comparative study with marketed products) refers to systematic study of the clinical performance of in-vitro diagnosis reagents in the corresponding clinical environment.

For in-vitro diagnosis reagents not requiring clinical trials, the applicant or filing applicant shall evaluate the clinical performance of the in-vitro diagnosis reagents through evaluation of clinical samples covering the intended uses and interference factors, summarization of literature data and other non-clinical test methods. The applicant or filing applicant shall ensure that the clinical samples used in evaluation are traceable.

Article 30 Clinical trials are not required for handling the filing of Class I in-vitro diagnosis reagents. To apply for registration of Class II and III in-vitro diagnosis reagents, clinical trials shall be conducted.

Under any of the following circumstances, in-vitro diagnosis reagents may be exempted from clinical trials:

(I) They have clear and definite working mechanisms, finalized designs and mature production technology, the marketed in-vitro diagnosis reagents of the same category have been put into clinical application for years with no record of serious adverse event, their general purposes remain unchanged, and the applicant can provide evaluation data proving equivalency with marketed products.

(II) The safety and effectiveness of such in-vitro diagnosis reagents can be proved through evaluation of clinical samples covering the intended uses and interference factors.

The catalogue of in-vitro diagnosis reagents exempted from clinical trials shall be established, adjusted and published by the CFDA.

Article 31 If the same registration application includes different packaging specifications, it is allowed to conduct clinical evaluation only on one packaging specification of the product.

Article 32 The applicant of Class III products shall select no less than 3 (including 3) clinical trial institutions and the applicant of Class II products shall select no less than 2 (including 2) clinical trial institutions, which have obtained the qualification to carry out clinical trials according to relevant provisions. The production of samples for clinical trials shall comply with the relevant requirements of the medical device quality management system.

Article 33 The applicant shall sign clinical trial contracts with the clinical trial institution, develop and improve the clinical trial protocol by referring to relevant technical guidelines, provide samples for clinical trials for free and bear clinical trial costs.

Article 34 The number of cases for a clinical trial shall be determined based on the purpose and statistical requirements of the clinical trial by referring to relevant technical guidelines. Technical guidelines for clinical trials will be issued separately.

For in-vitro diagnosis reagents used for rare diseases or urgently needed to cope with sudden public health incidents, where reduction of the case number of clinical trials or exemption of clinical trials are necessary, the applicant shall propose the application for reduction or exemption of clinical trials when submitting the registration application data, and explain the reason in detail. The technical review institutions of food and drug supervision and management departments shall make a decision after comprehensive technical review of the registration application data, and notify the applicant in the way of data supplementation and correction if clinical trials need to be supplemented.

Article 35 Overseas clinical evaluation data shall be provided in order to apply for registration of imported in-vitro diagnosis reagents. The applicant shall, according to the requirements of clinical evaluation, consider the epidemiological background, characteristics of different diseases, applicable positive judgment values or reference ranges for different groups and other factors in different countries or regions, and conduct well-targeted clinical evaluation in China.

Article 36 After completing clinical trials, clinical trial institutions shall issue clinical trial reports respectively. The applicant or leading organization of the clinical trial shall summarize the clinical trial results according to relevant technical guidelines, and complete a summary report on the clinical trial.

Article 37 For clinical trials on in-vitro diagnosis reagents for self-use by consumers themselves, evaluation of consumers without medical background on their cognitive ability of the product's instructions shall be included.

Article 38 If the clinical trial institution is found to have violated relevant provisions or failed to execute clinical trial protocols, the applicant shall urge them to correct; if the circumstances are serious, the applicant can require the institution to suspend or terminate clinical trials, and report the offense to the provincial (autonomous regional, central-government-directly-administered municipal) food and drug supervision and

management departments in the place where the clinical trial institutions are located and report to the CFDA.

Article 39 Institutions and personnel participating in clinical trials shall report to the provincial (autonomous regional, central-government-directly-administered municipal) food and drug supervision and management department in the place where the applicant is located and the CFDA if the applicant violates relevant provisions or demands to change trial data and conclusions.

Article 40 Clinical trials conducted on in-vitro diagnosis reagents shall be filed with the provincial (autonomous regional, central-government-directly-administered municipal) food and drug supervision and management department in the place where the applicant is located. The food and drug supervision and management departments accepting such filing shall report the filing conditions to the supervision and management departments of food and drug and competent health and family planning departments at the same level in the place where the clinical trial institutions are located.

The CFDA and provincial (autonomous regional, central-government-directly-administered municipal) food and drug supervision and management departments shall supervise and inspect the implementation status of clinical trials as needed.

Chapter 6 Product Registration

Article 41 To apply for registration of in-vitro diagnosis reagents, the applicant shall submit application data to the food and drug supervision and management departments according to relevant requirements.

Article 42 The food and drug supervision and management departments shall conduct formal examination after receiving the application, and handle cases respectively according to the following circumstances:

(1) Accept the application which falls into the function scope of the department, and the application data are complete and comply with the requirements for formal examination;

(2) Allow the applicant to make corrections on the spot if the application data have mistakes that can be corrected on the spot;

(3) Inform the applicant only once of all contents to be supplemented and corrected within 5 working days after receipt if the application data are incomplete or fail to comply with the requirements for formal examination; no informing within the time limit will be deemed as acceptance since the day when the application data are received;

(4) Tell the applicant that the application is not accepted if the application is beyond the function scope of the department.

To accept or not to accept the application for registration of in-vitro diagnosis reagents, the food and drug supervision and management department shall issue an acceptance or non-acceptance notice affixed with the department's special seal and specifying the date.

Article 43 The food and drug supervision and management department accepting the registration application shall transfer the application data to the technical review institution within 3 working days since the date of acceptance.

The technical review institution shall complete technical review of registration of Class II in-vitro diagnosis reagents within 60 working days and Class III in-vitro diagnosis reagents within 90 working days.

Where external experts need to be employed for review and the time required is not calculated within, the technical review institution shall inform the applicant of the time required in writing.

Article 44 When organizing product technical review, food and drug supervision and management departments may access the original study data, and organize quality management system inspection of the applicant related to product development and production.

Quality management system inspection for the registration of domestic Class II and III medical devices shall be carried out by provincial (autonomous regional, central-government-directly-administered municipal) food and drug supervision and management departments, wherein the technical review institution of the CFDA shall inform the food and drug supervision and management departments in the corresponding provinces, autonomous regions and municipalities directly under the central government to carry out quality management system inspection for the registration of domestic Class III medical devices, and participate in such inspection if necessary. Provincial (autonomous regional, central-government-directly-administered municipal) food and drug supervision and management departments shall complete system inspection according to relevant requirements within 30 working days.

When carrying out technical review of imported Class II and III in-vitro diagnosis reagents, if it considers it necessary to carry out quality management system inspection, the technical review institution of the CFDA shall notify the technical institution for quality management system inspection of the CFDA to carry out inspections according to relevant requirements, and the technical review institution shall participate in such inspections if necessary.

The time of quality management system inspection is not included within the time limit for the review.

Article 45 Where the applicant is required to supplement and correct data during the process of technical review, the technical review institution shall inform the applicant only once of all contents to be supplemented and corrected. The applicant shall provide supplementary data according to the requirements of the supplementation and correction notice within 1 year; the technical review institution shall complete technical review within 60 working days since the day when it receives the supplementary data. The time for the applicant to supplement data is not included within the time limit for the review.

If the applicant holds objection to the contents of the supplementation and correction notice, it may propose written opinions to the corresponding technical review institution, explain the reason, and provide the corresponding technical supportive data.

If the applicant fails to submit the supplementary data within the time limit, the technical review institution will terminate technical review and propose not to approve registration, and the food and drug supervision and management department will decide not to approve registration after verification and approval.

Article 46 The food and drug supervision and management department accepting registration applications shall make decisions within 20 working days after the completion of technical review. Products in line with the safety and effectiveness requirements will be approved for registration, medical device registration certificates shall be issued within 10 working days since the day when the review decision is made, and verified and approved technical requirements and instructions of the product will be issued to the applicant in the form of appendices. If registration is not approved, the food and drug supervision and management department shall explain the reason in writing, and inform the applicant that it enjoys the right to apply for re-review or to apply for administrative reconsideration or file administrative lawsuits.

The medical device registration certificate remains effective for 5 years.

Article 47 Issues concerning the registration of in-vitro diagnosis reagents include permission issues and registration issues. Permission issues include product name, packaging specifications, main ingredients, intended use, product technical requirements, product instructions, product's shelf life, production address of imported in-vitro diagnosis reagents, etc.; registration issues include the name and domicile of the registrant and the registrant's agent, production address of domestic in-vitro diagnosis reagents, etc..

Article 48 For in-vitro diagnosis reagents used for rare diseases or urgently needed to cope with sudden public health incidents, food and drug supervision and management departments may, when approving the registration of such in-vitro diagnosis reagents, require the applicant to further complete relevant work after product marketing, and specify such requirements in the medical device registration certificates.

Article 49 For registration applications that have been accepted, under any of the following circumstances, food and drug supervision and management departments will decide not to approve the registration, and will inform the applicant:

(I) Studies conducted by the applicant on the safety and effectiveness of the in-vitro diagnosis reagent to be marketed and their results cannot prove that the product is safe and effective;

(II) The registration application data are false;

(III) The contents of registration application data are messy and contradictory;

(IV) The contents of registration application data are obviously inconsistent with the application project;

(V) Other circumstances where registration shall not be approved.

Article 50 For a registration application that has been accepted, the applicant may apply to withdraw the registration application and relevant data to the food and drug supervision and management department accepting such application, and explain the reason.

Article 51 For a registration application that has been accepted, if there is evidence suggesting that the registration application data may be false, the food and drug supervision and management department may suspend the review, and decide to continue the review or not to approve registration after verification based on the verification conclusion.

Article 52 If the applicant holds objection to the decision not to approve registration made by the food and drug supervision and management department, it may propose a re-review application to the food and drug supervision and management department that has made such review decision within 20 working days since the day when it receives the notice of not approving registration. The contents of such re-review application are only limited to the original application issues and the original application data.

The food and drug supervision and management department shall make re-review decision within 30 working days since it accepts the re-review application, and inform the applicant in writing. Where the original decision is kept unchanged, the food and drug supervision and management department will no longer accept any re-review application proposed by the applicant again.

Article 53 If the applicant holds objection to the decision not to approve registration made made by the food and drug supervision and management department and has applied for administrative reconsideration or filed an administrative lawsuit, the food and drug supervision and management department will not accept its re-review application.

Article 54 If the medical device registration certification is lost, the applicant shall immediately publish a loss statement on the media designated by the original issuing authority. One month after the publishing of the loss statement, the applicant may apply to the original issuing authority for reissue, and the original issuing authority will reissue the certificate within 20 working days.

Article 55 After an in-vitro diagnosis reagent is marketed, its product technical requirements and instructions shall be consistent with the contents verified by food and drug supervision and management departments. The applicant or filing applicant shall track the product's safety and effectiveness after marketing, and propose an application for changes of the product technical requirements and instructions if necessary.

Article 56 Where the application for registration of in-vitro diagnosis reagents directly involves major conflict of interests between the applicant and other people, the food and drug supervision and management departments shall inform the applicant and stakeholders that they enjoy the right to apply for hearing according to laws, regulations and relevant provisions of the CFDA. When reviewing the application for registration of in-vitro diagnosis reagents, the food and drug supervision and management departments shall announce major permission issues deemed as involving public interests to society, and hold hearings.

Article 57 Any patent dispute arising in the process of registration application review and after approval shall be handled in accordance with the provisions of relevant laws and regulations.

Chapter 7 Registration Changes

Article 58 For Class II and III in-vitro diagnosis reagents that have been registered, in the event of changes of their medical device registration certificates and contents specified in the appendices thereto, the registrant shall apply to the original registration department for registration changes, and submit application data according to relevant requirements.

In the event of changes of the name and domicile of the registrant and the registrant's agent, the registrant shall apply to the original registration department for changes of registration issues; in the event of changes of the production address of domestic in-vitro diagnosis reagents, the registrant shall handle changes of the registration issues after the corresponding production license is changed.

In the event of the following changes of the registration certificate and contents specified in the appendices thereto, the applicant shall apply to the original registration department for changes of permission issues:

(I) Change of the suppliers of main materials such as antigen and antibody;

(II) Change of testing conditions, positive judgment values or reference ranges;

(III) Change of the items, indicators and test methods set in the registered product's technical requirements;

(IV) Change of the packaging specifications and applicable machine models'

(V) Change of the product's storage conditions or the product's shelf life;

(VI) Increase of the intended uses, such as increase of clinical indications, increase of the types of specimens for clinical determination;

(VII) Change of the production address of imported in-vitro diagnosis reagents;

(VIII) Other changes that could influence the safety and effectiveness of products.

Article 59 The following circumstances do not fall into change application issues stipulated by this Chapter, and shall be handled as registration applications:

(I) Change of the product's basic reaction principle;

(II) Change of the product's positive judgment value or reference range, and the change being of new clinical diagnosis significance;

(III) Other major changes that could influence the product's performance.

Article 60 If the data for change of registration issues comply with the requirements, food and drug supervision and management departments shall issue medical device registration change documents within 10 working days. If the data for change of registration issues are incomplete or do not comply with the requirements for formal examination, food and drug supervision and management departments shall inform the applicant only once of all contents to be supplemented and corrected.

Article 61 For changes of permission issues, the technical review institution shall focus on reviewing the changed parts and their influences on the product's performance, and evaluate whether the product is safe and effective after the changes.

The food and drug supervision and management department accepting applications for change of permission issues shall organize technical review according to the provisions in Chapter 6 hereof.

Article 62 Medical device registration change documents shall be used in combination with the original medical device registration certificates, and their shelf life shall be the same as such registration certificates. After obtaining registration change documents, the applicant shall independently modify the product's technical requirements, instructions and label according to the change contents.

Article 63 If this Chapter does not stipulate the acceptance and approval procedures for applications for change of permission issues, the relevant provisions in Chapter 6 hereof shall be applicable.

Chapter 8 Extended Registration

Article 64 If registrations need to be extended after the medical device registration certificates expire, the applicant shall apply for extended registration to food and drug supervision and management departments 6 months before the medical device registration certificates expire, and submit application data according to relevant requirements.

Except for circumstances stipulated in Article 65 hereof, food and drug supervision and management departments receiving applications for extended registration shall decide to approve extension before the medical device registration certificates expire. If no decision is made within the time limit, it will be deemed that the extension is approved.

Article 65 Under any of the following circumstances, extended registration will not be approved:

(I) The applicant fails to propose an application for extended registration within the stipulated time limit;

(II) Mandatory standards of in-vitro diagnosis reagents have been modified or there are new national standards and references available, and the in-vitro diagnosis reagents cannot meet the new requirements;

(III) For in-vitro diagnosis reagents used for rare diseases or urgently needed to cope with sudden public health incidents, the department approving registration has proposed requirements at the time of approval for marketing, but the applicant fails to complete the issues specified in the medical device registration certificate within the stipulated time limit.

Article 66 If this Chapter does not stipulate the acceptance and approval procedures for applications of extended registration of in-vitro diagnosis reagents, the relevant provisions in Chapter 6 hereof shall be applicable.

Chapter 9 Product Filing

Article 67 Product filing shall be handled before the production of Class I in-vitro diagnosis reagents.

Article 68 To handle the filing of in-vitro diagnosis reagents, the filing applicant shall submit filing data according to the provisions in Article 9 of the *Regulations on Supervision and Administration of Medical Devices*.

If the filing data comply with the requirements, the food and drug supervision and management departments shall file on the spot; if the filing data are incomplete or do not comply with the stipulated type, the food and drug supervision and management departments shall inform the filing applicant only once of all contents to be supplemented and corrected and file after the filing applicant's supplementation and correction.

For filed in-vitro diagnosis reagents, food and drug supervision and management departments shall produce filing vouchers according to the relevant format required, and publicize the information recorded in the filing information form on their websites.

Article 69 For in-vitro diagnosis reagents that have been filed, in the event of change of the contents recorded in the filing information form or technical requirements of the filed products, the filing applicant shall submit a description of the changes and relevant supporting documents, and shall propose to the original filing department to change the filing information. If the filing data comply with the type requirements, food and drug supervision and management departments shall record the changes in the change information, and archive the filing data.

Article 70 If the administration classes of in-vitro diagnosis reagents already filed are adjusted, the filing applicant shall take the initiative to propose to cancel the original filing to the food and drug supervision and management departments; if the administration class is adjusted to Class II or Class III in-vitro diagnosis reagents, registration shall be applied for according to the provisions of these Measures.

Chapter 10 Supervision and Administration

Article 71 The CFDA is responsible for supervising and administrating the registration and filing of in-vitro diagnosis reagents nationwide, and supervising and guiding the practice of local food and drug supervision and management departments in registration and filing of in-vitro diagnosis reagents.

Article 72 Provincial (autonomous regional, central-government-directly-administered municipal) food and drug supervision and management departments are responsible for supervising and administrating the registration and filing of in-vitro diagnosis reagents in their administrative areas, organizing the implementation of supervision and inspection, and timely reporting relevant situations to the CFDA.

Article 73 Provincial (autonomous regional, central-government-directly-administered municipal) food and drug supervision and management departments shall implement daily supervision and administration of work related to the registration and filing of agents of imported in-vitro diagnosis reagents in accordance with the principle of localized administration.

Article 74 Food and drug supervision and management departments at city level in places where districts are set shall periodically carry out inspections of filing work, and timely submit relevant information to provincial (autonomous regional, central-government-directly-administered municipal) food and drug supervision and management departments.

Article 75 If registered in-vitro diagnosis reagents comply with circumstances for cancellation as stipulated by laws and regulations, or the registration certificate expire but the registrant does to take the initiative to propose cancellation, food and drug

supervision and management departments shall cancel the registration certificate by law and announce to society.

Article 76 For registered in-vitro diagnosis reagents, if their administration class is adjusted from high to low, their medical device registration certificates continue to be effective within the shelf life. If the registration needs to be extended, the applicant shall apply for extended registration or handle filing to food and drug supervision and management departments 6 months before the medical device registration certificates expire by the changed class.

If the administration class of registered in-vitro diagnosis reagents is adjusted from low to high, the applicant shall apply to food and drug supervision and management departments for registration by the changed class according to the provisions in Chapter 6 hereof. The CFDA shall stipulate the time limit for the completion of adjustment in the administration class adjustment notice.

Article 77 If provincial (autonomous regional, central-government-directly-administered municipal) food and drug supervision and management departments implement registration of an in-vitro diagnosis reagent in violation of the provisions in these Measures, the CFDA shall order them to correct within a certain time limit; if they fail to correct within the tine limit, the CFDA may directly announce to cancel its medical device registration certificate.

Article 78 Food and drug supervision and management departments, relevant technical institutions and their staff are obliged to keep the trial data and technical secretes submitted by the applicant or filing applicant confidential.

Chapter 11 Legal Responsibilities

Article 79 Provision of false data or adoption of other deception means to obtain medical device registration certificates will be punished in accordance with the provisions in Paragraph 1 of Article 64 of the *Regulations on Supervision and Administration of Medical Devices*.

Provision of false data for filing will be punished in accordance with the provisions in Paragraph 2 of Article 65 of the *Regulations on Supervision and Administration of Medical Devices*.

Article 80 Forgery, alteration, purchase and sales, lease or lending of medical device registration certificates will be punished in accordance with the provisions in Paragraph 2 of Article 64 of the *Regulations on Supervision and Administration of Medical Devices*.

Article 81 Any breach of the provisions in these Measures and failure to handle filing of Class I in-vitro diagnosis reagent changes or changes of Class II and III in-vitro diagnosis reagent registration issues will be punished in accordance with the circumstances related to the failure of filing in the *Regulations on Supervision and Administration of Medical Devices*.

Article 82 Any breach of the provisions in these Measures and failure to handle changes of in-vitro diagnosis reagent registration permission issues will be punished in accordance with the circumstances related to the failure to obtain medical device registration certificate in the *Regulations on Supervision and Administration of Medical Devices*.

Article 83 If the applicant fails to carry out clinical trials according to the *Regulations on Supervision and Administration of Medical Devices* and the provisions of these Measures, food and drug supervision and management departments above the county level shall order the application to correct and may impose a fine of less than RMB 30,000; if the circumstances are serious, the clinical trial shall be immediately terminated.

Chapter 12 Supplementary Provisions

Article 84 The registration or filing unit of in-vitro diagnosis reagents shall be a single reagent or a single reagent kit, and a registration or filing unit may include different packaging specifications.

Article 85 The format of medical device registration certificates shall be uniformly developed by the CFDA.

The number in the registration certificate is arranged as follows:

×1 Xie Zhu ×2××××3×4××5××××6. Where,

×1 is the abbreviation for the place where the registration approval department is located;

"Guo" for domestic Class III in-vitro diagnosis reagents and imported Class II and III in-vitro diagnosis reagents;

The abbreviations of provinces, autonomous regions or municipalities directly under the central government where the registration approval departments are located for domestic Class II in-vitro diagnosis reagents;

×2 is the type of registration:

The word "Zhun" shall apply to domestic in-vitro diagnosis reagents;

The word "Jin" shall apply to imported in-vitro diagnosis reagents;

The word "Xu" shall apply to in-vitro diagnosis reagents from Taiwan, Hong Kong or Macao;

××××3 is the year in which the registration is approved for the first time;

×4 is the product's administration class;

××5 is the code of product classification;

××××6 is the serial number of registration for the first time.

For extended registration, the figures of ××××3 and ××××6 remain unchanged. If the product's administration class is adjusted, the number shall be rearranged.

Article 86 The number in the filing certificate of Class I in-vitro diagnosis reagents is arranged as follows:

×1 Xie Bei ××××2××××3 No.

Where,

×1 is the abbreviation for the place where the filing department is located;

"Guo" for imported Class I in-vitro diagnosis reagents;

The abbreviations of provinces, autonomous regions or municipalities directly under the central government where the filing department is located plus the abbreviations of city-level administrative regions where districts are set (if there is no city-level administrative region where districts are set, only the abbreviations of provinces, autonomous regions or municipalities directly under the central government) for domestic Class II in-vitro diagnosis reagents;

××××2 is the year of filing;

××××3 is the serial number of filing.

Article 87 Emergency approvals and innovative special approvals of in-vitro diagnosis reagents shall be executed according to the procedures for emergency approvals of medical devices and special approvals of innovative medical devices developed by the CFDA.

Article 88 According to the needs of work, the CFDA may entrust provincial (autonomous regional, central-government-directly-administered municipal) food and drug supervision and management departments or technical institutions or relevant social organizations to assume specific work related to the registration of in-vitro diagnosis reagents.

Article 89 Charges for in-vitro diagnosis reagents and charging standards shall be executed in accordance with the relevant provisions of financial and pricing authorities under the State Council.

Article 90 These Measures shall become effective as of October 1, 2014.