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Good Clinical Practice for Medical Devices

(No. 25 Order of CFDA and NHFPC)

Order of China Food and Drug Administration and National Health and Family Planning Commission of China

No. 25

Adopted at the meeting of CFDA and NHFPC, this practice is hereby promulgated, and shall take effect as of June 1, 2016.

Director Bi Jingquan

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March 1, 2016

Good Clinical Practice for Medical Devices

Chapter 1 General provisions

Article 1 The Practice is formulated in accordance with the Regulations on the Supervision and Administration of Medical Devices in order to further strengthen the management of clinical trials of medical devices, protect the rights and benefits of trial subjects and assure the clinical trial procedure standard, truthful, scientific, reliable and traceable.

Article 2 All the clinical trials of medical devices within the territory of the People's Republic of China shall be conducted according to the practice. The Practice covers the whole procedure of clinical trial of medical devices, including the protocol design, conduction, monitoring, audit, inspection, collection of data, record, analysis and summary and report of clinical trial, etc.

Article 3 Clinical trial of medical devices mentioned in this Practice refers to the process of confirming and verifying the safety and efficacy of the medical device intended to apply registration under normal condition in qualified clinical trial institutions of medical devices.

Article 4 Clinical trials of medical devices shall comply with the principle of legal, ethic and science.

Article 5 Food and drug regulatory authority above province level are responsible for the supervision and management of clinical trails of medical devices.

The competent department of National Health and Family Planning Commission shall strengthen the management of clinical trails of medical devices within the scope of its duties.

Food and drug regulatory authority and the competent department of NHFPC shall establish the information notification system on quality management of medical device clinical trials and strengthen the information notification on the

approval for conducting clinical trial of Class III medical devices and the medical devices listed in the management catalog of large medical equipment collocation in China and the data of the supervision and management on relevant clinical trial.

Chapter II Preparation before clinical trials

Article 6 There should be sufficient scientific basis and clear trial purpose to conduct clinical trials of medical devices, and the expected benefits and risks to the health of subjects and public shall be weighed, the expected benefits should exceed the possible damage.

Article 7 Before clinical trial, the sponsor shall complete the pre- clinical study of investigational medical devices, including the design of products (structure and composition, working principle and mechanism of action, intended use, application scope and applicable technical requirements) and quality inspection, animal trial and analysis report, etc, and the results shall support the clinical trial. The results of quality inspection include report of self-inspection and the qualified report for registration inspection issued by a qualified inspection agency within one year.

Article 8 Before clinical trial, the sponsor shall prepare adequate investigational medical devices. The development of investigational medical devices shall meet relevant requirements of quality management system of medical devices.

Article 9 Clinical trials of medical devices shall be conducted in two or more than two clinical trial institutions of medical devices. The selected trail institution shall be qualified clinical trial institution of medical devices and the facilities and conditions shall meet the requirements for conducting clinical trials safely and effectively. The investigator should have the professional expertise, qualifications and ability to undertake the clinical trial and should have been trained.

Administrative measures for the qualification recognition of clinical trial institutions of medical devices shall be formulated separately by China Food and Drug Administration and National Health and Family Planning Commission of China.

Article 10 Before clinical trial, the sponsor, clinical trial institution and investigator shall make a written agreement on trial design, quality control of trial, division of responsibilities in the trial, the cost of clinical trials undertaken by the sponsor and the treatment principle of injuries that may occur in the trial.

Article 11 Clinical trials should be approved by ethics committee of clinical trial institutions. Medical devices listed in the directory of Class III medical device clinical trial shall also be approved by CFDA.

Article 12 Before clinical trial, the sponsor should file to local food and drug regulatory authority of the province, the autonomous region or the municipality directly under the Central Government.

The food and drug regulatory authority accepting the filling should report the filing situations to the food and drug regulatory authority and the competent authority of NHFPC in the same level where the clinical trial institution is located.

Chapter III Protection of rights and benefits of trial subjects

Article 13 Clinical trials of medical devices should be conducted in accordance with the ethical principlesin World Medical Association Declaration of Helsinki .

Article 14 Ethical review and informed consent are the main measures to protect the rights and benefits of subjects. Each party involved in the clinical trial shall undertake corresponding ethical responsibilities according to their duties in the trial.

Article 15 The sponsor should avoid to cause undue influence or misleading to subjects, clinical trial institutions and the investigator and other clinical trial participants or related parties.

Clinical trial institution and the investigator should avoid to cause undue influence and misleading to subjects, the sponsor and other clinical trial participants or related parties.

Article 16 The sponsor, clinical trial institution and the investigator shall not exaggerate the compensation measures for participating in clinical trials and mislead the subjects to participate in clinical trials.

Article 17 Before clinical trial, the sponsor shall submit the following documents to ethics committee through the investigator and the management department of medical device clinical trial of clinical trial institution:

(1) Protocol of clinical trial;

(2) Investigator’ s brochure;

(3) Text of informed consent form and any other written documents provided to subjects;

(4) Procedural documents for recruiting subjects and publicity;

(5) Text of case report form;

(6) Self-inspection report and the inspection report for product registration;

(7) Resumes, professional expertise, ability, training of the investigator and other documents to prove qualifications;

(8) Overview of the facilities and conditions of clinical trial institution meeting trial;

(9) Declaration that the development of investigational medical devices meet relevant requirements of applicable quality management system of medical devices;

(10) Other documents related to ethical review.

Ethics committee should uphold the principles of ethics and science, review and supervise the implementation of clinical trials.

Article 18 If one of the following cases occur during the clinical trial, the investigator shall report in time to the management department of medical device clinical trial of clinical trial institution, inform the sponsor and report the ethics committee through the management department:

(1) Serious adverse events;

(2) Report of progress, including summary for safety and report of deviation;

(3) For any revise for the approved documents by ethics committee, the non substantive changes that do not affect the rights and benefits, safety and health of subjects or is not related to the purpose or endpoint of clinical trial don’ t need to be reported in advance, but shall be notified in written form afterwards.

(4) Suspension, termination or requiring for restoring the clinical trial after suspension;

(5) deviation of clinical trial protocol affecting the rights and benefits, safety and health of subjects or the scientific nature.

In order to protect the rights and benefits, safety and health of subjects, the deviation in an emergency that can’ t be reported in time shall be reported as soon as possible in written form afterwards according to relevant provisions.

Article 19 In the process of clinical trial, in the cast that revising the clinical trial protocol, informed consent form and other documents, requiring for deviation and restoring the suspended clinical trial, the trial shall continue to be implemented after being approved by the ethics committee.

Article 20 The minors, pregnant women, old people, persons with mental disability, patients in danger and others shall be avoided to be chosen as subjects; if they are needed to be chosen for some necessary reason, relevant additional requirements provided by the ethics committee shall be complied

with, and the special design shall be conducted for their health conditions in the clinical trial and it shall be helpful to their health.

Article 21 Before the subjects' participating in the clinical trial, the investigator shall explain the details of clinical trial to the subjects, the guardians of persons without or with limited capacity for civil conduct, including recognized, foreseeable risks and possible adverse events, etc.The subjects and guardians shall sign their name and the date on the informed consent form after sufficient and detained explanation, and the investigator shall also need to sign his name and the date.

Article 22 The following contents and explanations of the items shall be included in the informed consent form:

(1) Name of the investigator and relevant information;

(2) Name of clinical trial institution;

(3) Name, purpose, method and contents of the trial;

(4) Process and the term of validity of the trial;

(5) Sources of funding for the trial and possible conflict of interest;

(6) Expected possible benefits for subjects, recognized and foreseeable risks and possible adverse events;

(7) Alternative method of diagnosis and treatment that subjects can obtain and the potential benefits and risks;

(8) Different groups which the subjects will be assigned to in the trial shall be explained, if required;

(9) The subjects shall be voluntary to participate in the trial and have the right to withdraw at any stage of the trial without discrimination or retaliation, and their medical treatment, rights and interests are not affected;

(10) The personnel data that the subjects are informed to participate in the trial is confidential, but the ethics committee, food and drug regulatory authority,

the competent authority of NHFPC or the sponsor can look up the personnel data in the need to work according to the prescribed procedures;

(11) In case of injury related to the trial, the subjects shall receive treatment and economic compensation;

(12) The subjects shall know the information related to them at any time during the trial;

(13) Free items for diagnosis and treatment and other related support that subjects may obtain during the trial.

The language and words that the subjects or guardians can understand should be used for the informed consent form. The informed consent form shall not contain any contents that will cause the subjects to give up their legal rights and interests and will exempt from the responsibilities of clinical trial institutions and the investigator, the sponsor or the agent.

Article 23 The following requirements shall be met to obtain the informed consent:

(1) The disabled subjects can also participate in clinical trial if the ethics committee agree in principle and the investigator considers that participating in the trial can meet the subjects' interests, but the guardian of the subject should sign his name and note the date before the trial;

(2) If both the subject and the guardian have no reading ability, there should be a witness on the spot during the informed process. After being explained the informed consent form in detail and reading it which is the same with the oral informed consent and getting the oral agreement from the subject or guardian, the witness can sign on the informed consent and note the date, the sign of the witness and the investigator should be on the same day.

(3) When a minor is taken as a subject, the informed consent of the guardian shall be obtained and the informed consent form shall be signed. If the minor

can make an intention whether to participate in the trial or not, the consent of his own shall also be asked for.

(4) If important information or unexpected clinical effect related to the investigational medical devices are found, relevant contents of the informed consent form shall be modified, the modified informed consent form should be re-signed for confirmation by subjects or guardians after being approved by the ethics committee.

Article 24 The date of formulation or the date of the revised version shall be indicated in the informed consent form. If the informed consent form is revised during the trial, the revised informed consent form need to be approved by the ethics committee before implementation. After the revised informed consent form is submitted to the clinical trial institution, a new informed consent form shall be signed if the subjects of all the unfinished trial are affected.

Article 25 The subjects have the right to withdraw from any stage of clinical trials and are not liable for any economic responsibility.

Chapter IV Protocol of clinical trials

Article 26 When conducting clinical trials of medical devices, the sponsor should organize to formulate scientific and reasonable clinical trial protocol according to the classification, risks and intended use of investigational medical devices.

Article 27 For the new products that have not approved to market in China or abroad, the safety and performance have not confirmed by medical, the feasibility test of little sample should be carried out first before clinical trial protocol is designed. Then the sample size shall be determined according to statistical requirements and the follow-up clinical trials shall be carried out after the safety is initially confirmed.

Article 28 The clinical trial protocol of medical devices should contain the following contents:

(1) General information;

(2) Background data for clinical trials;

(3) Purpose for clinical trials;

(4) Design of clinical trials;

(5) Evaluation method for safety;

(6) Evaluation method for efficacy;

(7) Consideration for statistics;

(8) Provisions for revising clinical trial protocol;

(9) Provisions for adverse events and report of device defect;

(10) Direct access to source data and documents ;

(11) Ethical issues related to clinical trials and the description and the text of informed consent form;

(12) Data handling and record keeping;

(13) Financing and insurance;

(14) Agreement of trial results publishing.

Part of the above contents can be included in other relevant documentations of the protocol such as investigator’ s brochure. The detailed information of clinical trial institution, agreement of trial results publishing, finance and insurance can be indicated in the trial protocol or can also make another agreement to specified it.

Article 29 The clinical trial in multi- center shall be carried out by a number of investigators in accordance with the same trial protocol in different clinical trial institutions at the same time. The design and implementation of the trial protocol shall at least include the following contents:

(1) The trial protocol shall be organized to formulate by the sponsor and determined by each clinical trial institution and the investigator, and the case

should be cleared that the investigator of lead unit of clinical trial institution is coordinating investigator.

(2) The coordinating investigator is in charge of the work coordination of clinical trial institutions in the process of clinical trial and organizing the meeting of investigators in the early, middle, late stage of clinical trial, and responsible for the implementation of the whole trial with the sponsor;

(3) Each clinical trial institution should carry out and complete clinical trials at the same time in principle;

(4) Sample size of each clinical trial institution and the distribution and the reason for meeting statistics analysis requirements;

(5) The plan of the sponsor and clinical trial institutions on trial training and the requirement for training record;

(6) Establishing the procedure for the transmission, management, audit and query of trial data, and requiring clearly that the trial data of clinical trial institution and relevant documents should be managed and analyzed centrally by lead unit;

(7) After the clinical trials in multi- center are completed, the investigator of each clinical trial institution should provide a brief summary of the clinical trial, after the brief summary and case report form are checked according to the provisions, submit them to the coordinating investigator for summarizing to finish a summary report.

Chapter V　Responsibilities of ethics committee

Article 30 The ethics committee of clinical trial institution of medical devices shall at least be composed of 5 members with different genders, including medical professionals and non medical professionals. There should be at least one legal worker and one personnel not in the clinical trial institution among non medical professionals. The ethics committee should have the qualification

and experiences in science, medicine, and ethics and other aspects of assessing and evaluating the clinical trial. All the committee members should be familiar with ethical codes and relevant provisions for clinical trials of medical devices and comply with the rules of ethics committee.

Article 31 Ethics committee of medical devices should comply with the ethical codes of World Medical Association Declaration of Helsinki and the provisions of food and drug regulatory authority, establish corresponding working procedures and form documents, and fulfill the obligations in accordance with the working procedures.

The members independent of the investigator and sponsor in the ethics committee have the right to comment and participate in vote related to the trial.

Article 32 The ethics committee shall inform in advance when holding a meeting, the number of personnel participated in review and vote shall not be less than 5, and any decision shall be made in the case that more than half of the members in ethics committee have approved it.

The investigator shall provide any information related to the trial, but shall not participate in review, vote or comment.

The ethics committee shall invite experts in relevant fields when reviewing some special trials

Article 33 The ethics committee shall strictly review the trial protocol and relevant documentation from the perspective of protecting the rights and interests of subjects, and shall focus on the following contents:

(1) Qualification, experiences of the investigator and whether he has sufficient time to join the clinical trial;

(2) Whether the staffing and equipment conditions of clinical trial institutions meet the requirements of the trial.

(3) Whether the level of risks that the subjects may subjected to is suitable to the expected benefits of clinical trial.

(4) Whether the trial protocol take full account of ethical principles and meet the scientific nature, including whether the research purpose is appropriate, whether the rights and interests of subjects are protected, whether the protection against the risks that other persons may suffer and the methods for subjects inclusion are scientific.

(5) Method for subjects inclusion, whether the information data related to the trial that provided to the subjects or the guardians is complete, whether subjects can understand, the method for obtaining informed consent form is appropriate; The ethics committee should organize the representatives of subjects to test the level that they can understand the data if necessary and assess whether the informed consent form is appropriate, the assessment result shall be recorded in written form and kept for 10 years after the clinical trial is over.

(6) Whether the treatment and insurance measures are adequate if the injury or death related to the clinical trial happen to subjects.

(7) Whether the amendments on trial protocol can be accepted.

(8) Whether the possible hazards to subjects can be analyzed and evaluated regularly during the clinical trials.

(9) Whether the deviation of trial protocol that may affect the rights and interests of subjects, safety and health, or affecting the scientific nature and integrity of the trial can be accepted.

Article 34 A collaborative review process shall be established for the ethical review of clinical trial in multi center by the ethics committee of lead unit to ensure the consistency and timeliness of the review.

The ethics committee of lead unit shall be responsible for reviewing the ethical rationality and scientific nature of trial protocol before the trial is carried out by

each clinical trial institution, the ethics committee of other clinical trial institutions participated in the trial shall adopt meeting review or documentation review to review the feasibility of the trial in this clinical trial institution under the premise of taking the review opinions of the ethics committee of lead unit, including the qualification and experiences of the investigator, equipment and conditions, etc.. The ethics committee of other clinical trial institutions shall not propose amendments on the design of trial protocol any more, but he has the right to disapprove to carry out the trial in his clinical trial.

Article 35 The ethics committee should hold a meeting, review and discuss, issue written opinions, stamp it and attach the list, professional and signature of attendance. The opinions of ethics committee shall be：

(1) Approval;

(2) Approval after necessary modification;

(3) Disapproval;

(4) Suspending and terminating the approved trial.

Article 36 The ethics committee shall oversee and follow-up the trial carried out in this clinical trial institution and shall require to suspend or terminate the clinical trial in written form at any time if finding such cases that the right and interests of subjects can not be protected.

The suspended clinical trial should not be restored until the ethics committee approve it.

Article 37 The ethics committee shall keep all the relevant records for at least 10 years after the completion of clinical trials.

Chapter VI Responsibilities of sponsors

Article 38 The sponsor is in charge of the initiation, application, organization and monitoring of clinical trials and responsible for the authenticity and

reliability of clinical trials. The sponsor is usually a manufacturer of medical devices. If the sponsor is a overseas institution, he shall appoint an agent within the territory of china.

Article 39 The sponsor is responsible for organizing to formulate and modify investigator’ s brochure, clinical trial protocol, informed consent form, case report form, relevant standard operation procedure and other relevant documents, and is responsible for organizing to carry out the training necessary for clinical trials.

Article 40 The sponsor shall choose clinical trial institutions and investigators in qualified clinical trial institutions of medical devices according to the characteristics of investigational medical devices. Before the sponsor signs the clinical trial agreement with clinical trial institution, the newest investigator’ s brochure and other relevant documents shall be provided to the clinical trial institution and investigator to decide whether they can undertake the clinical trial or not.

Article 41 The investigator’ s brochure should contain the following contents:

(1) Basic information of the sponsor and investigator;

(2) Summary of investigational medical devices;

(3) Summary and evaluation supporting the intended use of investigational medical devices and design reason of clinical trial;

(4) Declaration that the manufacturing of investigational medical devices meet the requirements of applicable quality management system of medical devices.

Article 42 The sponsor shall not exaggerate to publicize the mechanism and effect of investigational medical devices when organizing the formulation of clinical trial protocol.

Article 43 In the process of clinical trial, the sponsor shall modify the investigator’ s brochure and relevant documents in time when obtaining the important information that affect the clinical trial, and submit the modified

documents to the ethics committee for approving through the management department of medical device clinical trial in this clinical trial institution.

Article 44 The sponsor shall reach a written agreement with the clinical trial institution and investigator on the following issues:

(1) Clinical trials shall be carried out according to relevant laws and regulations and clinical trial protocol and shall be monitored, audited and inspected;

(2) Complying with data record and report procedure;

(3) Basic documents related to the trial shall be kept for not less than the legal time until the sponsor inform the clinical trial institution and investigator that the documents are not needed any more;

(4) The sponsor is responsible for providing investigational medical devices to clinical trial institutions and investigators after being approved by the ethics committee, and confirming the transportation condition, storage condition, time of storage and the term of validity, etc.

(5) The investigational medical devices shall be qualified and have special identification for easy recognition and with correct coding and label with" for trial", and shall be packed and kept in accordance with the requirements of clinical trial protocol;

(6) The sponsor shall formulate a standard operation procedure related to the quality control of clinical trial for clinical trial institutions and the investigator to comply with, such as the transportation, receiving, storage, distribution, processing and recycling of investigational medical devices.

Article 45 The sponsor is responsible for the safety of investigational medical devices in clinical trials. The sponsor should inform all the clinical trial institutions and investigators immediately and take corresponding actions when he finds the safety of subjects may be affected or the conduction of the trial may change the approval of ethics committee on the continuation of the trial.