Provisions for Clinical Trials of Medical Devices

(SFDA Order No. 5)

The Provisions for Clinical Trials of Medical Devices were passed by the State Food and Drug Administration at the administration affairs meeting on December 22 of 2003, are hereby promulgated and shall go into effect as of April 1,2004.

Zheng Xiaoyu
Commissioner of State Food and Drug Administration
January 17, 2004

Provisions for Clinical Trials of Medical Devices

Chapter I General Provisions

Article 1 The provisions are formulated to strengthen the administration of clinical trials of medical devices and to ensure the rights and benefits of testing subjects protected and assuring the truthfulness and reliability of the trials result is based on the Regulations for the Supervision and Administration of Medical Devices.

Article 2 The implementation of, supervision over, and examination into clinical trials of medical devices shall be conducted in accordance with the provisions.

Article 3 Clinical trial under the provisions refers to the process in which the medical institutions qualified for conducting clinical trial of medical devices (medical institutions, for short hereunder) testing and verifying the safety and effectiveness of the medical device submitted to register in normal condition.

The purpose of clinical trials of medical devices is to evaluate the intended safety and effectiveness of the testing products.

Article 4 Clinical trials of medical devices should be conducted in accordance with the ethical principles contained in World Medical Association Declaration of Helsinki (see Appendix 1), respecting human dignity, striving for maximal benefit for the testing subject, and avoiding harm as best one may.

Article 5 The clinical trials of medical devices are divided into clinical testing and clinical verification.

Clinical testing refers to verifying if such factors as the theoretical principle, basic structure and performance of the concerned medical devices are able to guarantee their operating safety and effectiveness, by means of clinical application.

Clinical verification refers to verifying the testing products and the products already in the market are virtually the same in terms of the basic structure, performance, safety and effectiveness.

Scope of clinical testing: those medical devices that have not yet been available in the market, or whose

safety and effectiveness are subject to verification.

Scope of clinical verification: those medical devices whose identical products of similar kinds have already been launched onto the market, or whose safety and effectiveness need to be further verified.

Article 6 Medical devices entering clinical trials must possess the following conditions:
(1) The concerned product has measured up to the registered product standard or corresponding state or industrial standard undergoing re-examination.
(2) The concerned product is accompanied by a self-examination report.
(3) The concerned product possess qualified testing report from the testing center recognized by SFDA or State National Quality Standard Supervision department.
(4) If the product to be tested is some medical device that is implanted into human body for the first time, it is necessary to present the animal experiment report for the product.
For other products whose safety to human body in the clinical trials has to be verified by means of animal experiment, it is required to render an animal testing report, too.

Chapter II Assurance of Rights and Interests of Human Subjects

Article 7 It is not allowed to levy any charges upon the testing subjects involved in the clinical trials of medical devices.

Article 8 The person responsible for clinical trials of medical devices or his or her authorized proxy must explain the following to the testing subjects or their authorized legal representatives:
(1) The testing subjects participating the clinical trials are voluntary and may withdraw from clinical trials at any stage.
(2) The personal information and data of the testing subjects participating in the clinical trials are confidential. The Ethics committee, the department of (food and) drug administration, and the implementer may look up the personal information and data of the testing subjects, but must not disclose to the outside.
(3) The Clinical trials proposal for Medical Devices, in particular the purpose, process and time duration of the clinical trials; the expected benefits and possible risks that may occur in the testing subjects.
(4) During the course of clinical trials, medical institutions shall have the obligation to provide the testing subjects with information and data in relation to the clinical trials.
(5) Implementer should provide appropriate compensation for the testing subject. The related content of compensation should be described in the clinical trials contract of the medical devices.

Article 9 After sufficient understanding of content of clinical trials, testing subjects may receive “Notice of Informed Consent”. The content of “Notice of Informed Consent” shall include the related content stipulated under Article Eight.
(1) Signature and date of signature of the person responsible for clinical trials of medical devices.
(2) Signature and date of signature of each of the testing subjects or his or her authorized legal representatives.
(3) In case of any unexpected clinical results discovered by medical institutions, “Notice of Informed Consent” should be amended and such amendments shall sign again by the testing subjects or their authorized legal representatives.

Chapter III Clinical Trials Protocol

Article 10 The clinical trials protocol is a document, which includes contents illustrating testing purpose, risks analysis, overall scheme and testing methods and steps. Prior to start of the clinical trials , it is required to formulate a test protocol. Clinical trials must be carried out in accordance with the clinical

Trials protocol.

Article 11 The clinical trials protocol shall stick to a primary principle of protecting the rights and interests, safety and health of the testing subjects to the maximum degree, and must be designed and formulated jointly by the medical institution liable for the clinical trials and the implementer as the stipulated format (see Appendix 2), as well as be submitted to the ethical committee for ratification. Any amendments should be approved by the ethics committee.

Article 12 With regard to those class III medical devices implanted into human body, which is not available yet in the market or those medical device based on the theory of traditional Chinese medicines, the clinical trials protocol shall be filed with the technical evaluation agency of medical Devices.

Article 13 If adverse event occurs from the same category of marketed medical device, or the product whose curative effects remain uncertain, State Food and Drug Administration may set a unified guideline on clinical trials protocol.

To conduct the clinical trials of such medical devices, the implementer, the medical institutions and the clinical trials personnel shall follow the unified guideline.

Article 14 The clinical trials protocol for medical devices shall refer to the characteristics of the concerned products to be tested, determine the number of testing case, time duration of the test and clinical evaluation standard, and to make the test results to be of statistical significance.

The Clinical trials protocol shall verify the general descriptions of such factors as the theoretical principle, basic structure, performance, safety and effectiveness of the testing products.

The clinical trials protocol shall verify the testing products and the products already in the market are virtually the same in terms of the basic structure, performance, safety and effectiveness.

Article 15 The clinical trials protocol shall include the following content:
(1) Title of the clinical trials.
(2) Purpose, background and contents of the clinical trials.
(3) Clinical evaluation standard.
(4) Analysis of risks and benefits of clinical trials.
(5) Name, title, post and the corresponding department of the clinical personnel.
(6) Overall scheme, including success or failure feasibility analysis.
(7) Time duration of clinical trials and reasons for it.
(8) Number of testing cases of each disease category and reasons for it.
(9) Scope of selecting subjects, quantity of subjects and reasons for the selection, and setup control group when necessary.
(10) Specific indication or scope of application for those curative products.
(11) Evaluation method of clinical performance and statistical processing method.
(12) Expected adverse effects and the necessary measures to be taken.
(13) Notice of Informed Consent for testing subjects
(14) Descriptions of duties of the parties.

Article 16 Clinical trials institution and the implementer shall sign a clinical trials protocol that both parties have agreed to, and sign the clinical trials contract.

Article 17 The clinical trials of medical devices shall be conducted in two or more medical institutions.

Chapter IV Implementer of Clinical Trials

Article 18 The implementer shall be responsible for initiating, implementing, organizing, sponsoring and supervising over the clinical trials. The implementer is the unit applying to register the concerned medical device product.

Article 19 Duties of the implementer cover:
(1) To select a medical institution according to regulations
(2) To provide Medical Device Clinical Trials Notice for the medical institution.
(3) To work together with the medical institution to design and formulate the clinical trials protocol and sign the clinical trials protocol and the contract which both parties have agreed to.
(4) To provide the medical institution with the products to be tested for free.
(5) To train the personnel for clinical trials.
(6) To render a guarantee for medical institutions.
(7) In case of occurrence of severe side effects, be sure to report to the department of (food and) drug administration of the concerned province or autonomous region or municipality originally handling the application of the registration and State Food and Drug Administration respectively in time and truthfully, and also notify all the other medical institutions conducting the clinical trials.
(8) Before the implementer discontinues the clinical trials, it is necessary to notify the medical institution, ethic committee and the department of (food and) drug administration of the concerned province or autonomous region or municipality originally handling the application of the registration and State Food and Drug Administration respectively, and explain the reasons.
(9) If the testing products have caused any damage to the testing subjects, the implementer shall compensate in accordance with the contract of clinical trials.

Article 20 The “Medical Device Clinical Trials Notice” shall cover the following contents:
(1) Description of functional principal of testing product, expected indications, functionality and expected aims, description of operational requirement and description of installation requirement.
(2) Technical indicators of the testing products.
(3) Type testing report of testing products issued by testing institutions recognized by the regulatory department of food and drug and the department of quality and technical supervision under the State Council.
(4) Risks that may arise, recommended preventive method and emergency treatment method;
(5) Confidentiality issues that may be involved.

Chapter V Medical Institutions and Personnel of Clinical Trials

Article 21 Medical institutions undertaking the clinical trials of medical devices refer to those institutions liable for clinical trials of drugs recognized by the regulatory department of food and drug and the administrative department of health under the State Council jointly.

Article 22 The personnel of clinical trials for medical devices must have the following qualifications:
(1) To have required the expertise, qualifications and capabilities for undertaking the clinical trials.
(2) To be acquainted with those documents and data in relation to the clinical trials provided by the implementer.

Article 23 The medical institution responsible for clinical trials of medical devices and the clinical personnel shall undertake the following duties:
(1) To be acquainted with related documents rendered by the implementer, and to be familiar with application of the testing product;
(2) To work with the implementer jointly to design and formulate a clinical trials protocol, sign the clinical trials protocol and contract.
(3) To explain to the testing subjects the details of the products to be tested truthfully; before the clinical trials, enough time should be given to the testing subjects to consider whether or not to get involved in the clinical trials.

(4) To faithfully record the side effects and adverse events of the testing products, and analyze the causes; in case of occurrence of any adverse events and severe side effects, be sure to report to the (food and) drug administration of the concerned province or autonomous region or municipality originally handling the application for registration of the medical devices and State Food and Drug Admonition respectively in time and truthfully; in case of occurrence of severe side effects, be sure to report to these authorities within the ensuing 24 hours.
(5) In case of occurrence of any side effects, the clinical personnel shall make clinical judgment in time, adopt measures to protect the rights and interests of the testing subjects; when necessary, the ethic committee shall have the right to discontinue the clinical trials immediately.
(6) When the clinical trials is discontinued, be sure to notify the testing subjects, the implementer, the ethic committee and the (food and) drug administration of the concerned province or autonomous region or municipality originally handling the application for registration of the medical devices and State Food and Drug Admonition respectively of such a discontinuity case, and also explain the reasons.
(7) To present a clinical trials report, and be responsible for the correctness and reliability of the report.
(8) To be liable for keeping the documents rendered by the implementer as confidential.

Article 24 The medical institution responsible for the clinical trials of medical devices shall determine and appoint a medical person in charge of the clinical trials as the person responsible for clinical trials. Such a person responsible for clinical trials must possess a technical title at the physician-in-charge level or above.

Chapter VI Clinical Trials Report

Article 25 After completion of the clinical trials, the medical institution shall present a clinical trials report in the form as specified (see Appendix 3), and pursuant to the requirements under the clinical trials protocol for medical devices. The report shall bear the signature of the testing personnel, the date, and comments made by the management department of the clinical trials institution, plus the date of issuance of such comments and the stamp of the same department.

Article 26 The clinical trials report shall include the following information:
(1) Categories of illnesses subject to test; total number of cases; gender, age and analysis by grouping of patients; establishment of a control group (when necessary);
(2) Clinical trials method;
(3) Statistical method and evaluation method in use;
(4) Clinical evaluation standard;
(5) Clinical trials results;
(6) Clinical trials conclusion;
(7) Adverse event and side effect during the clinical trials and treatment measures
(8) Analysis of clinical trials effects.
(9) Indications, scope of application, contraindications and precautions.
(10) Existing problems and suggestions for improvement.

Article 27 Clinical trials data of medical devices must be kept in good conditions and controlled properly. The medical institution shall keep clinical trials data within the ensuing five years after completion of the test. The implementer shall keep clinical trials data within the ensuing ten years after the products that are produced lastly have been put into use.

Chapter VII Supplementary Provisions

Article 28 The State Food and Drug Administration is responsible for the interpretation of the provisions.

Article 29 The provisions shall go into effect as of April 1, 2004.

Appendixes:

1. World Medical Association Declaration of Helsinki
2. Clinical trials Protocol for Medical Devices
3. Clinical Trials Report for Medical Devices

Appendix1

WORLD MEDICAL ASSOCIATION DECLARATION OF HELSINKI

Ethical Principles for Medical Research Involving Human Subjects

Adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964, and amended by the
29th WMA General Assembly, Tokyo, Japan, October 1975
35th WMA General Assembly, Venice, Italy, October 1983
41st WMA General Assembly, Hong Kong, September 1989
48th WMA General Assembly, Somerset West, Republic of South Africa, October 1996
and the 52nd WMA General Assembly, Edinburgh, Scotland, October 2000

A. Introduction

1. The World Medical Association has developed the Declaration of Helsinki as a statement of ethical principles to provide guidance to physicians and other participants in medical research involving human subjects. Medical research involving human subjects includes research on identifiable human material or identifiable data.
2. It is the duty of the physician to promote and safeguard the health of the people. The physician's knowledge and conscience are dedicated to the fulfillment of this duty.
3. The Declaration of Geneva of the World Medical Association binds the physician with the words, "The health of my patient will be my first consideration," and the International Code of Medical Ethics declares that, "A physician shall act only in the patient's interest when providing medical care which might have the effect of weakening the physical and mental condition of the patient."
4. Medical progress is based on research which ultimately must rest in part on experimentation involving human subjects.
5. In medical research on human subjects, considerations related to the well-being of the human subject should take precedence over the interests of science and society.
6. The primary purpose of medical research involving human subjects is to improve prophylactic, diagnostic and therapeutic procedures and the understanding of the aetiology and pathogenesis of disease. Even the best proven prophylactic, diagnostic, and therapeutic methods must continuously be challenged through research for their effectiveness, efficiency, accessibility and quality.
7. In current medical practice and in medical research, most prophylactic, diagnostic and therapeutic procedures involve risks and burdens.
8. Medical research is subject to ethical standards that promote respect for all human beings and protect their health and rights. Some research populations are vulnerable and need special protection. The particular needs of the economically and medically disadvantaged must be recognized. Special attention is also required for those who cannot give or refuse consent for themselves, for those who may be subject to giving consent under duress, for those who will not benefit personally from the research and for those for whom the research is combined with care.
9. Research Investigators should be aware of the ethical, legal and regulatory requirements for research on human subjects in their own countries as well as applicable international requirements. No national ethical, legal or regulatory requirement should be allowed to reduce or eliminate any of the protections for human subjects set forth in this Declaration.

B. Basic Principles For All Medical Research

10. It is the duty of the physician in medical research to protect the life, health, privacy, and dignity of the human subject.
11. Medical research involving human subjects must conform to generally accepted scientific principles, be based on a thorough knowledge of the scientific literature, other relevant sources of information, and on

adequate laboratory and, where appropriate, animal experimentation.
12. Appropriate caution must be exercised in the conduct of research which may affect the environment, and the welfare of animals used for research must be respected.
13. The design and performance of each experimental procedure involving human subjects should be clearly formulated in an experimental protocol. This protocol should be submitted for consideration, comment, guidance, and where appropriate, approval to a specially appointed ethical review committee, which must be independent of the investigator, the sponsor or any other kind of undue influence. This independent committee should be in conformity with the laws and regulations of the country in which the research experiment is performed. The committee has the right to monitor ongoing trials. The researcher has the obligation to provide monitoring information to the committee, especially any serious adverse events. The researcher should also submit to the committee, for review, information regarding funding, sponsors, institutional affiliations, other potential conflicts of interest and incentives for subjects.
14. The research protocol should always contain a statement of the ethical considerations involved and should indicate that there is compliance with the principles enunciated in this Declaration.
15. Medical research involving human subjects should be conducted only by scientifically qualified persons and under the supervision of a clinically competent medical person. The responsibility for the human subject must always rest with a medically qualified person and never rest on the subject of the research, even though the subject has given consent.
16. Every medical research project involving human subjects should be preceded by careful assessment of predictable risks and burdens in comparison with foreseeable benefits to the subject or to others. This does not preclude the participation of healthy volunteers in medical research. The design of all studies should be publicly available.
17. Physicians should abstain from engaging in research projects involving human subjects unless they are confident that the risks involved have been adequately assessed and can be satisfactorily managed. Physicians should cease any investigation if the risks are found to outweigh the potential benefits or if there is conclusive proof of positive and beneficial results.
18. Medical research involving human subjects should only be conducted if the importance of the objective outweighs the inherent risks and burdens to the subject. This is especially important when the human subjects are healthy volunteers.
19. Medical research is only justified if there is a reasonable likelihood that the populations in which the research is carried out stand to benefit from the results of the research.
20. The subjects must be volunteers and informed participants in the research project.
21. The right of research subjects to safeguard their integrity must always be respected. Every precaution should be taken to respect the privacy of the subject, the confidentiality of the patient's information and to minimize the impact of the study on the subject's physical and mental integrity and on the personality of the subject.
22. In any research on human beings, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail. The subject should be informed of the right to abstain from participation in the study or to withdraw consent to participate at any time without reprisal. After ensuring that the subject has understood the information, the physician should then obtain the subject's freely-given informed consent, preferably in writing. If the consent cannot be obtained in writing, the non-written consent must be formally documented and witnessed.
23. When obtaining informed consent for the research project the physician should be particularly cautious if the subject is in a dependent relationship with the physician or may consent under duress. In that case the informed consent should be obtained by a well-informed physician who is not engaged in the investigation and who is completely independent of this relationship.
24. For a research subject who is legally incompetent, physically or mentally incapable of giving consent or is a legally incompetent minor, the investigator must obtain informed consent from the legally authorized representative in accordance with applicable law. These groups should not be included in research unless the research is necessary to promote the health of the population represented and this research cannot instead be performed on legally competent persons.
25. When a subject deemed legally incompetent, such as a minor child, is able to give assent to decisions about participation in research, the investigator must obtain that assent in addition to the consent of the legally authorized representative.
26. Research on individuals from whom it is not possible to obtain consent, including proxy or advance

consent, should be done only if the physical/mental condition that prevents obtaining informed consent is a necessary characteristic of the research population. The specific reasons for involving research subjects with a condition that renders them unable to give informed consent should be stated in the experimental protocol for consideration and approval of the review committee. The protocol should state that consent to remain in the research should be obtained as soon as possible from the individual or a legally authorized surrogate.
27. Both authors and publishers have ethical obligations. In publication of the results of research, the investigators are obliged to preserve the accuracy of the results. Negative as well as positive results should be published or otherwise publicly available. Sources of funding, institutional affiliations and any possible conflicts of interest should be declared in the publication. Reports of experimentation not in accordance with the principles laid down in this Declaration should not be accepted for publication.
C. Additional Principles For Medical Research Combined With Medical Care
28. The physician may combine medical research with medical care, only to the extent that the research is justified by its potential prophylactic, diagnostic or therapeutic value. When medical research is combined with medical care, additional standards apply to protect the patients who are research subjects.
29. The benefits, risks, burdens and effectiveness of a new method should be tested against those of the best current prophylactic, diagnostic, and therapeutic methods. This does not exclude the use of placebo, or no treatment, in studies where no proven prophylactic, diagnostic or therapeutic method exists. See footnote
30. At the conclusion of the study, every patient entered into the study should be assured of access to the best proven prophylactic, diagnostic and therapeutic methods identified by the study.
31. The physician should fully inform the patient which aspects of the care are related to the research. The refusal of a patient to participate in a study must never interfere with the patient-physician relationship.
32. In the treatment of a patient, where proven prophylactic, diagnostic and therapeutic methods do not exist or have been ineffective, the physician, with informed consent from the patient, must be free to use unproven or new prophylactic, diagnostic and therapeutic measures, if in the physician's judgement it offers hope of saving life, re-establishing health or alleviating suffering. Where possible, these measures should be made the object of research, designed to evaluate their safety and efficacy. In all cases, new information should be recorded and, where appropriate, published. The other relevant guidelines of this Declaration should be followed.

Top

Appendix 2:

Clinical Trials Protocol for Medical Devices

Product name:
Model and specification:
Implementer:
Medical institution undertaking the clinical trial:
Category of the clinical trial:

Person responsible for the clinical trial: (Signature)

_____ (Month) _____ (Date), _____ (Year)

Annotations:
1. Prior to putting medical device products to a clinical trial, it is required to formulate a clinical trials protocol.
2. The clinical trials protocol shall be designed and formulated jointly by the medical institution and the implementer. The implementer and the medical institution shall sign a clinical trials protocol that they have both agreed to, and also enter into a clinical trials contract.
3. With regard to those class III medical devices implanted into human body, which is not available yet in

market or those medical device based on the theory of traditional Chinese medicine, the clinical trials protocol shall be filed with medical devices technical evaluation agency.
4. The medical institution and the implementer shall work together to settle the number of illness case of each category for the clinical trial and the time duration of such a clinical trials, so as to ensure the anticipated test objective to be attained.
5. The clinical trials of medical devices are divided into clinical testing and clinical verification.

-- Background of clinical trial:

-- Functional scheme, characteristics of the product and test scope:

-- Indications or functions of the product:

-- The content of the clinical trials and its objective:

-- Overall design (including success and failure feasibility analysis):

-- Clinical evaluation standard:

-- Time duration of clinical trials and reasons:

-- Number of case of each disease category for clinical trial and reasons:

-- Scope of subject selection (including selection of the control group when necessary), quantity of selection and reasons:

-- Expected side effects and necessary measures to be taken:

-- Evaluation method and statistic processing method of clinical performance:

-- Notice of Informed Consent:

-- Duties undertaken by the parties:

Clinical personnel	Post	Technical Title	Department

Comments of the Ethical Committee:

(Stamp)

_____ (Month) _____ (Date), _____ (Year)

Comments of the medical institution undertaking the clinical trial:

(Stamp)

_____ (Month) _____ (Date), _____ (Year)

Comments of the implementor:

(Stamp)

_____ (Month) _____ (Date), _____ (Year)

Top

Appendix 3:

Clinical Trials Report

Product name:
Model and specification:
Implementer:
Medical institution undertaking the clinical trial:
Category of clinical trial:
Person responsible for the clinical trial: (signature)

_____ (Month) _____ (Date), _____ (Year)

Annotations:

1. The medical institution liable for the clinical trials shall be of responsible attitude to conduct the clinical trials and fill in the present report pursuant to the clinical trials protocol in an impartial and objective manner.

2. This report must bear the signature of the person responsible for the clinical trials, who is experienced and with a technical title at the physician-in-charge level or above in the clinical trials institution.

3. Clinical trials are categorized into two types: clinical testing and clinical verification

-- General clinical data (illness types, total number of illness cases and selection of cases):

-- Clinical trials method (including establishment of a control group when necessary):

-- Statistical method and evaluation method in use:

-- Clinical evaluation standard:

-- Clinical trials results:

-- Adverse event and side effect during the clinical trials and treatment measures:

-- Analysis of clinical trials effects:

-- Clinical trials conclusion:

-- Indications, scope of application, contraindications and precautions

-- Existing problems and suggestion:

Clinical personnel	Post	Technical Title	Department

Comments of the clinical trials management department of the medical institution responsible for clinical trials

(Stamp)

_____ (Month) _____ (Date), _____ (Year)