Machine Translated by Google

appendix

Good Clinical Practice for Drugs

Chapter 1 General Provisions

Article 1 In order to ensure the standardization of the drug clinical trial process, the scientific, authentic and reliable data and results, and to protect the rights and safety of the subjects, in accordance with the Drug Administration Law of the People's Republic of China, the Vaccine Administration Law of the People's Republic of China, and the People's Republic of China Regulations for the Implementation of the Drug Administration Law of the Republic of China, which formulates this specification. This standard applies to drug clinical trials conducted for the purpose of applying for drug registration. Activities related to drug clinical trials shall comply with this specification.

Article 2 The quality management standards for drug clinical trials are the quality standards for the entire process of drug clinical trials, including program design, organization and implementation, monitoring, auditing, recording, analysis, summarization and reporting. Article 3 Drug clinical trials shall comply with the principles of the Declaration of Helsinki of the World Medical Congress and relevant ethical requirements. The rights and safety of subjects are the primary factors to be considered, taking precedence over the benefits to science and society. Ethical review and informed consent are important measures to protect the rights and interests of subjects. Article 4 Clinical trials of drugs shall have sufficient scientific basis. Clinical trials should weigh the expected risks and benefits of subjects and society, and only when the expected benefits outweigh the risks, clinical trials can be implemented or continued.

Article 5 The test plan shall be clear, detailed and operable. The test plan is being

It can only be executed with the consent of the Ethics Committee.

Machine Translated by Google

Article 6 Investigators shall abide by the trial protocol during the clinical trial, and any medical judgment or clinical decision shall be made by clinicians. Researchers participating in the implementation of clinical trials shall have the corresponding education, training and experience to undertake the work of clinical trials.

Article 7 The paper or electronic data of all clinical trials shall be properly recorded, processed and preserved, and can be accurately reported, interpreted and confirmed. The subject's privacy and the confidentiality of relevant information should be protected.

Article 8 The preparation of the experimental drug shall conform to the production quality of the clinical trial drug. requirements for volume management. The use of the test drug should conform to the test protocol.

Article 9 The quality management system of clinical trials shall cover the whole process of clinical trials, focusing on subject protection, reliable test results, and compliance with relevant laws and regulations.

Article 10 The implementation of clinical trials shall comply with the principle of avoiding conflicts of interest.

Chapter 2 Terms and Definitions

Article 11 The meanings of the following terms in this specification are:

(1) Clinical trials refer to trials conducted on humans (patients or healthy subjects) with the purpose of discovering or verifying the clinical medicine, pharmacology and other pharmacodynamic effects, adverse reactions, or adverse reactions of an experimental drug. Systematic trials of absorption, distribution, metabolism and excretion to determine the efficacy and safety of drugs. (2) Compliance of clinical trials, which means that all parties involved in clinical trials comply with the relevant requirements of clinical trials, this specification and relevant laws and regulations. (3) Non-clinical research refers to biomedical research that is not conducted on humans.

Machine Translated by Google

(4) Independent data monitoring committee (data and safety monitoring committee, monitoring committee, data monitoring committee), refers to an independent data monitoring committee established by the sponsor, which regularly monitors the progress and safety data of clinical trials. and important efficacy endpoints, and recommend to the sponsor whether to continue, adjust, or stop the trial. (5) Ethics committee, which refers to a committee composed of people with medical, pharmaceutical and other backgrounds, whose responsibilities are to independently review, agree, follow-up review of the experimental protocol and related documents, and obtain and record the methods and materials used for the informed consent of the subjects. etc., to ensure that the rights and safety of subjects are protected.

(6) Investigator, refers to conducting clinical trials and assessing the quality of clinical trials and subjects. Owner of the test site responsible for equity and safety.

(7) Sponsor, refers to the sponsor responsible for the initiation, management and provision of clinical trials. An individual, organization or institution that examines the funds.

(8) Contract research organization refers to a unit authorized by signing a contract to perform certain duties and tasks of the sponsor or investigator in the clinical trial. (9) Subjects, refer to those who participated in a clinical trial and used as an investigational drug.

Recipients, including patients, healthy subjects.

(10) Vulnerable subjects refer to subjects with insufficient or lost ability to maintain their own will and rights, their willingness to voluntarily participate in clinical trials, and may be unfairly punished by the expected benefits of the trial or by refusing to participate in retaliation. influences. Including: Investigator's students and subordinates, sponsor's employees, military personnel, prisoners, patients with incurable diseases, patients in critical conditions, people in welfare institutions, homeless, minors, and those without the ability to give informed consent people and so on.

(11) Informed consent, which means that the subject is informed that it may influence his decision to participate in clinical trials.

Machine Translated by Google

The process of confirming consent to voluntarily participate in the clinical trial after all aspects of the trial decision. The process should be documented by written, signed and dated informed consent

Bright.

(12) Impartial witnesses refer to individuals who have nothing to do with the clinical trial and are not unjustly affected by the relevant personnel of the clinical trial. When the subjects or their guardians are incapable of reading, they serve as impartial witnesses to read informed consent and other written information, see also

Evidence of informed consent.

(13) Monitoring refers to the actions of supervising the progress of clinical trials, and ensuring that clinical trials are implemented, recorded and reported in accordance with the requirements of the trial protocol, standard operating procedures and relevant laws and regulations.

(14) Monitoring plan, which refers to the document describing the monitoring strategy, methods, responsibilities and requirements. document.

(15) Monitoring report refers to the written report submitted by the monitor to the sponsor after each on-site visit or other clinical trial-related communication according to the sponsor's standard operating procedures.

(16) Audit, which refers to the systematic and independent inspection of clinical trial-related activities and documents to evaluate and determine whether the implementation of clinical trial-related activities, the recording, analysis and reporting of trial data conform to the trial protocol, standard operating procedures and related requirements of laws and regulations. (17) Audit report, which refers to the written evaluation report on the audit results written by the auditor appointed by the sponsor. (18) Inspection, which refers to the conduct of the drug

supervision and administration department to review and inspect the relevant documents, facilities, records and other aspects of the clinical trial.

Machine Translated by Google

The site, the location of the sponsor or contract research organization, and other sites deemed necessary by the drug regulatory authority. (19) Direct access refers to the direct inspection, analysis, verification or duplication of important records and reports for evaluating drug clinical trials. Any party that directly consults shall, in accordance with relevant laws and regulations, take reasonable measures to protect the privacy of subjects and avoid revealing the sponsor's ownership information and other information that needs to be kept confidential. (20) The trial protocol, which refers to the document describing the purpose, design, methodology, statistical considerations and organization of the clinical trial. The trial protocol should usually also include the background and rationale for the clinical trial, which may also be given in other references. The trial protocol includes the protocol and its revisions.

(21) Investigator's Manual, which refers to the investigational drugs related to the conduct of clinical trials Compilation of clinical and non-clinical studies of the product.

(22) Case report form, which refers to the form designed in accordance with the requirements of the trial protocol and submitted to the sponsor Subject-reported paper or electronic file recording subject-related information.

(23) Standard operating procedures, which refer to detailed written requirements formulated to ensure the consistency of a particular operation. (24) Investigational drugs, refer to the experimental drugs, control drugs used in clinical trials
drug.

(25) Control drug, which refers to the reference drug used in clinical trials for comparison with the test drug other investigational drugs, marketed drugs, or placebo.

(26) Adverse events refer to all adverse medical events that occur after subjects receive the investigational drug, which may be manifested as symptoms, signs, diseases, or abnormal laboratory tests, but are not necessarily causally related to the investigational drug.

Machine Translated by Google

(27) Serious adverse events refer to death, life-threatening, permanent or severe disability or functional loss of subjects after receiving investigational drugs, subjects requiring hospitalization or prolonged hospitalization, and congenital anomalies or birth defects. Defects and other adverse medical events.

(28) Adverse drug reaction refers to any harmful or undesired reaction that may be related to the investigational drug that occurs in the clinical trial. There is at least a reasonable probability of a causal relationship between the investigational medicinal product and the adverse event, i.e. an association cannot be ruled out. (29) Suspicious and unexpected serious adverse reactions, which refer to suspicious and unexpected serious adverse reactions whose nature and severity of clinical manifestations exceed the existing data and information such as the investigational drug investigator's manual, the instruction manual of the marketed drug, or the summary of product characteristics. Adverse reactions.

(30) Subject identification code, which refers to the unique code assigned to subjects in clinical trials to identify their identity. Investigators use this code in place of the subject's name to protect their privacy when reporting adverse events and other trial-related data.

(31) Source documents, which refer to the original records, documents and data generated in the clinical trial, such as hospital medical records, medical images, laboratory records, memoranda, subjects' diaries or evaluation forms, drug distribution records, and automatic records of instruments. Data, microfilms, photographic negatives, magnetic media, X-rays, subject files, clinical trial related documents and records maintained by pharmacies, laboratories and medical technology departments, including certified copies, etc. Source files include source data, which can exist in paper or electronic forms.

(32) Source data, which refers to the original records or certified copies of clinical trials

Machine Translated by Google

All information recorded above, including clinical findings, observations, and other relevant activity records required for the reconstruction and evaluation of clinical trials. (33) Necessary documents refer to documents that can be used individually or collectively to evaluate the implementation process of clinical trials and the quality of trial data. (34) A certified copy refers to a copy that has been verified and verified to be the same as the original in content and structure. The copy is signed and dated by the reviewer, or is directly generated by a verified system. , which can exist in the form of paper or electronic carriers.

(35) Quality assurance refers to the planned and systematic measures established in clinical trials to ensure that the implementation of clinical trials and the generation, recording and reporting of data comply with the trial protocol and relevant laws and regulations.

(36) Quality control refers to the techniques and activities implemented in the clinical trial quality assurance system to confirm whether all relevant activities of clinical trials meet the quality requirements.

(37) Trial site, refers to the place where clinical trial-related activities are carried out. (38) Blinding refers to the procedure in which one or more parties in a clinical trial are unaware of the subject's treatment allocation. Single-blind generally means that subjects do not know, and double-blind generally means that subjects, investigators, monitors, and data analysts are unaware of treatment assignments.

(39) Computerized system verification refers to the process of establishing and recording that a computerized system can meet specific requirements throughout its life cycle from design to decommissioning, or conversion to other systems. Validation protocols should be developed based on a risk assessment that considers factors such as the intended use of the system, the potential impact of the system on subject protection and the reliability of clinical trial results.

Machine Translated by Google

(40) The audit trail refers to the records that can be traced back to restore the process of the occurrence of the incident.

Chapter 3 Ethics Committee

Article 12 The duty of the ethics committee is to protect the rights and safety of subjects, and should pay special attention to vulnerable subjects. (1) The documents that should be reviewed by the ethics committee include: the trial protocol and the revised version of the trial protocol; the informed consent form and its updates; the method and information for recruiting subjects; other written materials provided to the subjects; the investigator's manual; Existing safety data; Documentation containing subject compensation information; Documentation of investigator qualifications; Other documentation required by the Ethics Committee to perform its responsibilities.

(2) The ethics committee shall review the scientific and ethical nature of clinical trials. check.

(3) The ethics committee shall review the qualifications of investigators. (4) In order to better judge whether the rights and safety of subjects and basic medical care can be ensured in clinical trials, the ethics committee may request the provision of materials and information other than those contained in the informed consent form.

(5) When conducting non-therapeutic clinical trials (i.e. trials with no expected direct clinical benefit to the subjects), if the informed consent of the subjects is carried out by their guardians, the ethics committee should pay special attention to whether the trial protocol contains The corresponding ethical issues and laws and regulations are fully considered. (6) If the trial protocol clearly states that the subjects or their guardians cannot sign the informed consent form before the trial in an emergency, the ethics committee shall review whether the corresponding ethical issues and laws and regulations are fully considered in the trial protocol.

Machine Translated by Google

(7) The ethics committee shall examine whether there is any undue influence such as coercion or inducement of subjects to participate in clinical trials. The ethics committee should review that the informed consent cannot contain any content that makes subjects or their guardians give up their legal rights, nor can it contain content that exempts investigators, clinical trial institutions, sponsors and their agencies from their responsibilities.

(8) The ethics committee shall ensure that the informed consent form and other written materials provided to the subjects state the information on the compensation to the subjects, including the compensation method, amount and plan.

(9) The ethics committee shall complete the review or filing process of clinical trial related materials within a reasonable time limit, and give clear written review opinions. The review opinion shall include the name, document (including version number) and date of the clinical trial reviewed.

(10) The review opinions of the ethics committee include: agree; agree with necessary modifications; disagree; terminate or suspend the agreed research. The review opinion shall state the content required to be revised, or the reasons for rejection.

(11) The ethics committee should pay attention to and clearly require the investigator to report in a timely manner: Deviation or modification of the trial protocol in order to eliminate the emergency harm to the subjects during the implementation of the clinical trial; changes that increase the risk to the subjects or significantly affect the implementation of the clinical trial; All suspected and unexpected serious adverse reactions; new information that may adversely affect the safety of subjects or the conduct of clinical trials.

(12) The Ethics Committee has the right to suspend or terminate the non-compliance with relevant requirements. Or a clinical trial in which the subject has unexpected serious damage.

(13) The ethics committee should regularly follow up and review the ongoing clinical trials, and the frequency of review should be determined according to the risk level of the subjects, but at least one year.

Machine Translated by Google

Check it once.

(14) The ethics committee shall accept and properly handle the relevant complaints of the subjects.

beg.

Article 13 The composition and operation of the ethics committee shall meet the following requirements:

(1) The composition of the members of the ethics committee and the record management should be in line with health

requirements of the competent authority.

(2) All members of the ethics committee shall receive training in ethical review and be able to review ethical and

scientific issues related to clinical trials. (3) The ethics committee shall perform its work in accordance with its system and standard

operating procedures

Responsibilities, the review should have a written record, and indicate the meeting time and discussion content.

(4) The voting members of the review opinions of the ethics committee meeting shall participate in the review and

discussion of the meeting, including members of various categories, with different gender composition, and meet the prescribed

number of members. The review opinions of the meeting shall be formed into written documents. (5) The committee members who

vote or put forward the review opinions shall be independent from the clinical staff under review.

Pilot projects.

(6) The ethics committee shall have detailed information on its members, and ensure that its members

Qualified for ethical review.

(7) The ethics committee shall require the researcher to provide all kinds of

information and answer questions from the ethics committee.

(8) The Ethics Committee may invite relevant experts other than members to participate in the review as needed, but

cannot participate in voting.

Article 14 The Ethics Committee shall establish and implement the following written documents:

(1) Provisions on the composition, organization and filing of the ethics committee.

Machine Translated by Google

(2) Ethics committee meeting schedule, meeting notice and meeting review schedule

sequence.

(3) Procedures for the initial review and follow-up review by the ethics committee. (4) Minor

amendments to the trial protocol agreed by the ethics committee, using rapid

Procedure for review and agreement.

(5) Procedures for timely notification of review opinions to investigators. (6)

Review procedures for disagreeing opinions on ethics review.

Article 15 The ethics committee shall keep all records of the ethics review, including the written records of the ethics review, member information, submitted documents, meeting minutes and relevant transaction records, etc. All records should be kept for at least 5 years after the end of the clinical trial. Investigators, sponsors or drug regulatory authorities may request the ethics committee to provide its standard operating procedures and the list of ethics reviewers.

Chapter 4 Researcher

Article 16 The qualifications and requirements that investigators and clinical trial institutions should possess include:

(1) Possess the qualification to practice in a clinical trial institution; possess the professional knowledge, training experience and ability required for clinical trials; be able to provide the latest work resume and relevant qualification documents according to the requirements of the sponsor, ethics committee and drug supervision and administration department. (2)

Familiar with the trial protocol, investigator's manual, and trial drugs provided by the sponsor

relevant information.

(3) Familiar with and abide by the regulations and the laws and regulations related to clinical trials. (4)

Keep a copy of the authorization form for the division of responsibilities signed by the researcher.

Machine Translated by Google

(5) Investigators and clinical trial institutions shall accept the supervision and audits, and inspections by drug regulatory authorities.

(6) Investigators and clinical trial institutions authorize individuals or entities to undertake clinical trial-related duties and functions, and should ensure that they have corresponding qualifications, and should establish complete procedures to ensure that they perform clinical trial-related duties and functions and generate reliable data. Investigators and clinical trial institutions authorizing units other than clinical trial institutions to undertake trial-related responsibilities and functions shall obtain the consent of the sponsor.

Article 17 Investigators and clinical trial institutions shall have the necessary conditions for completing clinical trials:

(1) The investigator has the ability to enroll a sufficient number of subjects according to the trial protocol within the time limit agreed upon in the clinical trial. (2) The investigator has enough time to implement and

Completion of clinical trials.

(3) During the clinical trial, the investigator has the right to control the personnel participating in the clinical trial, has the authority to use the medical facilities required for the clinical trial, and implements it correctly and safely. Clinical Trials.

(4) During the clinical trial, the investigator shall ensure that all personnel participating in the clinical trial fully understand the trial protocol and investigational drugs, clarify their respective division of labor and responsibilities in the trial, and ensure the authenticity, integrity and accuracy of the clinical trial data.

(5) The investigator supervises the implementation of the trial protocol by all investigators, and takes measures to implement the quality management of clinical trials. (6) Clinical trial institutions shall establish corresponding internal management departments to undertake clinical trials.

Management of bed tests.

Machine Translated by Google

Article 18 The investigator shall give the subjects appropriate medical treatment:

(1) The investigator is a clinician or an authorized clinician and needs to bear all the

Responsibility for medical decision-making related to clinical trials.

(2) During the clinical trial and follow-up period, when the subjects have adverse events related to the trial, including clinically significant laboratory abnormalities, the investigator and the clinical trial institution shall ensure that the subjects receive proper medical treatment, and Inform the subjects of the relevant information truthfully. When researchers realize that subjects have co-morbidities that require treatment, they should inform subjects and pay attention to concomitant drugs that may interfere with the results of clinical trials or the safety of subjects.

(3) With the consent of the subjects, the researcher may add the subjects to the trial.

Inform the relevant clinician about the test results.

(4) Subjects can withdraw from the clinical trial without any reason. While respecting the individual rights of subjects, researchers should try their best to understand the reasons for their withdrawal.

Article 19 The communication between the researcher and the ethics committee

includes: (1) Before the clinical trial is carried out, the researcher shall obtain a written letter from the ethics committee. Consent; subjects cannot be screened without prior written consent from the ethics committee.

(2) Before the implementation of the clinical trial and during the clinical trial, the investigator shall provide the ethics committee with all the documents required for the ethical review.

Article 20 Investigators shall abide by the experimental protocol.

(1) Investigators should carry out clinical trials in accordance with the experimental protocol agreed by the ethics committee. test.

(2) Without the consent of the sponsor and the ethics committee, the investigator shall not revise or deviate from the trial protocol, except in order to eliminate the emergency harm to the subjects in a timely manner or

Machine Translated by Google

The change of monitor, telephone number, etc. only involves changes in clinical trial management.

(3) The researcher or the researcher designated by him shall give notice of any deviation from the trial protocol. to record and explain.

(4) In order to eliminate the emergency harm to the subjects, if the investigator modifies or deviates from the trial protocol without the consent of the ethics committee, he shall report to the ethics committee and the sponsor in a timely manner, explain the reasons, and report to the drug supervision department if necessary. Management Door.

(5) Investigators should take measures to avoid using combinations prohibited by the trial protocol Medication.

Article 21 Investigators and clinical trial institutions are responsible for the management of investigational drugs provided by sponsors.

(1) Investigators and clinical trial institutions shall assign qualified pharmacists or other personnel to manage investigational drugs. (2) The management of receipt, storage, distribution, recovery, return and unused disposal of investigational drugs in clinical trial institutions shall comply with relevant regulations and keep records.

record.

The records of investigational drug management should include date, quantity, batch/serial number, expiration date, distribution code, signature, etc. The investigator should keep records of the quantity and dose of the investigational drug used by each subject. The amount used and the remaining amount of the investigational drug should be consistent with the amount provided by the sponsor. (3) The storage of the investigational drug should meet the corresponding storage conditions. (4) The investigator shall ensure that the investigational drug is used in accordance with the experimental protocol, and shall

Explain to the subjects the correct use of the investigational drug.

Machine Translated by Google

(5) Investigators shall randomly select and reserve samples of the clinical trial drugs for bioequivalence trials. The clinical trial institution shall keep the reserved samples for at least 2 years after the drug is marketed. Clinical trial institutions may entrust the retained samples to qualified independent third parties for preservation, but shall not return them to the sponsor or a third party related to their interests.

Article 22 Investigators shall abide by the randomization procedure of clinical trials. Blind trials should be unblinded in accordance with the requirements of the trial protocol. In case of accidental unblinding or emergency unblinding due to serious adverse events, the investigator shall explain the reasons in writing to the sponsor. Article 23 When implementing informed consent, researchers should abide by the Declaration of Helsinki

the ethical principles and meet the following requirements:

(1) Investigators should use the latest version of the informed consent form approved by the ethics committee and other information provided to the subjects. If necessary, subjects during the clinical trial should sign the informed consent form again.

(2) The investigator obtains new information that may affect the subject's continued participation in the trial The subjects or their guardians should be informed in a timely manner, and corresponding records should be made.

(3) Researchers shall not use illegitimate means such as coercion and inducement to influence subjects; subjects to participate in or continue clinical trials.

(4) The investigator or the designated investigator shall fully inform the subjects of all relevant matters of the clinical trial, including written information and the consent of the ethics committee.

See.

(5) The oral and written materials provided to the subjects, such as the informed consent form, shall be in easy-to-understand language and expressions, so that the subjects or their guardians and witnesses can easily understand them.

Machine Translated by Google

(6) Before signing the informed consent, the researcher or the designated researcher shall give the subjects or their guardians sufficient time and opportunity to learn about the details of the clinical trial, and give detailed answers to the subjects or their guardians' questions related to the clinical trial. The problem. (7) The subjects or their guardians, as well as the researcher who executes the informed consent, shall sign and date the informed consent form.

(8) If the subjects or their guardians lack the ability to read, there should be an impartial witness to witness the entire informed consent process. The researcher shall explain the content of the informed consent and other written materials to the subjects or their guardians and witnesses in detail. If the subjects or their guardians verbally agree to participate in the trial, they should sign the informed consent form as far as they can, and the witnesses should also sign and date the informed consent form to prove that the subjects or their guardians have signed the informed consent form. The book and other written materials were accurately explained by the investigators, and the relevant contents were understood and agreed to participate in the clinical trial. (9) Subjects or their guardians should obtain the original or copy of the signed and dated informed consent form and other written materials provided to the subjects, including the original or copy of the updated informed consent form, and other written information provided to the subjects. Revised text of the written information of the author. (10) If the subject is incapable of civil conduct, the written informed consent of his guardian shall be obtained; if the subject is a person with limited capacity for civil conduct, the written informed consent of himself and his guardian shall be obtained. When the guardian represents the subject's informed consent, the subject should be informed of the relevant information of the clinical trial within the scope of the subject's understanding, and the subject should try to sign the informed consent form and indicate the date.

Machine Translated by Google

(11) In an emergency, when the subject's informed consent cannot be obtained before participating in the clinical trial, the guardian can represent the subject's informed consent. If the subject's guardian is not present, the subject's selection method shall be specified in the trial protocol and other documents, and obtain the written consent of the ethics committee; at the same time, the informed consent of the subjects or their guardians to continue participating in the clinical trial should be obtained as soon as possible. (12) When a subject participates in a non-therapeutic clinical trial, the subject himself/herself shall sign and date the informed consent form. A non-therapeutic clinical trial can be given informed consent by a guardian on behalf of the subject only if the following conditions are met: the clinical trial can only be conducted in subjects who are not capable of informed consent; the expected risk to the subject is low; the negative impact on the subject's health has been The implementation of this type of clinical trial is not prohibited by laws and regulations; the selection of this type of subjects has been reviewed and approved by the ethics committee. In principle, such clinical trials can only be conducted in patients with diseases or conditions for which the investigational drug is applicable. During the clinical trial, the subjects should be closely observed. If the subjects show excessive pain or discomfort, they should be withdrawn from the trial, and necessary measures should be given to ensure the safety of the subjects. (13) The specific time and date of the subject's informed consent should be recorded in the medical history record.

personnel.

(14) Children, as subjects, should obtain the informed consent of their guardians and sign the informed consent form. When a child has the ability to make a decision to agree to participate in a clinical trial, his or her own consent should also be obtained. If the child subject does not agree to participate in the clinical trial or decides to withdraw from the clinical trial midway, even if the guardian has agreed to participate or is willing to continue to participate , it should also be subject to the decision of the child subject, unless in a clinical trial for the treatment of a serious or life-threatening disease, the investigator, his or her guardian

Machine Translated by Google

It is believed that the life of a child subject will be endangered if he does not participate in the research, and the consent of his guardian can allow the patient to continue to participate in the research. During the clinical trial, if the child subjects meet the conditions for signing informed consent, they need to sign the informed consent before proceeding. Article 24 The informed consent form and other materials provided to the subjects shall be include:

(1) Overview of clinical trials. (2)
The purpose of the test. (3) The
possibility of trial treatment and random assignment to each group. (4) The
experimental procedures that subjects need to follow, including traumatic medical operations. (5)
Obligations of subjects. (6) The experimental content involved in the clinical trial. (7) The experiment
may cause risks or inconveniences to the subjects, especially when there is a risk of affecting the
embryo, fetus or nursing infant. (8) The expected benefit of the trial, and the possibility of no benefit.
(9) Other optional drugs and treatments, their important potential benefits and risk.

(10) When the subject suffers damage related to the test, he can obtain compensation and treatment.
treatment.

(11) Compensation that subjects may receive for participating in clinical trials.

(12) The expected cost of the subjects participating in the clinical trial. (13)

Subjects participating in the trial are voluntary, they may refuse to participate or have the right to withdraw from the trial at any stage of the trial without being discriminated against or retaliated against.

Machine Translated by Google

Benefits and rights will not be affected. (14) In

the case of not violating the principle of confidentiality and relevant regulations, inspectors, auditors, ethics committees and inspectors of drug regulatory authorities may consult the original medical records of subjects to verify the process and data of clinical trials .

(15) Confidentiality of subjects' relevant identification records shall not be used publicly.

If clinical trial results are released, subject identities remain confidential.

(16) When there is new information that may affect subjects' continued participation in the trial, the

Inform the subjects or their guardians in a timely manner.

(17) When there are questions about the trial information and the rights and interests of the subjects, as well as the occurrence of trial-related damages, the investigators and ethics committees that the subjects can contact and their contact information. (18) The circumstances and reasons why subjects may be terminated from the trial. (19) The

expected duration of the subjects participating in the trial. (20) The estimated number of subjects participating

in the trial.

Article 25 The records and reports of tests shall meet the following requirements:

(1) The researcher shall supervise the data collection at the trial site and the performance of each researcher.

performance of their job responsibilities.

(2) Investigators should ensure that all clinical trial data obtained from the source documents and trial records of the clinical trial are accurate, complete, readable and timely. Source data should be attributable, legible, contemporaneous, original, accurate, complete, consistent, and durable. Modifications to source data should leave traces that do not obscure the original data, and the reasons for modification should be recorded. For clinical trials with patients as subjects, the relevant medical records shall be recorded in the outpatient or inpatient medical record system.

Informatization of clinical trial institutions

Machine Translated by Google

When the system meets the conditions for establishing electronic medical records for clinical trials, researchers should use it first, and the corresponding computerized system should have complete authority management and audit trails, which can be traced back to the creator or modifier of the records, ensuring that the source data collected can be traced to the source. .

(3) Investigators should fill in and amend the case report forms in accordance with the instructions provided by the sponsor to ensure that the data in various case report forms and other reports are accurate, complete, clear and timely. The data in the case report form should be consistent with the source document, and if there is any inconsistency, a reasonable explanation should be given. The modification of the data in the case report form should make the initial record clear and identifiable, keep the modification track, explain the reasons if necessary, and sign and date the modification. The sponsor should have written procedures to ensure that changes to the case report form are necessary, documented, and approved by the investigator. Investigators should keep relevant records of revisions and corrections.

(4) Investigators and clinical trial institutions should follow the "Required Documents for Clinical Trials" and the relevant requirements of the drug supervision and administration department, and properly keep the test documents.

(5) Care should be taken to avoid illegal or unauthorized access, disclosure, dissemination, modification, damage, and loss of information during the processing of clinical trial information and subject information. The recording, processing and preservation of clinical trial data shall ensure the confidentiality of records and subject information.

(6) The sponsor shall specify in the contract with the investigator and the clinical trial institution the retention time, cost and disposal of the necessary documents after expiration. (7) According to the requirements of supervisors, auditors, ethics committees or drug regulatory authorities, investigators and clinical trial institutions should cooperate and provide necessary and trial

Machine Translated by Google

relevant records.

Article 26 The safety report of the investigator shall meet the following requirements: Except for serious adverse events that are not required to be reported immediately in the trial protocol or other documents (such as the investigator's handbook), the investigator shall immediately report in writing to the sponsor all For serious adverse events, a detailed and written follow-up report should be provided in a timely manner. Serious adverse event reports and follow-up reports should indicate the subject's identification code in the clinical trial, rather than the subject's real name, citizenship number and address and other identification information. Adverse events and laboratory abnormal values specified in the trial protocol and important for safety evaluation should be reported to the sponsor according to the requirements and time limit of the trial protocol.

Investigators should report to the sponsor and the ethics committee for reports of fatal events. For other required information such as autopsy report and final medical report.

After receiving the relevant safety information of the clinical trial provided by the sponsor, the researcher should sign and read it in time, and consider the treatment of the subjects, whether to make corresponding adjustments, communicate with the subjects as soon as possible if necessary, and report to the ethics committee. Suspected and unexpected serious adverse reactions provided by the sponsor.

Article 27 When a clinical trial is terminated or suspended early, the investigator shall Subjects were notified when appropriate, and subjects were given appropriate treatment and follow-up. also:

(1) If the investigator terminates or suspends the clinical trial without consulting with the sponsor, the investigator shall immediately report to the clinical trial institution, the sponsor and the ethics committee, and provide a detailed written explanation.

(2) If the sponsor terminates or suspends the clinical trial, the investigator shall immediately report to the clinical trial Bed testing institutions, ethics committee reports, and provide detailed written instructions.

(3) The ethics committee terminates or suspends the agreed clinical trials, research

Machine Translated by Google

Those who fail to do so shall immediately report to the clinical trial institution and sponsor, and provide detailed written instructions. Article 28 The investigator shall provide a trial progress report. (1) The investigator shall submit the annual report of the clinical trial to the ethics committee, or shall provide the progress report as required by the ethics committee. (2) In the event of a situation that may significantly affect the implementation of the clinical trial or increase the risk of the subjects, the investigator shall report in writing to the sponsor, the ethics committee and the clinical trial institution as soon as possible. (3) After the clinical trial is completed, the investigator shall report to the clinical trial institution; the investigator shall provide the ethics committee with a summary of the clinical trial results, and provide the sponsor with the relevant clinical trial reports required by the drug regulatory authority.

Chapter V Sponsors

Article 29 The sponsor shall protect the rights and safety of the subjects and The authenticity and reliability of clinical trial results are the basic considerations for clinical trials.

Article 30 The sponsor shall establish a quality management system for clinical trials. The quality management system of the sponsor's clinical trial should cover the whole process of the clinical trial, including the design, implementation, recording, evaluation, result reporting and document filing of the clinical trial. Quality management includes effective trial protocol design, data collection methods and processes, and information collection necessary for decision-making in clinical trials.

Methods for quality assurance and quality control of clinical trials should be consistent with the risks inherent in clinical trials and the importance of the information collected. Sponsors should ensure the operability of all aspects of the clinical trial, and avoid overly complicated trial procedures and data collection. Protocols, case report forms, and other relevant documents should be clear, concise, and consistent.

Machine Translated by Google

The sponsor shall perform management duties. According to the needs of clinical trials, a clinical trial research and management team can be established to guide and supervise the implementation of clinical trials. Work within the research and management teams should be communicated in a timely manner. During inspections by the drug regulatory authorities, both the research and management teams should send personnel to participate. Article 31 The sponsor conducts quality management based on risk. (1) The key links and data for protecting the rights and interests of subjects and ensuring the reliability of clinical trial results should be clearly defined when the trial protocol is formulated. (2) Risks affecting key links and data of clinical trials should be identified. This risk should be considered at two levels: system level, such as facility equipment, standard operating procedures, computerized systems, personnel, suppliers; and clinical trial level, such as investigational drug, trial design, data collection and recording, informed consent process.

(3) The risk assessment shall consider the possibility of errors occurring under the existing risk control; the impact of the errors on the protection of the rights and safety of the subjects and the reliability of the data; the extent to which the errors are monitored. (4) Risks that can be mitigated or acceptable should be identified. Control measures to reduce risk should be reflected in the design and implementation of the trial protocol, monitoring plans, contracts with clear responsibilities of all parties, compliance with standard operating procedures, and various types of training.

When presetting tolerances for quality risk, the medical and statistical characteristics of the variables and the statistical design should be considered to identify systemic issues affecting subject safety and data reliability. When a quality risk tolerance is exceeded, it should be assessed whether further action is required.

(5) During clinical trials, quality management should be recorded and communicated with relevant parties in a timely manner to promote risk assessment and continuous quality improvement.

Machine Translated by Google

(6) Sponsors should regularly evaluate risk control measures based on new knowledge and experience during clinical trials to ensure the effectiveness and applicability of current quality management. (7) The sponsor shall state the quality management adopted in the clinical trial report method, and outline incidents and remedial actions that significantly deviate from tolerance for quality risk.

Article 32 The quality assurance and quality control of the sponsor shall meet the following requirements:

(1) The sponsor is responsible for formulating, implementing and timely updating the standard operating procedures related to the quality assurance and quality control system of clinical trials, to ensure that the implementation of clinical trials, data generation, recording and reporting comply with the trial protocol, this specification and relevant laws and regulations requirements. (2) The whole process of clinical trials and laboratory tests shall be carried out in strict accordance with the standard operating procedures for quality management. Each stage of data processing is subject to quality control to ensure that all data is reliable and that the data processing process is correct. (3) The sponsor shall sign a contract with all relevant units participating in the clinical trial, including investigators and clinical trial institutions, to clarify the responsibilities of each party. (4) The contract signed between the sponsor and each relevant unit should indicate that the sponsor's supervision and inspection, and the inspection of the drug regulatory department can directly go to the trial site to check the source data, source documents and reports. Article 33 The sponsor entrusting a contract research organization shall meet the following requirements: (1) The sponsor may entrust part or all of its clinical trial work and tasks to the contract research organization, but the sponsor is still responsible for the quality and reliability of clinical trial data. The ultimate responsible person shall supervise the work undertaken by the contract research organization. Contract research organizations should implement quality assurance and quality control.

Machine Translated by Google

(2) Contracts shall be signed for the work entrusted by the sponsor to the contract research organization. The contract should specify the following: the specific work entrusted and the corresponding standard operating procedures; the sponsor has the right to confirm the implementation of the standard operating procedures for the entrusted work; the written requirements for the entrusted party; the entrusted party needs to submit to the sponsor. Reporting requirements; matters related to damage compensation measures for subjects; other matters related to commissioned work. If the contract research organization has subcontracting tasks, it should obtain the written approval of the sponsor. (3) The work and tasks are not clearly entrusted to the contract research organization, and its responsibilities are s It is the responsibility of the sponsor.

(4) The requirements for sponsors in this specification are applicable to contract research organizations that undertake sponsor-related work and tasks. Article 34 The sponsor shall designate competent medical experts to promptly Consultation on medical issues related to bed testing.

Article 35 The sponsor shall select qualified biostatisticians, clinical pharmacologists and clinicians to participate in the trial, including designing trial protocols and case report forms, formulating statistical analysis plans, analyzing data, writing mid-term and final reports Trial summary report. Article 36 The sponsor shall meet the following requirements in trial management, data processing and record keeping:

(1) The sponsor shall select qualified personnel to supervise the implementation of clinical trials, Data processing, data checking, statistical analysis and writing of trial summary report.

(2) The sponsor may establish an independent data monitoring committee to regularly evaluate the progress of clinical trials, including safety data and important efficacy endpoint data. An independent data monitoring committee can advise sponsors on whether to continue implementing,

Machine Translated by Google

Modify or stop ongoing clinical trials. An independent data monitoring committee should have written work procedures and should keep minutes of all relevant meetings. (3) The electronic data management system used by the sponsor shall pass reliable system verification and conform to the preset technical performance, so as to ensure the integrity, accuracy and reliability of the test data, and to ensure that the system is always in a valid state during the entire test process. state.

(4) The electronic data management system shall have complete standard operating procedures for use, covering the setup, installation and use of electronic data management; the standard operating procedures shall describe the verification, functional testing, data collection and processing, system maintenance, and system security of the system testing, change control, data backup, recovery, system contingency plans and software scrapping; standard operating procedures should specify the responsibilities of sponsors, investigators and clinical trial institutions when using computerized systems. All personnel using computerized systems should be trained. (5) The method of data modification in the computerized system shall be pre-specified, the modification process shall be completely recorded, and the original data (such as the retention of electronic data audit trail, data track and editing track) shall be retained; the integration, content and structure of electronic data shall be Clearly stipulated to ensure the integrity of electronic data; when there are changes to computerized systems, such as software upgrades or data transfers, ensuring the integrity of electronic data is more important.

want.

If data conversion occurs during data processing, ensure that the converted data is consistent with the original data and the visibility of the data conversion process.

(6) Ensure the security of the electronic data management system, and unauthorized persons cannot access it; keep a list of persons authorized to modify data; electronic data shall be prepared in a timely manner;

Machine Translated by Google

A blinded design clinical trial should remain blinded at all times, including data entry and processing.

(7) The sponsor shall use the subject identification code to identify all clinical trial data of each subject. After the blinded trial is unblinded, the sponsor shall promptly notify the investigator in writing of the subject's investigational drug.

(8) The sponsor shall save the clinical trial data related to the sponsor, and other data obtained by some relevant units participating in the clinical trial shall also be retained in the necessary documents of the clinical trial as the sponsor's specific data.

(9) If the sponsor suspends or terminates the clinical trial in implementation in advance, it shall communicate with Know all relevant investigators and clinical trial institutions and drug regulatory authorities.

(10) The transfer of ownership of test data shall comply with the requirements of relevant laws and regulations.

(11) The sponsor shall inform the investigator and the clinical trial institution in writing of the requirements for the preservation of trial records; when the relevant records of the trial are no longer required, the sponsor shall also notify the investigator and the clinical trial institution in writing. Article 37 When selecting investigators, sponsors shall meet the following requirements:

(1) The sponsor is responsible for selecting investigators and clinical trial institutions. Investigators should be trained in clinical trials, have experience in clinical trials, and have sufficient medical resources to complete clinical trials. For clinical trials involving multiple clinical trial institutions, the sponsor is responsible for selecting the team leader unit.

(2) Sample testing laboratories involved in medical judgment shall comply with relevant regulations and have corresponding qualifications. The management, testing, transportation and storage of specimens collected in clinical trials shall ensure quality. The implementation of biological sample testing (such as genetics, etc.) that is not related to the experimental protocol agreed by the ethics committee is prohibited. Continuation of the remaining specimens after the clinical trial

Machine Translated by Google

In the case of preservation or possible use in the future, the subject should sign an informed consent form, and explain the preservation time and confidentiality of the data, and under what circumstances the data and samples can be shared with other researchers, etc.

(3) The sponsor shall provide the investigator and the clinical trial institution with the trial protocol and the latest investigator's manual, and shall provide sufficient time for the investigator and the clinical trial institution to review the trial protocol and relevant materials.

Article 38 Before all parties involved in a clinical trial participate in a clinical trial, the sponsor shall Confirm their responsibilities and specify them in the signed contract.

Article 39 The sponsor shall take appropriate measures to ensure that the subjects and investigators can be compensated or compensated. (1) The sponsor shall provide the investigator and the clinical trial institution with legal and economic insurance or guarantee related to the clinical trial, which shall be commensurate with the nature and degree of risk of the clinical trial. But it does not include the damage caused by the fault of the investigator and the clinical trial institution itself.

(2) The sponsor shall bear the cost of diagnosis and treatment for the damage or death of the subjects related to the clinical trial, as well as the corresponding compensation. Sponsors and investigators shall pay compensation or compensation to subjects in a timely manner.

(3) The methods and methods of compensation provided by the sponsor to the subjects shall comply with relevant laws and regulations. (4) The sponsor shall provide the experimental drug to the subjects free of charge, and the payment shall be Medical testing costs associated with bed testing.

Article 40 The contract signed between the sponsor and the investigator and the clinical trial institution shall specify the responsibilities, rights and interests of all parties involved in the trial, as well as the responsibilities, rights and interests that should be avoided by all parties.

Machine Translated by Google

possible conflicts of interest. The trial expenses of the contract shall be reasonable and in line with market laws. The sponsor, investigator and clinical trial institution shall sign and confirm the contract.

The content of the contract should include: compliance with this specification and relevant clinical trial laws and regulations during the implementation of clinical trials; implementation of the trial protocol determined through consultation between the sponsor and the investigator and agreed by the ethics committee; compliance with data recording and reporting procedures; consent Supervision, audit and inspection; preservation and period of necessary documents related to clinical trials; agreement on publication of articles, intellectual property rights, etc.

Article 41 Before the start of a clinical trial, the sponsor shall submit the relevant clinical trial materials to the drug regulatory department, and obtain the license for the clinical trial or complete the filing. The submitted documents should indicate the version number and version date.

Article 42 The sponsor shall obtain the name and address of the ethics committee, the list of members of the ethics committee participating in the project review, the review statement in compliance with this specification and relevant laws and regulations, and the documents approved by the ethics committee from the investigator and the clinical trial institution. and other related information. Article 43 When drawing up a clinical trial protocol, the sponsor shall have sufficient safety and

efficacy data to support its administration route, dosage and duration of administration. Sponsors should update the Investigator Brochure in a timely manner when important new information becomes available. Article 44 The preparation, packaging, labeling and coding of investigational drugs shall comply with the

The following

requirements are met: (1) The preparation of the investigational drug shall comply with the relevant requirements for the production quality management of the drug for clinical investigation; Ability to remain blinded during the trial

state.

Machine Translated by Google

(2) The sponsor should clearly stipulate the storage temperature, transportation conditions (whether it needs to be protected from light), storage time limit, preparation method and process of the drug solution, and device requirements for drug infusion, etc. of the investigational drug. The use method of the investigational drug should be informed to all relevant personnel of the trial, including supervisors, investigators, pharmacists, and drug custodians

Wait.

(3) The packaging of the investigational drug should be able to ensure that the drug can be stored during transportation and storage. not contaminated or deteriorated.

(4) In a blinded trial, the coding system of the investigational drug should include an emergency unblinding procedure, so that the investigational drug can be quickly identified in an emergency medical state without destroying the blindness of the clinical trial.

Article 45 The supply and management of investigational drugs shall meet the following requirements: (1) The sponsor is responsible for providing investigational drugs to investigators and clinical trial institutions

Product.

(2) Sponsors shall not provide investigational drugs to investigators and clinical trial institutions until the clinical trial is approved by the ethics committee and approved or filed by the drug regulatory authority.

(3) The sponsor shall provide the investigator and the clinical trial institution with a written description of the investigational drug, stating that the use, storage and relevant records of the investigational drug shall be clarified. The sponsor shall formulate the supply and management procedures of the investigational drug, including the receipt, storage, distribution, use and recovery of the investigational drug. The investigational drug recovered from the subject and the researcher who did not use the investigational drug should be returned to the sponsor, or destroyed by the clinical trial institution after authorization by the sponsor.

(4) The sponsor shall ensure that the investigational drug is delivered to the investigator and clinical trial in a timely manner.

Machine Translated by Google

testing institutions to ensure timely use by subjects; keep records of the transportation, receipt, distribution, recovery and destruction of investigational drugs; establish a management system for the recovery of investigational drugs to ensure the recall of defective products, the recovery after the test, and the recovery after expiration; Establish a destruction system for unused investigational drugs. The management process of all investigational drugs shall be recorded in writing, and the whole process shall be counted accurately.

(5) The sponsor shall take measures to ensure the stability of the investigational drug during the trial. The storage period of the retained samples of the investigational drug, within the storage time limit of the investigational drug, shall be stored until the end of the clinical trial data analysis or the time limit required by relevant regulations, whichever is longer if the two are inconsistent. Article 46 The sponsor shall clarify the access rights of the trial records.

(1) The sponsor shall specify in the trial protocol or contract that investigators and clinical trial institutions allow inspectors, auditors, reviewers of ethics committees, and inspectors of drug regulatory authorities to directly access source data related to clinical trials. and source files.

(2) The sponsor should confirm that each subject agrees in writing to inspectors, auditors, reviewers of ethics committees, and inspectors of drug regulatory authorities to directly access their original medical records related to clinical trials.

Article 47 The sponsor is responsible for the safety assessment of the investigational drug during the drug trial. Sponsors shall promptly notify investigators, clinical trial institutions, and drug regulatory authorities of any issues found in clinical trials that may affect the safety of subjects, the implementation of clinical trials, or the changes in the ethics committee’s consent.

Article 48 The sponsor shall report adverse drug reactions according to the requirements and time limit.

answer.

Machine Translated by Google

(1) After the sponsor receives safety-related information from any source, it should immediately analyze and evaluate it, including the severity, the correlation with the trial drug, and whether it is an expected event, etc. The sponsor should promptly report suspicious and unexpected serious adverse reactions to all investigators participating in the clinical trial, as well as the clinical trial institutions and ethics committees; the sponsor should report suspicious and unexpected serious adverse reactions to the drug regulatory authority and the health and health authority .

(2) The safety update report during drug research and development provided by the sponsor shall include the assessment of the risks and benefits of the clinical trial, and the relevant information shall be communicated to all investigators participating in the clinical trial, the clinical trial institution, and the ethics committee.

Article 49 The supervision of clinical trials shall meet the following requirements:

(1) The purpose of monitoring is to ensure the rights and interests of the subjects in the clinical trial, to ensure that the data recorded and reported in the trial is accurate and complete, and to ensure that the trial complies with the agreed protocol, this specification and relevant regulations. (2) The supervisors appointed by the sponsor shall have received corresponding training and have medical,

The knowledge required for the supervision of clinical trials such as pharmacy can be effectively performed.

(3) The sponsor shall establish a systematic, prioritized, and risk-based approach to monitor clinical trials. The scope and nature of audits can be flexible, allowing different audit methods to be used to improve the efficiency and effectiveness of audits. Sponsors should document the rationale for selecting a monitoring strategy in the monitoring plan. (4) The sponsor shall formulate a monitoring plan. The monitoring plan should place special emphasis on protecting the rights and interests of subjects, ensuring the authenticity of data, and ensuring that various risks in clinical trials are dealt with. The monitoring plan should describe the monitoring strategy, the monitoring responsibilities for all parties to the trial, the methods of monitoring, and the reasons for applying the different monitoring methods. The monitoring plan should emphasize

Machine Translated by Google

Monitoring of key data and processes. The monitoring plan shall comply with relevant laws and regulations.

(5) The sponsor shall formulate the standard operating procedures for inspection, and the inspector shall

Standard operating procedures should be implemented during the operation.

(6) The sponsor shall implement clinical trial monitoring. The scope and nature of the monitoring depends on the purpose, design, complexity, blinding, sample size, and clinical trial endpoints of the clinical trial.

(7) On-site supervision and centralized supervision shall be carried out based on the combination of risks of clinical trials. On-site monitoring is carried out at the clinical trial site, which should usually be carried out before, during, and after the clinical trial begins. Centralized monitoring is the timely remote evaluation of ongoing clinical trials, as well as the aggregation of data collected by different clinical trial institutions for remote evaluation. The process of centralized monitoring helps to improve the monitoring effect of clinical trials and is a supplement to on-site monitoring.

The application of statistical analysis in centralized monitoring can determine the trend of data, including the scope and consistency of data within different clinical trial institutions and between clinical trial institutions, and can analyze the characteristics and quality of data, which is helpful for the selection of monitoring sites and monitoring procedures.

(8) Under special circumstances, the sponsor may combine monitoring with other trial work, such as researcher training and meetings. During the monitoring, the statistical sampling survey method can be used to check the data. Article 50 Responsibilities of supervisors include: (1) Supervisors should be familiar with the relevant knowledge of the investigational drug, the test protocol, the informed consent form and other written materials provided to the subjects, and the clinical trial standards. Operating procedures and relevant regulations such as this specification. (2) Supervisors shall conscientiously perform supervisory duties in accordance with the requirements of the sponsor and ensure that

Machine Translated by Google

Ensure that clinical trials are conducted and documented correctly in accordance with the trial protocol.

(3) The monitor is the main contact between the sponsor and the investigator. Before the clinical trial, confirm that the investigator has sufficient qualifications and resources to complete the trial, that the clinical trial institution has appropriate conditions for completing the trial, including staffing and training, the laboratory is well-equipped and functioning well, and has various inspection-related inspections. condition.

(4) The inspector should verify that the investigational drug is within the validity period, the storage conditions are acceptable, and the supply is sufficient during the clinical trial; the investigational drug is only provided to the appropriate subjects at the dose specified in the trial protocol; Instructions for proper use, handling, storage and return of investigational drugs; clinical trial institutions have appropriate controls and records for receipt, use and return of investigational drugs; clinical trial institutions dispose of unused investigational drugs in compliance with relevant laws and regulations and Sponsor's request. (5) The inspector shall verify the investigator's implementation of the trial protocol during the implementation of the clinical trial; confirm that all subjects or their guardians have signed the informed consent before the trial; and ensure that the investigator receives the latest version of the investigator's handbook , All test related documents and necessary supplies for the test, and implement it in accordance with the requirements of relevant laws and regulations; ensure that researchers have a full understanding of clinical trials. (6) Monitors verify that researchers perform the duties specified in the trial protocol and contract, and whether these duties are delegated to unauthorized personnel; confirm that the selected subjects are qualified and report the enrollment rate and the progress of the clinical trial; Confirm that data records and reports are correct and complete, that trial records and documents are updated in real time and are well preserved; verify that all medical reports, records and documents provided by investigators are traceable, clear, synchronized, original, accurate and Complete, dated and trial numbered. (7) The inspector checks the accuracy and completeness of the entry in the case report form, and communicates with the

Machine Translated by Google

source file comparison. Monitors should pay attention to check that the data specified in the trial protocol are accurately recorded in the case report form and consistent with the source documents; confirm the subjects' dose changes, treatment changes, adverse events, concomitant medications, complications, loss to follow-up, inspections Omissions, etc., are recorded in the case report form; confirming that the investigators failed to follow up, tests that were not performed, inspections that were not performed, and whether errors and omissions were corrected, etc., were recorded in the case report form; Verify that withdrawals and loss to follow-up of enrolled subjects have been recorded and explained in the case report form.

(8) Supervisors shall notify the investigator of any errors, omissions or unclear handwriting in the case report form; supervisors shall ensure that corrections, additions or deletions are made by the investigator or an authorized person, and there is an amendment Sign, date, and explain the reason for modification if necessary.

(9) Monitors confirm that adverse events are in accordance with relevant laws and regulations, trial protocols, The ethics committee and the sponsor's request were reported within the prescribed time limit.

(10) The inspector confirms whether the researcher has kept the necessary documents in accordance with this specification. (11) Supervisors shall communicate with investigators in a timely manner regarding deviations from the trial protocol, standard operating procedures, and relevant laws and regulations, and take appropriate measures to prevent recurrence. Article 51 After each monitoring, the monitor shall report to the sponsor in writing in a timely manner; the report shall include the date and place of the monitoring, the name of the monitor, the names of the investigators and other personnel that the monitor has contacted, etc.; The report should include a summary of the monitoring work, problems found in the clinical trial and statement of facts, deviations and defects from the trial protocol, and monitoring conclusions; the report should state the corrective measures that have been taken or to be taken for the problems found in the monitoring. , to ensure that the trial complies with the recommendations for the implementation of the trial protocol; the report should

Machine Translated by Google

Provide sufficient detail to review compliance with the monitoring plan. The centralized inspection report can be submitted separately from the on-site inspection report. The sponsor should review and follow up the problems in the monitoring report, and keep it on file.

Article 52 The audit of clinical trials shall meet the following requirements:

(1) In order to evaluate the implementation of clinical trials and compliance with laws and regulations, sponsors may conduct audits in addition to routine monitoring. (2) The sponsor selects a person who is independent of the clinical trial to serve as an auditor, and cannot be an auditor concurrently. Auditors shall have appropriate training and experience in auditing, and be able to effectively perform their auditing duties. (3) The sponsor shall formulate audit procedures for clinical trials and trial quality management systems to ensure the implementation of audit procedures in clinical trials. The regulations shall formulate the audit purpose, audit method, audit frequency and the format and content of the audit report. The problems observed and discovered by the auditors during the auditing process shall be recorded in writing.

(4) The sponsor shall formulate the audit plan and procedures, which shall be based on the content of the materials submitted to the drug regulatory department, the number of subjects in the clinical trial, the type and complexity of the clinical trial, the risk level affecting the subjects and other factors. Known related questions

question.

(5) The drug regulatory department may require the sponsor to provide an audit report according to the needs of the work. (6) When necessary, the sponsor shall provide an audit certificate.

Article 53 The sponsor shall ensure the compliance of clinical trials.

(1) When it is found that the personnel of investigators, clinical trial institutions and sponsors do not abide by the trial protocol, standard operating procedures, this specification, and relevant laws and regulations during the clinical trial,

Machine Translated by Google

Sponsors should take immediate measures to correct and ensure good compliance of clinical trials.

(2) When important compliance problems are discovered, which may have a significant impact on the safety and rights of subjects, or on the reliability of clinical trial data, the sponsor shall conduct root cause analysis in a timely manner and take appropriate corrective and preventive measures. If the trial protocol is violated or the problems of this specification are serious, the sponsor may hold relevant personnel accountable and report to the drug regulatory department.

(3) When an investigator or clinical trial institution is found to have serious non-compliance problems or be discouraged from correcting, the sponsor shall terminate the investigator or clinical trial institution from continuing to participate in the clinical trial, and report to the drug regulatory department in writing in a timely manner. At the same time, sponsors and investigators should take corresponding emergency safety measures to protect the safety and rights of subjects.

Article 54 If the sponsor terminates or suspends the clinical trial in advance, it shall immediately notify the investigator, the clinical trial institution, and the drug regulatory department, and explain the reasons. Article 55 When a clinical trial is completed or terminated early, the sponsor shall

Submit clinical trial reports to drug regulatory authorities in accordance with relevant laws and regulations. The clinical trial summary report shall comprehensively, completely and accurately reflect the clinical trial results, and the safety and efficacy data of the clinical trial summary report shall be consistent with the clinical trial source data. Article 56 The sponsors conducting multi-center trials shall meet the following requirements:

(1) The sponsor shall ensure that all centers participating in the clinical trial can comply with the trial Program.

(2) The sponsor shall provide the same trial protocol to each center. Center by

Machine Translated by Google

Follow the same protocol for harmonized evaluation of clinical and laboratory data and instructions for completing case report forms.

(3) Each center should use the same case report form to record the trial data obtained in the clinical trial. If the sponsor needs the investigator to collect additional trial data, this content should be indicated in the trial protocol, and the sponsor will provide the investigator with an additional case report form. (4) Before the start of the clinical trial, there should be written documents specifying the responsibilities of the investigators of each center participating in the clinical trial. (5) The sponsor shall ensure the communication among the investigators of each center.

Chapter 6 Test Plan

Article 57 The experimental protocol usually includes basic information, research background information, experimental purpose, experimental design, implementation (method, content, steps) and other contents. Article 58 The basic information in the test protocol generally includes: (1) The title, serial number, version number and date of the test protocol. (2) The name and address of the sponsor. (3) The names, positions and positions of the personnel authorized by the sponsor to sign and modify the trial protocol.

unit.

(4) The name, position, address and telephone number of the medical expert of the sponsor.

(5) Investigator’s name, title, position, address and email address of the clinical trial institution talk.

(6) The name and address of the unit and relevant department participating in the clinical trial.

Article 59 The research background information in the experimental protocol usually includes:

Machine Translated by Google

(1) The name and introduction of the investigational

drug. (2) The trial drug is related to the clinical trial in non-clinical research and clinical research.

and potentially clinically meaningful findings.

(3) Known and potential risks and benefits to the subject population. (4) A description

of the administration route, dosage, administration method and treatment time course of the investigational

drug, and the reasons. (5) Emphasize that clinical trials need to be in accordance with the trial protocol, this specification

and relevant laws

Regulations are implemented.

(6) The target population of the clinical trial. (7)

Research background information, references and data sources related to the clinical trial.

Article 60 The purpose of the clinical trial shall be described in detail in the trial protocol. Article 61

The scientific nature of clinical trials and the reliability of trial data, mainly

Depending on the trial design, the trial design usually includes: (1)

Defining the primary and secondary endpoints of the clinical trial. (2) The reason

for the selection of the control group and the description of the trial design (eg double-blind, placebo-

controlled, parallel group design), and the study design, process and different stages are shown in the form of a

flowchart. (3) Measures taken to reduce or control bias, including methods and procedures for randomization and

blinding. The use of single-blind or open-label trials requires justification and measures to control bias.

(4) Treatment method, dosage and administration plan of the investigational drug; dosage form, packaging

and labelling of the investigational drug. (5) The expected duration and specific arrangements for subjects to participate

in clinical trials, including follow-up

Machine Translated by Google

visit, etc.

(6) "Test suspension criteria" and "Trial termination criteria" for subjects, some clinical trials and all clinical trials. (7) Management process of investigational drugs. (8) Procedures for the preservation and unblinding of blind bottoms. (9) Clarify which test data can be directly recorded in the case report as source data

in the

table. Article 62 Items of clinical and laboratory examinations are usually included in the experimental protocol. eye content.

Article 63 Subject selection and withdrawal usually include:

(1) Inclusion criteria of subjects. (2) Exclusion

criteria for subjects. (3) Standards and

procedures for subjects to withdraw from clinical trials.

Article 64 Treatment of subjects usually includes:

(1) The names of all investigational drugs used by the subjects in each group of the clinical trial, Dosage, regimen, route of administration, duration of treatment, and duration of follow-up.

(2) Concomitant medications (including first aid) permitted before and during clinical trials therapeutic drugs) or treatments, and prohibited drugs or treatments.

(3) Methods for assessing subject compliance.

Article 65 Develop a clear visit and follow-up plan, including the clinical trial period, clinical trial endpoints, adverse event evaluation, and follow-up and medical treatment after the end of the trial.

reason.

Article 66 Effectiveness evaluation usually includes:

Machine Translated by Google

(1) Describe in detail the efficacy indicators of clinical trials. (2) Describe in detail the evaluation, recording, and analysis methods and time of the effectiveness indicators point.

Article 67 Safety evaluation usually includes:

(1) Describe in detail the safety indicators of clinical trials. (2) Describe in detail the evaluation, recording and analysis methods and time of safety indicators point.

(3) Recording and reporting procedures for adverse events and concomitant diseases.

(4) Methods and duration of follow-up for adverse events.

Article 68 Statistics usually include:

(1) Determine the sample size of the subjects, and explain the reasons based on the preliminary test or literature data. (2) Significance level, if there is adjustment, it will be considered. (3) Explain the statistical assumptions of the main evaluation indicators, including the null hypothesis and the alternative hypothesis, and briefly describe the specific statistical methods and statistical analysis software to be used. If an interim analysis is required, the reasons, analysis time points and operating procedures should be explained.

(4) Handling methods for missing data, unused data and illogical data. (5) Clearly deviate from the original statistical analysis plan modification procedures. (6) A clearly defined subject data set for statistical analysis, including all subjects participating in randomization, all subjects who have taken investigational drugs, all subjects who are eligible for inclusion and can be used for clinical trial results evaluated subjects.

Article 69 The trial protocol shall include the implementation of clinical trial quality control and quality assurance.

Machine Translated by Google

Article 70 The trial protocol usually includes ethical issues related to the trial consideration.

Article 71 The test plan usually describes the test data collection and management process, the system used for data management and collection, the steps and tasks of data management, and the quality assurance measures for data management.

Article 72 If not specified in the contract or agreement, the trial protocol usually includes direct access to source documents, data processing and record keeping, finance and insurance related to the clinical trial.

Chapter 7 Investigator Handbook

Article 73 The "Investigator's Manual" provided by the sponsor is a compilation of pharmaceutical, non-clinical and clinical data about the investigational drug, including the chemical, pharmaceutical, toxicological, pharmacological and clinical data and data of the investigational drug . The purpose of the Investigator's Handbook is to help investigators and others involved in the trial better understand and comply with the trial protocol, and to help investigators understand many key basic elements of the trial protocol, including the dose, frequency of administration, and administration of clinical trials. Interval time, mode of administration, etc., observation and monitoring of primary and secondary efficacy indicators and safety.

Article 74 When a marketed drug is undergoing clinical trials and the researcher has fully understood its pharmacology and other relevant knowledge, the researcher's manual may be simplified. Parts of the investigator's handbook can be replaced by drug inserts and other forms, and the investigators only need to provide the investigators with relevant, important, and recent, comprehensive, and detailed information about the investigational drug. Article 75 The sponsor shall formulate written procedures for revision of the investigator's handbook.

Machine Translated by Google

Review the Investigator Brochure at least once a year during the clinical trial. According to the research and development steps of the clinical trial and the new information about drug safety and efficacy obtained during the clinical trial, the sponsor should inform the investigator before updating the investigator's handbook, and communicate with the ethics committee and drug regulatory department if necessary. . The sponsor is responsible for updating the investigator's manual and delivering it to the investigator in a timely manner, and the investigator is responsible for submitting the updated manual to the ethics committee.

Article 76 The title page of the Investigator's Handbook shall indicate the name of the sponsor, the serial number or name of the trial drug, the version number, the release date, the replacement version number, and the replacement date. Article 77 The researcher's manual should include:

(1) Catalog entry: confidentiality statement, signature page, table of contents, abstract, preface, physics, chemistry, pharmaceutical properties and structural formula of the investigational drug, non-clinical studies (non-clinical pharmacology, in vivo pharmacokinetics, toxicology)), in vivo effects (in vivo pharmacokinetics, safety and efficacy, marketing use), data summaries and investigator guidelines, precautions, references (published literature, reports, at the end of each chapter) listed).

(2) Abstract: Focus on the information content of physics, chemistry, pharmacy, pharmacology, toxicology, pharmacokinetics and clinical that are of great significance in the process of research and development of experimental drugs.

(3) Preface: Briefly describe the chemical name or approved generic name and approved trade name of the test drug; all active ingredients, pharmacological classification of the test drug, and their expected status (such as advantages) among similar drugs; The basis for the establishment of clinical trials of drugs; the proposed experimental drugs are used for the prevention, diagnosis and treatment of diseases. The preamble should describe routine methods for evaluating the investigational drug.

Machine Translated by Google

(4) The chemical formula and structural formula of the investigational drug should be clearly stated in the investigator's handbook, and its physicochemical and pharmaceutical properties should be briefly described. Describe the storage method and use method of the test drug. When the preparation information of the test drug may affect the clinical trial, the ingredients of the excipients and the reasons for the formulation should be explained, so as to ensure that the necessary safety measures are taken in the clinical trial. Shi.

(5) If the structure of the test drug is similar to other known drugs, it should be stated that Bright.

(6) Introduction to non-clinical research: Briefly describe the relevant results of the non-clinical research on pharmacology, toxicology and pharmacokinetics of the test drug. Explain the methodology and research results of these non-clinical studies, and discuss the implications of these findings for clinical treatment in humans, possible adverse effects on humans, and the relevance of unintended effects on humans. (7) The Investigator's Manual should provide information in non-clinical research: species of experimental animals, number and sex of animals in each group, dosage unit, dosage interval, route of administration, duration of administration, system distribution data, and duration of follow-up after exposure. The research results should include the characteristics and frequency of the pharmacological effects and toxic effects of the test drug; the severity or intensity of the pharmacological effects and toxic effects; the onset time; the reversibility of the drug effect; the duration of drug action and the dose response. The most important findings in nonclinical studies, such as dose-response, possible relevance to humans, and possible aspects of conducting human studies should be discussed. If the results of effective doses and non-toxic doses in the same species of animals can be compared, the results can be used in the discussion of the therapeutic index and the correlation of the research results with the proposed human dose. Comparative studies are based as much as possible on the blood or organ tissue level.

(8) Introduction to non-clinical pharmacology research: should include the pharmacology of the experimental drug

Machine Translated by Google

The abstract should also include, if possible, important metabolic studies of the experimental drug in animals. The abstract should include studies evaluating the potential therapeutic activity of the investigational drug (eg, efficacy models, receptor binding, and specificity), as well as studies evaluating the safety of the investigational drug (eg, specialized studies evaluating pharmacological effects as opposed to evaluating therapeutic effects). . (9) Introduction to the pharmacokinetics of animals: should include a summary of the pharmacokinetics, biotransformation and distribution of the test drug in the species under study. Discussions of findings should address the absorption, local and systemic bioavailability and metabolism of the test drug, and their relationship to species pharmacological and toxicological findings.

(10) Toxicology introduction: The summary of toxicological effects found in relevant studies in different animal species should include single-dose administration, repeated administration, carcinogenicity, special toxicology studies (such as irritation and sensitization), Reproductive toxicity, genotoxicity (mutagenicity), etc. (11) Effects in humans: The known effects of the test drug in humans should be fully discussed, including information on pharmacokinetics, pharmacodynamics, dose-response, safety, efficacy and other areas of pharmacology. A summary of all completed clinical trials of the investigational drug should be provided whenever possible. The use of the investigational drug outside the clinical trial, such as experience during the marketing period, should also be provided. (12) Summary of pharmacokinetic information of the test drug in humans, including pharmacokinetics (absorption and metabolism, plasma protein binding, distribution and elimination); bioavailability (absolute, relative bioavailability) of a reference dosage form of the test drug availability); population subgroups (eg, gender, age, and organ dysfunction); interactions (eg, drug-drug interactions and effects of food); other pharmacokinetic data (eg, populations completed during clinical trials) Research result).

Machine Translated by Google

(13) Safety and efficacy of the investigational drug: a summary and discussion of the safety, pharmacodynamics, efficacy and dose-response information of the investigational drug (including metabolites) obtained from preliminary human trials should be provided. If multiple clinical trials have been completed, safety and efficacy data from multiple studies and subgroups should be pooled. Consideration may be given to a clear overview of adverse drug reactions in all clinical trials (including all investigated indications) in a form such as a table. Important differences in the type and incidence of adverse drug reactions between indications or subgroups should be discussed. (14) Status of marketed use: The major countries and regions where the trial drug has been marketed or approved should be stated. Important information from marketing use (eg, prescription, dosage, route of administration, and adverse drug reactions) should be summarized. The major countries and regions where the investigational drug has not been approved for marketing or withdrawn from marketing should be stated. (15) Data Summary and Investigator Guidelines: non-clinical and clinical data should be comprehensively analyzed and discussed, and information on different aspects of the trial drug from various sources should be summarized to help researchers predict adverse drug reactions or clinical trials. other issues. (16) The Investigator's Handbook should allow the investigator to clearly understand the possible risks and adverse reactions of the clinical trial, as well as the special inspections, observation items and preventive measures that may be required; this understanding is based on the information about the investigational drug obtained from the Investigator's Handbook. physical, chemical, pharmaceutical, pharmacological, toxicological and clinical information. Based on previous human application experience and the pharmacology of the test drug, the investigator should also be provided with guidance on the identification and management of possible overdose and adverse drug reactions.

(17) The contents of the researcher's manual of traditional Chinese medicine and ethnic medicine shall be formulated with reference to the above requirements. It should also indicate the theoretical basis, screening information, compatibility, functions, indications, existing

Machine Translated by Google

The human experience in drug use, the origin and origin of the medicinal materials, etc.; the traditional Chinese medicine compound preparations derived from ancient classic prescriptions, and the source thereof shall be indicated; the relevant medicinal materials and prescriptions and other information.

Chapter 8 Necessary Document Management

Article 78 Necessary documents for clinical trials refer to documents for evaluating clinical trial implementation and data quality, which are used to prove that investigators, sponsors and monitors have complied with this specification and relevant laws on drug clinical trials during clinical trials. regulatory requirements.

The necessary documents are an important part of the audit of the sponsor and the inspection of the clinical trial by the drug regulatory department, and serve as the basis for confirming the authenticity of the implementation of the clinical trial and the integrity of the collected data. Article 79 Sponsors, investigators and clinical trial institutions shall confirm that there are

places and conditions for keeping the necessary documents for clinical trials. The equipment conditions for the preservation of documents shall meet the conditions of preventing direct light exposure, waterproofing, fireproofing, etc., which is conducive to the long-term preservation of documents. Standard operating procedures for document management should be developed. The files that are saved need to be easy to identify, find, retrieve and relocate. The media used to save clinical trial data should ensure that the source data or its certified copies are kept intact and readable during the retention period, and the ability to recover and read is regularly tested or checked to prevent them from being intentionally or unintentionally altered or lost.

If some documents generated during the implementation of clinical trials are not listed in the management catalogue of necessary documents for clinical trials, sponsors, investigators and clinical trial institutions may also list them in their respective necessary documents according to their necessity and relevance save.

Article 80 For clinical trials used to apply for drug registration, the necessary documents shall be kept for at least 5 years after the trial drug is approved for marketing;

Machine Translated by Google

For clinical trials, the necessary documents shall be kept for at least 5 years after the clinical trial is terminated.

Article 81 The sponsor should ensure that the investigator can always access and enter and correct the data in the case report form reported to the sponsor during the trial process, and the data should not be controlled by the sponsor alone.

The sponsor should ensure that the investigator retains case reports that have been submitted to the sponsor table data. Copies used as source documents should meet the requirements for certified copies.

Article 82 When a clinical trial begins, both the investigator, the clinical trial institution, and the sponsor shall establish archive management of necessary documents. At the end of the clinical trial, the monitor shall review and confirm the necessary documents of the investigator, the clinical trial institution, and the sponsor, and these documents shall be properly kept in their respective clinical trial archives.

Chapter IX Supplementary Provisions

Article 83 This specification shall come into force on July 1, 2020.