Article Content

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Chapter I General Provisions

Article 1 This Regulations are enacted pursuant to Paragraph 2, Article 42 of the Pharmaceutical Affairs Act.

Article 2 The Competent Authority as referred to herein means the Ministry of Health and Welfare.

Article 3 Terms used in this Regulations are defined as follows:
1.Clinical Trial: Any investigation in human subjects intended to discover or verify the clinical, pharmacological or other pharmaceutical effects of an investigational product(s).
2.Nonclinical Study: Biomedical studies not performed on human subjects.
3.Subject/Trial Subject: An individual who participates in a clinical trial, either as a recipient of the investigational product(s) or as a control.
4.Informed Consent Form: A written documentation signed and dated by a subject who voluntarily confirms his or her willingness to participate in a particular trial, after having been informed and understand all aspects of the trial that are relevant to the subject's decision to participate.
5.Ethics Committee/ Institutional Review Board (IRB): An independent committee constituted of medical professionals and impartial persons with no medical professions, whose responsibility is to ensure the protection of the rights, safety and well-being of human subjects involved in a trial.
6.Institution/Trial Site: A medical institution where clinical trials are conducted.
7.Investigator: A person responsible for the conduct of the clinical trial at a trial site.
8.Sponsor: An individual, company, institution, or organization which takes responsibility for the initiation and management of a clinical trial.
9.Contract Research Organization (CRO): A person or an organization (commercial, academic, or other) contracted by the sponsor to perform one or more of a sponsor's trial-related duties and functions.

10.Investigational Product: A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial, including a product with a marketing authorization when used or assembled (formulated or packaged) in a way different from the approved form, or when used for an unapproved indication, or when used to gain further information about an approved use.
11.Protocol: A document that describes the objective(s), design, methodology, statistical considerations, and organization of a trial. The protocol usually also gives the background and rationale for the trial, but these could be provided in other protocol referenced documents.
12.Investigator's Brochure (IB): A compilation of the clinical and nonclinical data on the investigational product(s) which is relevant to the study of the investigational product(s) in human subjects.
13.Adverse Drug Reaction (ADR): All noxious and unexpected response to a medicinal product. An adverse drug reaction should be reasonably related to the use of the investigational product(s).
14.Adverse Event (AE): Any untoward medical occurrence in a clinical investigation subject administered an investigational product and which does not necessarily have a causal relationship with the use of the investigational product(s).
15.Blinding/Masking: A procedure in which one or more parties to the trial are kept unaware of the treatment assignment(s). Single-blinding usually refers to the subject(s) being unaware, and double-blinding usually refers to the subject(s), investigator(s), monitor, and, in some cases, data analyst(s) being unaware of the treatment assignment(s).

Article 4 Clinical trials should be conducted in accordance with the ethical principles of the Declaration of Helsinki.
Before a trial is initiated, foreseeable risks and inconveniences should be weighed against the anticipated benefit for the individual trial subject and society. A trial should be initiated and continued only if the anticipated benefits justify the risks and inconveniences.
The rights, safety, and well-being of the trial subjects are the most important considerations and should prevail over interests of science and society.
The Ethics Committee should safeguard the rights, safety, and well-being of all trial subjects. Special attention should be paid to trials that may include vulnerable subjects.

Article 5 The investigator should obtain the informed consent form freely given by the subjects prior to the beginning of the trial.
The investigator, or a person designated by the investigator,

should fully inform the subject of all pertinent aspects of the trial, including the contents of the informed consent form and the documentations approved by the Ethics Committee. The investigator, or designated person, should ensure the content of inform consent form and other trial-related documentations are well understood, signed and dated by the subject.
For the consent mentioned in the preceding two paragraphs, where the subject is incompetent, the consent should be performed by his or her legal representative; where the subject is of limited legal capacity, consent should be obtained from his or her legal representative; where the subject who is neither incompetent nor of limited legal capacity, yet is unable to give consent due to insanity or the absence of discernment, the consent could be given by the subject's legally acceptable representative.
The subject's legally acceptable representative refers to the subject’s spouse and cohabiting families.

Article 6 During and following a subject's participation in a trial, the investigator and the institution should ensure that adequate medical care is provided to a subject for any adverse events related to the trial. The investigator should inform a subject when medical care is needed for intercurrent illness(es) of which the investigator becomes aware.

Article 7 The investigator should inform the subject's primary physician about the subject's participation in the trial if the subject has a primary physician and if the subject agrees to the primary physician being informed.

Article 8 Neither the investigator, nor the trial staff, should coerce or unduly influence a subject to participate in a trial.
During the trial, neither the investigator, nor the trial staff, should coerce or unduly influence a subject to continue the trial.

Article 9 A subject is entitled to withdraw from a clinical trial at any time without giving reason(s).
Under the circumstances referred to in the preceding paragraph, the investigator should make a reasonable effort to ascertain the reason(s) while fully respecting the subject's rights and will.

Article 10 In the aspect of amount and method of payment to subjects, the sponsor should not impose coercion or undue influences on the trial subjects.
The payment to a subject should be prorated and subject to the progress of the trial, instead of payment in full only after completion of the trial.

Information regarding payment to subjects, including the methods, amounts, and schedule of payment to trial subjects, should be clearly stated in the written informed consent form and any other written information to be provided to subjects. The way that the payment will be prorated should be specified.

Article 11 Identities and records of the subjects that are related to the trial should be kept confidential.

Article 12 Clinical trials should be scientifically based, and the protocol should be clearly defined and detailed.

Article 13 No trials shall be conducted without approval from an Ethics Committee.
After reviewing the informed consent form, protocol and all other relevant documents, the Ethics Committee can approve the institution to conduct the clinical trial.

Article 14 All trial staff should have qualified education, training and working experiences to assume their responsibilities in the trial.

Article 15 All clinical trial documents should be recorded and retained.

Chapter II Protection of Trial Subjects

Article 16 Prior to the beginning of the trial, the investigator shall obtain the approval from the Ethics Committee for the informed consent form and any other written information to be provided to subjects.
The approval referred to in the preceding paragraph should be made in writing.

Article 17 The informed consent form and any other written information to be provided to subjects should be revised whenever important new information becomes available that may be relevant to the subject’s consent. The subject or the subject’s legally acceptable representative should be informed in a timely manner if new information becomes available.
Any revised informed consent form, and written information shall be approved by the Ethics Committee in advance of use; For those clinical trials which are approved by the Competent Authority, the revised documents shall be resubmitted for approval.
The communication and approval referred to in preceding paragraph1 and paragraph 2 should be made in writing.

Article 18 None of the informed consent form and any other written information to be provided to subjects shall contain any language that causes the subject or the subject's legally

acceptable representative to waive or to appear to waive any legal rights, or that releases or appears to release the investigator, the institution, the sponsor, or their agents from liability for negligence.
Statements in contradiction to the rules specified in the preceding paragraph are invalid.

Article 19 The language used in the oral and written information about the trial, including the informed consent form, should be as non-technical as practical and should be understandable to the subject or the subject's legally acceptable representative and the impartial witness, where applicable.

Article 20 Prior to a subject’s participation in the trial, the informed consent form shall be signed and personally dated by the subject or by the subject's legal representative and the legally acceptable representative.
Before informed consent may be obtained, the investigator, or a person designated by the investigator, should provide the subject or the subject's legally acceptable representative ample time and opportunity to inquire about details of the trial.
All questions about the trial should be answered to the satisfaction of the subject or the subject's legal representative and the legally acceptable representative.
Informed consent forms shall be signed by all parties mentioned in paragraph 2.
In clinical trials of emergency cases, prior consent of the subject or the subject’s legally representatives could be waived only when the emergency procedures are well described in the protocol. When consent of the subject or the subject's legal representative and the legally acceptable representative is possible, the consent shall be obtained immediately.

Article 21 If the subject or the subject's legal representative and legally acceptable representative. is unable to read, an impartial witness shall be present during the entire informed consent discussion.
The impartial witness should read the informed consent form and any other written information to be provided to subjects and attests that the information were accurately explained by the investigator or designated person, and were fully understood by the subject or by the subject's legal representative and the legally acceptable representative.
Under the circumstances referred to in paragraph 1, the subject or the subject's legal representative and legally acceptable representative. shall still sign and date the informed consent form. Finger print is an acceptable substitute for signature.
After finishing the work described in paragraph 2, the impartial

witness attests that informed consent was freely given by the subject or the subject's legal representative and legally acceptable representative. by signing and dating the informed consent form.
Trial staff shall not acts as the impartial witness.

Article 22 The informed consent form and any other written information to be provided to subjects shall include explanations of the following:
1.That the trial involves research.
2.The purpose of the trial.
3.The trial treatment(s) and the probability for random assignment to each treatment.
4.The trial procedures to be followed, including all invasive procedures.
5.The subject's responsibilities.
6.Those aspects of the trial that are experimental.
7.The reasonably foreseeable risks or inconveniences to the subject and, when applicable, to an embryo, fetus, or nursing infant.
8.The reasonably expected benefits.
9.The alternative procedure(s) or course(s) of treatment that may be available to the subject, and their important potential benefits and risks.
10.The compensation and/or treatment available to the subject in the event of trial-related injury.
11.The anticipated prorated payment, if any, to the subject for participating in the trial.
12.The anticipated expenses, if any, to the subject for participating in the trial.
13.That the subject's participation in the trial is voluntary and that the subject may refuse to participate or withdraw from the trial, at any time, without penalty or loss of benefits to which the subject is otherwise entitled.
14.That the monitor(s), the auditor(s), the Ethics Committee, and the Competent Authority will be granted direct access to the subject's original medical records for verification of clinical trial procedures and/or data, without violating the confidentiality of the subject, to the extent permitted by the applicable laws and regulations and that, by signing a written informed consent form, the subject is authorizing such access.
15.That records identifying the subject will be kept confidential and, to the extent permitted by the applicable laws and/or regulations, will not be made publicly available. If the results of the trial are published, the subject’s identity will remain confidential.
16.That the subject or the subject's legally acceptable

representative will be informed in a timely manner if information becomes available that may be relevant to the subject's willingness to continue participation in the trial.
17.The person(s) to contact for further information regarding the trial and the rights of trial subjects, and whom to contact in the event of trial-related injury.
18.The foreseeable circumstances and/or reasons under which the subject's participation in the trial may be terminated.
19.The expected duration of the subject's participation in the trial.
20.The approximate number of subjects involved in the trial.

Article 23 Prior to participation in the trial, the subject or the subject's legal representative and the legally acceptable representative shall receive a copy of the signed and dated informed consent form and any other written information provided to the subjects. The clinical trials intended for treating emergency cases when prior consent is not possible are exceptional.
During a subject’s participation in the trial, the subject or the subject's legal representative and the legally acceptable representative. shall receive a copy of the signed and dated consent form updates and a copy of any amendments to the written information provided to subjects.

Article 24 The subject’s legally acceptable representative can not represent the subject to provide consent to participate in non-therapeutic trials, except for those non-therapeutic trials with the following conditions are fulfilled:
1.The objectives of the trial can not be met by means of a trial in subjects who can give informed consent personally.
2.The foreseeable risks to the subjects are low.
3.The negative impact on the subject’s well-being is minimized and low.
4.The trial is not prohibited by law.
5.The written approval of the Ethics Committee.
Under the exceptional circumstances referred to in the preceding paragraph, those trials shall be conducted in patients having a disease or condition for which the investigational product is intended. Subjects in these trials shall be particularly closely monitored and shall be withdrawn if they appear to be unduly distressed.

Chapter III Ethics Committee

Article 25 For the purpose of clinical trials review, an institution shall establish an Ethics Committee consisting of members, with the qualifications and experiences to review and evaluate the

science, medical aspects and ethics of the proposed trial.
The Ethics Committee should include at least five members, with at least one member with non-scientific background, and at least one member who is independent of the institution.
The Ethics Committee should perform its functions according to written operating procedures, should maintain written records of its activities and minutes of its meetings.
The constitution and operation should be in compliance with the regulations stipulated by the Competent Authority.

Article 26 The Ethics Committee should make its decision in accordance with the regulations specified in the paragraph 4 of the preceding Article.

Article 27 Members who do not participate in the Ethics Committee review and discussion should not vote or provide their opinion.

Article 28 The investigator may provide information on any aspect of the trial, but should not participate in the deliberations, decision or vote of the Ethics Committee.
The Ethics Committee may invite nonmembers with expertise in special areas for assistance.

Article 29 The Ethics Committee should retain written procedures, membership lists, lists of occupations/affiliations of members, submitted documents, minutes of meetings, correspondence and any other relevant records for a period of at least 3 years after completion of the trial and make them available upon request from the Competent Authority.
The Ethics Committee may be asked by investigators, sponsors or regulatory authorities to provide its written procedures and membership lists. Upon requests, the Ethics Committee shall not reject.

Chapter IV Investigator

Article 30 The investigator(s) shall meet all the qualifications and abilities specified by the Competent Authority, and shall have experiences and resources for the proper conduct of the trial.

Article 31 The investigator should be thoroughly familiar with the appropriate use of the investigational product(s), as described in the protocol, in the current Investigator's Brochure, in the product information and in other information sources provided by the sponsor.

Article 32 The investigator shall be aware of, and shall comply with, this Regulations and the applicable regulatory requirements.

Article 33 The investigator and the institution shall permit monitoring and auditing by the sponsor, and inspection by the Competent Authority or the delegated agencies.

Article 34 The investigator should maintain a list of appropriately qualified persons to whom the investigator has delegated significant trial-related duties.

Article 35 The investigator should be able to demonstrate a potential for recruiting the required number of suitable subjects within the agreed recruitment period.

Article 36 The investigator should have sufficient time to properly conduct and complete the trial within the agreed trial period.

Article 37 The investigator should have available an adequate number of qualified staff and adequate facilities to conduct the trial properly and safely.
The investigator shall supervise the individual and party delegated by him/her to perform duties related to the trial.

Article 38 The investigator should ensure that all persons assisting with the trial are adequately informed about the protocol, the investigational product(s), and their trial-related duties and functions.

Article 39 If the protocol and Investigator's Brochure are updated during the trial, the investigator and the institution shall supply a copy of the updated ones to the Ethics Committee.

Chapter V Sponsor

I. General Rules

Article 40 The sponsor is responsible for selecting the investigator(s).

Article 41 Before entering an agreement with an investigator and an institution to conduct a trial, the sponsor should provide the investigator(s) and the institution(s) with the protocol and an up-to-date Investigator's Brochure, and should provide sufficient time for the investigator to review the protocol and the information provided.

Article 42 The sponsor should obtain the investigator's and the institution's agreement:
1.to conduct the trial in compliance with this Regulations and the applicable regulatory requirement(s), and with the protocol agreed to by the sponsor and given approval by the Ethics Committee;
2.to comply with procedures for data recording and reporting;

3.to permit monitoring, auditing and inspection;
4.to retain the essential documents that the investigator and the institution should file within the time period sponsor specified.
The sponsor, the investigator and the institution should sign the protocol, or an alternative document, to confirm this agreement.

Article 43 A sponsor may transfer any or all of the sponsor's trial-related duties and functions to a CRO.
The ultimate responsibility for the quality and integrity of the trial data always resides with the sponsor.
The delegation referred to in the preceding paragraph should be made in writing.
Within the scope of the transferred duties and obligations referred to paragraph 1, CRO shall apply mutatis mutandis to the relevant provisions of the sponsor in this Regulations.

Article 44 The sponsor may consider establishing an independent data-monitoring committee (IDMC) to assess the progress of a clinical trial, including the safety data and the critical efficacy endpoints at intervals.
The IDMC can recommend to the sponsor whether to continue, modify, or stop a trial.
The IDMC should have written operating procedures and maintain written records of all its meetings.

Article 45 The sponsor should designate appropriately qualified medical personnel who will be readily available to advise on trial related medical questions or problems. If necessary, outside consultant(s) may be appointed for this purpose.

Article 46 Prior to initiating a trial, the sponsor should define, establish, and allocate all trial-related duties and functions.

Article 47 The sponsor should provide insurance or should indemnify (legal and financial coverage) the investigator and the institution against claims arising from the trial, except for claims that arise from malpractice and/or negligence.

Article 48 When the investigator, the institution or any trial staff fails to comply with the protocol or this Regulations, the sponsor should adopt immediate measures to ensure the compliance.
While the investigator or the institution does not adopt the measures referred to in the preceding paragraph, the sponsor should take action in accordance with Article 116.

II. Quality Assurance and Quality Control

Article 49 The sponsor is responsible for implementing and maintaining quality assurance and quality control systems with written SOPs to ensure that trials are conducted and data are generated, documented (recorded), and reported in compliance with the protocol, this Regulations, and the applicable regulatory requirement(s).

Article 50 The sponsor is responsible for securing agreement from all involved parties to ensure direct access to all trial related sites, source data/ documents, and reports for the purpose of monitoring and auditing by the sponsor, and inspection by the Competent Authority.

Article 51 Agreements, made by the sponsor with the investigator, the institution and any other parties involved with the clinical trial, should be in writing, as part of the protocol or in a separate agreement.

Article 52 The sponsor should utilize appropriately qualified individual to design the protocol, produce case report forms (CRFs), plan the analysis, and prepare interim and final clinical trial reports.

III. Data Handling and Record Keeping

Article 53 Quality control should be applied to each stage of data handling to ensure that all data are reliable and have been processed correctly.

Article 54 The sponsor should utilize appropriately qualified individuals to be responsible for the following work:
1.to supervise the overall conduct of the trial,
2.to handle the data and to verify the data,
3.to conduct the statistical analyses, and to prepare the trial reports.
4.to perform operations related to conducting the trial.

Article 55 When using electronic trial data handling or remote electronic trial data systems, the sponsor should:
1. Based on the risk assessment, ensure that the electronic data processing system(s) conforms to the sponsor’s established requirements for completeness, accuracy, reliability, and consistent intended performance (i.e. validation).
2.Follow and maintain SOPs for using these systems.
3.Ensure that the systems are designed to permit data changes in such a way that the data changes are documented and that there is no deletion of entered data; the system shall maintain an audit trail, data trail, edit trail separately.
4.Maintain a security system that prevents unauthorized access to the system or data.

5.Maintain a list of the individuals who are authorized to make data changes.
6.Maintain adequate backup of the data.
7.Safeguard the blinding.
8.Ensure the data integrity in the case of any change in the computer system.

Article 56 If data are transformed during processing, it should always be possible to compare the original data and observations with the processed data.

Article 57 The sponsor should use an unambiguous subject identification code that allows identification of all the data reported for each subject.

Article 58 The sponsor, or other owners of the data, shall retain all of the sponsor-specific essential documents pertaining to the trial for at least 2 years after approval of the marketing application of the investigational product(s) in Taiwan. However, these documents shall be retained for a longer period if required by other applicable regulatory requirements.

Article 59 If the sponsor discontinues the clinical development of an investigational product, the sponsor should notify all the trial investigators, institutions and the Competent Authority.
Under the preceding circumstance, the sponsor shall maintain all sponsor-specific essential documents for at least 2 years after formal discontinuation. However, these documents shall be retained for a longer period if required by other applicable regulatory requirements.

Article 60 Any transfer of ownership of the data shall be reported to the Competent Authority.

Article 61 The sponsor should inform the investigator(s) and the institution(s) in writing of the need for record retention. When the trial related records are no longer needed, the sponsor should notify the investigator(s) and the institution(s) in writing.

IV. Management of Investigational Product(s)

Article 62 When planning trials, the sponsor should ensure that sufficient safety and efficacy data from nonclinical studies and/or clinical trials are available to support human exposure by the route, at the dosages, for the duration, and in the trial population to be studied.

Article 63

The sponsor should update the Investigator's Brochure as significant new information becomes available.

Article 64 The characters of the investigational product(s), including active comparator(s) and placebo should be appropriate to the stage of development of the product(s).The manufacturing, handling and storage of the investigational product(s) shall comply with the GMP. The labeling and codes should protect the blinding design.

Article 65 The sponsor should determine, for the investigational product(s), acceptable storage temperatures, storage conditions, storage times, reconstitution fluids and procedures, and devices for product infusion, and should inform monitors, investigators, pharmacists, storage managers and any other involved parties.

Article 66 The investigational product(s) should be packaged to prevent contamination and unacceptable deterioration during transport and storage.

Article 67 In blinded trials, the coding system for the investigational product(s) should include a mechanism that permits rapid identification of the product(s) in case of a medical emergency, but does not permit undetectable breaks of the blinding.

Article 68 If significant formulation changes are made in the investigational or comparator product(s) during the course of clinical development, studies about whether the new formulated product(s) significantly alter the stability, dissolution rate, bioavailability and other pharmacokinetic profile of the product(s) should be completed prior to the use of the new formulation in clinical trials.

Article 69 The sponsor should not supply an investigator and an institution with the investigational product(s) before the trial is approved.

Article 70 The sponsor should ensure that written procedures include:
1.The instructions that the investigator and the institution should follow for the handling and storage of investigational product(s).
2.Procedures about handling, storage, dispensing, retrieval of unused product from subjects, and return of unused investigational product(s) to the sponsor.

Article 71 In the aspect of the handling of investigational product(s), the sponsor should:
1.Ensure timely delivery of investigational product(s) to the investigator(s).

2.Maintain records that document shipment, receipt, disposition, return, and destruction of the investigational product(s).
3.Follow and maintain a system for retrieving investigational products and documenting this retrieval.
4.Follow and maintain a system for the disposition of unused investigational product(s) and for the documentation of this disposition.
5.Ensure that the investigational product(s) are stable over the period of use.
6.Maintain sufficient quantities of the investigational product(s) used in the trials to reconfirm specifications if necessary.
7.Maintain records of batch sample analyses and characteristics.
For samples referred to in item 6 and item 7 for extending storage permits, samples should be retained either until the analyses of the trial data are complete or as required by the applicable regulatory requirement(s), whichever represents the longer retention period.

Article 72 The sponsor is responsible for the ongoing safety evaluation of the investigational product(s).

V. Monitoring

Article 73 The sponsor shall take into account the risk over subjects' protection and data integrity when establishing a monitoring plan, in order to ensure that the trial is conducted under appropriate monitoring.
The sponsor may choose on-site monitoring, system remote monitoring, or both.
Where the system remote monitoring referred to in the preceding paragraph is adopted, the same shall be implemented only upon a reasonable assessment to verify the adequacy thereof.
The contents of the plan referred to in Paragraph 1 cover the monitoring strategies, the monitoring responsibilities, the monitoring methods and reasons for adoption of the plan, as well as key data and processes to be monitored.

Article 74 The purposes of trial monitoring are to verify that:
1.The rights and well-being of human subjects are protected.
2.The reported trial data are accurate, complete, and verifiable from source documents.
3.The conduct of the trial is in compliance with the currently approved protocol/amendment(s), with this Regulations, and with the applicable regulatory requirement(s).

Article 75 Selection and qualifications of monitors should comply with:
1.Monitors should be appointed by the sponsor.

2.Monitors should be appropriately trained, and should have the scientific and clinical knowledge needed to monitor the trial adequately.
3.A monitor’s qualifications should be documented.
4.Monitors should be thoroughly familiar with the investigational product(s), the protocol, informed consent form and any other written information to be provided to subjects, the sponsor’s SOPs, this Regulations, and the applicable regulatory requirement(s).

Article 76 The sponsor should determine the appropriate scope and nature of monitoring. The determination of the scope and nature of monitoring should be based on considerations such as the objective, purpose, design, complexity, blinding, scale, and endpoints of the trial.
On-site monitoring should be conducted before, during, and after the trial. However, the sponsor may increase some monitoring procedures such as investigators’ training or meetings.
Statistically controlled sampling can be an acceptable method for monitor(s) to select the data to be verified.

Article 77 The monitor(s) should carry out the following activities in accordance with the sponsor’s requirements to ensure that the trial is conducted and documented properly:
1.Acting as the main line of communication between the sponsor and the investigator.
2.Verifying that the investigator has adequate qualifications and resources and remain adequate throughout the trial period.
3.Verifying trial staff and the facilities, including laboratories, equipment, are adequate, safely and properly to conduct the trial and remain adequate throughout the trial period.
4.Verifying, for the investigational product(s):
(1)That storage times and conditions are complies with the requirement(s), and that supplies are sufficient throughout the trial.
(2)That the investigational product(s) are supplied only to subjects who are eligible to receive it and at the protocol specified dose(s).
(3)That subjects are provided with necessary instruction on properly using, handling, storing, and returning the investigational product(s).
(4)That the receipt, use, and return of the investigational product(s) at the trial sites are controlled and documented adequately.
(5)That the disposition of unused investigational product(s) at the trial sites complies with applicable regulatory requirement(s) and is in accordance with the sponsor.

5.Verifying that the investigator follows the approved protocol and amendment(s).
6.Verifying that informed consent was obtained before each subject's participation in the trial.
7.Ensuring that the investigator receives the current Investigator's Brochure, all documents, and all trial supplies needed to conduct the trial properly.
8.Ensuring that the investigator and the investigator's trial staff are adequately informed about the trial details.
9.Verifying that the investigator and the investigator's trial staff are performing the specified trial functions, in accordance with the protocol and any other written agreement between the sponsor and the investigator and the institution, and have not delegated these functions to unauthorized individuals.
10.Verifying that the investigator is enrolling only eligible subjects.
11.Reporting the subject recruitment rate.
12.Verifying that source data, documents and other trial records are accurate, complete, and maintained.
13.Verifying that the investigator provides all the required reports, notifications, applications, and submissions, and that these documents are accurate, complete, timely, legible, dated, and identify the trial.
14.Checking the accuracy and completeness of the CRF entries, source documents, files and other trial-related records against each other. The monitor specifically should verify that:
(1)The data required by the protocol are reported accurately on the CRFs and are consistent with the source documents.
(2)Any dose or therapy modifications are well documented for each of the trial subjects.
(3)Adverse events, concomitant medications and intercurrent illnesses are reported in accordance with the protocol on the CRFs.
(4)Visits that the subjects fail to make, tests that are not conducted, and examinations that are not performed are clearly reported as such on the CRFs.
(5)All dropout subjects from the trial are reported and explained on the CRFs.
15.Informing the investigator of any CRF entry error, omission, or illegibility. The monitor should ensure that appropriate corrections, additions, or deletions are made, dated, explained, and initialled by the investigator or by a member of the investigator's trial staff who is authorized to initial CRF changes for the investigator. This authorization should be documented and filed.
16.Checking all adverse events (AEs) are appropriately reported

within the time periods required by Article 106.
17.Determining whether the investigator is maintaining the essential documents of the trial.
18.Communicating deviations from the protocol, SOPs, this Regulations, and the applicable regulatory requirements to the investigator and taking appropriate action designed to prevent recurrence of the detected deviations.

Article 78 The monitor(s) should follow the sponsor’s established written SOPs as well as those procedures that are specified by the sponsor for monitoring a specific trial.

Article 79 The monitoring report should comply with the following requirements:
1.The monitor should submit a written report to the sponsor after each trial-site visit or trial-related communication.
2.Reports should include the date, site, name of the monitor, and name of the investigator or other individual(s) contacted.
3.Reports should include a summary of what the monitor reviewed and the monitor's statements concerning the significant findings/facts, deviations and deficiencies, conclusions, actions taken or to be taken and actions recommended to secure compliance.
4.The sponsor should designate representatives to record, review and follow-up of the monitoring report.

VI. Audit

Article 80 A sponsor's audit should be independent of and separate from routine monitoring or quality control functions. The purpose of auditing is to evaluate trial conduct and compliance with the protocol, SOPs, this Regulations, and the applicable regulatory requirements.

Article 81 Selection and qualification of auditors should comply with:
1.The sponsor should appoint individuals, who are independent of the clinical trials and data capture systems, to conduct audits.
2.The sponsor should ensure that the auditors are qualified by training and experience to conduct audits properly. An auditor’s qualifications should be documented.

Article 82 The auditing procedures should comply with:
1.The auditing procedures is conducted in accordance with the sponsor's written procedures on what to audit, how to audit, the frequency of audits, and the form and content of audit reports.
2.The sponsor's audit plan and procedures for a trial audit should be guided by the importance of the trial, the number of subjects in the trial, the type and complexity of the trial, the level of risks to the trial subjects, and any identified

problem(s).
3.The observations and findings of the auditor(s) should be documented in writing.
4.To preserve the independence and value of the audit function, the Competent Authority should not routinely request the audit reports, except when evidence of serious non-compliance with this Regulations exists, or in the course of legal proceedings, the Competent Authority may seek access to an audit report on a case by case basis.
5.The sponsor should provide an audit certificate.

Chapter VI Application and Assessment of Clinical Trials

Article 83 For applying for a clinical trial approval, an application form and the following documents are needed to submit:
1.Protocol;
2.Informed Consent From;
3.Advertisement on subject recruitment or any other documents regarding the recruitment procedures;
4.All written information to be provided to subjects;
5.Investigator’s Brochure;
6.Currently available safety data on the investigational product(s);
7.Descriptions of the payments and compensations to trials subjects;
8.The investigator’s current curriculum vitae or any other documents supported his/her qualifications;
9.Other essential documents specified by the Ethics Committee.

Article 84 The Ethics Committee shall review a proposed clinical trial within one month and make a decision for one of the four review results:
1.Approval;
2.Reassessment after modification;
3.Disapproval;
4.Termination or suspension of any prior approval trials.

Article 85 The review decision should be made in writing and include the following contents:
1.The title of the trial;
2.The institution and the investigator;
3.The reviewed documents and the version numbers;
4.The review results and reasons;
5.Year, Month and date.

Article 86 The Ethics Committee should review the qualifications, curriculum vitae and any other relevant documentation of the investigator.

Article 87 The Ethics Committee should depend on the degree of risk to human subjects, conduct continuing review of each ongoing trial at appropriate interval.
The preceding continuing review shall be conducted at least once a year.

Article 88 A clinical trial is to be carried out with the consent of the subject’s legally acceptable representative, the Ethics Committee should ensure that the proposed protocol and other document(s) adequately addresses relevant ethical concerns.

Chapter VII Conduction of Clinical Trials

I. Clinical Trial Protocol

Article 89 The investigator and the institution should conduct the trial in compliance with the protocol agreed to by the sponsor, by the Ethics Committee and by the Competent Authority. The investigator, the institution and the sponsor should sign the protocol, or an alternative contract, to confirm agreement.

Article 90 The investigator should not implement any deviation, or changes of the protocol without agreement by the sponsor and prior approval from the Ethics Committee, except where necessary to eliminate an immediate hazard(s) to trial subjects, or when the change(s) involves only administrative aspects of the trial.
For a deviation, or a change of, the protocol implemented to eliminate an immediate hazard(s) to trial subjects, the investigator should submit the implemented deviation or change, the reasons for it, or the proposed protocol amendment(s) to the Ethics Committee and the sponsor, and to the Competent Authority if the trials are approved by the Competent Authority.

Article 91 The investigator, or person designated by the investigator, should document and explain any deviation from the protocol.

II. Investigational Products

Article 92 The investigator or the institution should be responsible for the accountability and storage of the investigational product(s).
The investigator or the institution may assign some or all of the duties for investigational product(s) accountability and storage at the trial site(s) to designated pharmacists or other appropriate individuals.

Article 93 The investigator, the institution and the designated pharmacist or other appropriate individual should maintain following records:
1.Records of the product's delivery to the trial site;

2.The inventory at the site;
3.The use of the investigational product(s) by subjects;
4.The return to the sponsor or alternative disposition of unused investigational product(s).
The preceding records should include dates, quantities, batch/serial numbers, expiration dates, and the unique code numbers assigned to the investigational product(s) and trial subjects.
The investigator should maintain records that document adequately that the subjects were provided the doses specified by the protocol and reconcile all investigational product(s) received from the sponsor.

Article 94 The investigational product(s) should be stored as specified by the sponsor and in accordance with applicable regulatory requirement(s).

Article 95 The investigational product(s) should be used only in the approved protocol.

Article 96 The investigator, or a person designated by the investigator, should explain the correct use of the investigational product(s) to each subject and should check, at intervals appropriate for the trial, that each subject is following the instructions properly.

Article 97 The investigator should follow the trial's randomization procedures.
Under the preceding randomization procedures, the code should be broken only in accordance with the protocol.
If the trial is blinded, the investigator should promptly document and explain to the sponsor any premature unblinding of the investigational product(s).

III. Records and Reports

Article 98 The investigator should ensure the accuracy, completeness, legibility, and timeliness of the data reported to the sponsor in the CRFs and in all required reports.

Article 99 Data reported on the CRF should be consistent with the source documents. The discrepancies should be explained.

Article 100 Any change or correction to a CRF should be dated, initialed, and explained and should not obscure the original entry.
The preceding regulation applies to both written and electronic changes or corrections.
The investigator should designate a person to document changes or corrections in CRF. All changes or corrections should be

endorsed by the investigator.
The investigator should retain records of the changes and corrections.

Article 101 The investigator and the institution should pay sufficient attention to properly maintain all the important trial documents, and take measures to prevent accidental or premature destruction of these documents.
The documents referred to in the preceding paragraph shall be retained until at least 2 years after approval of the marketing application of the investigational product(s) in Taiwan. However, these documents shall be retained for a longer period if required by other applicable regulatory requirements.

Article 102 The financial aspects of the trial should be documented in an agreement between the sponsor and the institution or the investigator.

Article 103 The monitor, auditor, the Ethics Committee, or the Competent Authority, can request for direct access to all trial-related records. However, prior to access to the subject's personal identity information, confirmation of the subject's written consent is required.

Article 104 The Competent Authority may request the investigator to submit written reports to the institution, elaborating the trial status.
The investigator and the institution should submit written summaries of the trial status to the Ethics Committee annually. If necessary, the Ethics Committee may request to shorten the interval of the routine reports.

Article 105 The investigator shall promptly provide written reports to the sponsor, the Ethics Committee and the Competent Authority on any situation significantly affecting the conduct of the trial, and/or increasing the risk to subjects.

Article 106 The investigator shall immediately report any serious adverse events to the sponsor, and shall provide detailed, written reports as soon as possible. The investigator shall immediately report any suspected unexpected serious adverse drug reactions to the Ethics Committee. However, those SAEs that the protocol or other document identifies as not needing immediate reporting shall not apply.
The sponsor shall report any suspected unexpected serious adverse reactions that are fatal or life-threatening to the Competent Authority or the contracted organization within 7 days after being aware of the event, and shall provide detailed written documents within 15 days after being aware of the event.

The sponsor shall report all the other suspected unexpected serious adverse reactions to the Competent Authority or the contracted organization and provide detailed written documents within 15 days after being aware of the event.
The subjects' identity should be coded in the oral and written reports mentioned in paragraph 1 that should not reveal subjects' names, ID numbers, addresses, or any other information which may reveal subject's personal identity.
The serious adverse events and serious adverse drug reactions are defined and announced by the Competent Authority.

Article 107 When adverse events or laboratory abnormalities are identified as critical to safety evaluations, the investigator should report to the sponsor within the time periods specified by the sponsor in the protocol.

Article 108 For reported deaths, the sponsor, the Ethics Committee, and the Competent Authority may request the investigator to provide autopsy reports, terminal medical reports and any additional information.

Article 109 The sponsor shall promptly notify all investigator(s), institution(s) and the Competent Authority for any of the following situations:
1.New findings that could affect adversely the safety of subjects.
2.New findings that impact the conduct of the trial.
3.New findings that alter the Ethics Committee's approval to continue the trial.

Article 110 The sponsor shall submit the latest safety reports to the Competent Authority.

Article 111 Upon the trial is completed or prematurely terminated, the investigator and the institution shall provide the sponsor and the Competent Authority with any reports required, and provide the Ethics Committee with a summary of the trial's outcome.
Under the circumstances referred to in the preceding paragraph, the sponsor shall provide the Competent Authority with a complete and detailed clinical trial report.
The format of the clinical trial reports referred to in the preceding paragraph is announced by the Competent Authority.

IV. Suspension and Termination of a Trial

Article 112 If the trial is suspended or terminated, the investigator and the institution shall promptly inform the trial subjects, should assure appropriate therapy and follow-up for the subjects.
Under the circumstances referred to in the preceding paragraph,

the investigator and the institution shall inform the Competent Authority of the reasons for suspension or termination of the trial in writing.

Article 113 If the investigator suspended or terminated a trial without prior agreement of the sponsor, the investigator and the institution shall promptly inform the sponsor and the Ethics Committee, and provide detailed written reports.

Article 114 If the sponsor suspended or terminated a trial, the sponsor shall promptly inform the investigators, the institutions, the Ethics Committee, and the Competent Authority and the reason(s) for the termination or suspension, and provide detailed written reports.

Article 115 If the Ethics Committee terminated or suspended a trial, the investigator and the institution shall promptly inform the sponsor, and provide the detailed written reports.

Article 116 If the investigator or the institution seriously or repeatedly violates the protocol, the sponsor should stop the investigator or the institution from conducting the trial and promptly notify the Competent Authority.

V. Multicenter Trials

Article 117 When conducting a multicenter trial, all investigators should conduct the trial in compliance with the protocol agreed to by the sponsor and approved by the Competent Authority, and by the Ethics Committee.

Article 118 When conducting a multicenter trial, for those investigators who are collecting additional data according to the protocol, the sponsor should provide supplemental CRFs that are designed to capture the additional data.

Article 119 The coordination approaches and responsibilities of the investigator(s) and the other participating investigators should be documented in writing prior to the start of a multicenter trial.

Article 120 When conducting a multicenter trial, all investigators should comply with a uniform set of standards for the assessment of clinical and laboratory findings, and on completing the CRFs.

Article 121 When conducting a multicenter trial, the sponsor should facilitate communication between all investigators.

Chapter VIII Supplemental Provisions

Article 122 For clinical trials initiated in accordance with the original Guideline for Good Clinical Practice prior to the implementation of this Regulations, this Regulations shall be applied after taking effect.

Article 123 This Regulations shall take effect immediately upon the date of promulgation hereof.

NOTE
This English version of the Regulations for Good Clinical Practice is provided for reference purposes only. In the event of any inconsistency between the Chinese original and the English translation, the former shall prevail.