Consensus on Contracts for Drug Clinical Trials in Beijing

(2024)

Beijing Pharmaceutical Association

R&D-based Pharmaceutical Association Committee (RDPAC)

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Preface

A drug clinical trial is a systematic trial conducted in human subjects (patients or healthy subjects) that is intended to discover or verify an investigational product's clinical, pharmacological and pharmacodynamic effects, identify any adverse reactions that may arise from its use, or study its absorption, distribution, metabolism and excretion, thus to ascertain its efficacy and safety. Given that a drug developer (e.g., pharmaceutical company, Institution, etc.) does not necessarily have the clinical conditions and qualifications to conduct the trial of an investigational product, the clinical trial requires full cooperation among all parties concerned, including the Sponsor and/or its agent (e.g., the contract research organization ("CRO")), the clinical trial institution and principal investigator ("Investigator") as well as the site management organization ("SMO") contracted and managed thereby, and the clinical research coordinator ("CRC") designated by the SMO. The drug clinical trial-related contract is an agreement concluded by and between the Sponsor and the clinical trial institution, the Investigator, and other parties involved in the clinical trial pertaining to specific tasks within a particular drug clinical trial, which serves as a key document outlining the responsibilities and rights of all parties involved and specifying the clinical trial's funds, payment arrangements and/or dispute resolution procedures, etc.

The drug clinical trial-related contract should comply with and be protected by the *Civil Code of the People's Republic of China,* the *Drug Administration Law of the People's Republic of China*, the *Vaccine Administration Law of the People's Republic of China*, the *Personal Information Protection Law of the People's Republic of China,* the *Regulations on Management of Human Genetic Resources of the People's Republic of China*, the *Rules for the Implementation of Regulations on Management of Human Genetic Resources*, the *Drug Registration Regulations*, the *Good Clinical Practice* ("GCP"), the *Good Manufacturing Practice (2010 Revision) - Annex on Investigational Products (Interim)* ("GMP - Annex on Investigational Products"), the *Standards and Procedures for Expedited Reporting of Safety Data During Drug Clinical Trials*, relevant guidelines issued by the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use ("ICH"), other applicable laws and regulations (e.g., anti-commercial bribery law), and technical guidelines in the industry. Meanwhile, the contract shall be developed in alignment with the specific clinical trial protocol, informed consent form and other essential trial documents. Subject to compliance with the aforementioned regulatory provisions, the drug clinical trial contract may address the major concerns of the parties based on the specific needs of the clinical trial. The Sponsor is prohibited from transferring undue benefits to the clinical trial institution and Investigator by falsifying a project or under the guise of conducting a clinical trial.

The drug clinical trial contract may be drafted by the Sponsor (or its contracted CRO), the clinical trial institution, or other parties; and should be concluded by the Sponsor (or its contracted CRO) and the clinical trial institution and the Investigator through negotiation on the basis of equality, mutual trust, and full expression of their respective wishes for mutual observation. The contract may take various forms, such as bipartite or multipartite agreements governing clinical trials; master contracts (framework contracts) and project contracts concerning a specific trial/trials.

In a bid to enhance the efficiency of clinical trial contract sign-off in Beijing, this Consensus addresses the primary concerns of Sponsors and clinical trial institutions in Beijing, including the responsibilities of the Sponsor and the Investigator, insurance and injury compensation, and intellectual property, and establishes principled solutions to these issues to minimize repetitive discussions on the aforesaid issues during the contract sign-off process. However, the contract for a specific clinical trial should be customized to the unique conditions of that trial.

This Consensus, as recommended, applies to drug clinical trials conducted for registration purpose within the territory of the Peoples' Republic of China, where the clinical trials mentioned herein are interventional in nature. Other types of trials may be performed with reference to this Consensus. This Consensus does not involve essential patents.

I. Responsibilities of the Sponsor

An applicant, defined as one that makes the application for drug registration and the right holder of drug regulation, must ensure the authenticity, integrity and standardization of clinical trial data involved in registration application, supervise the conduct of the clinical trial, and shoulder legal responsibilities for the reliability of the submitted application dossiers and related trial data. The applicant approved to conduct a drug clinical trial is the Sponsor of the drug clinical trial ("Sponsor"). This section is based on the description in GCP, including China's GCP (July 1, 2020) and ICH E6 (R2) *Good Clinical Practice*, and is drawn up with reference to relevant contents of the *Guangdong Consensus on Drug Clinical Trial Management*. It is hoped that relevant requirements for the Sponsor will be further refined through this Consensus, thereby improving self-discipline in the industry.

In this section, the following key issues will be discussed: payment of trial funds, provision of trial-related supplies, protection of personal information, use of biological samples, management and control of the quality of clinical trial data and safety reporting, and division of rights and responsibilities between the Sponsor and the CRO. It should be noted that compensation for subject injuries, a topic that often comes up in contractual discussions, will be detailed in other sections and thus will not be covered in this section.

1. Payment of trial funds: The Sponsor bears the corresponding trial funds as detailed in the attachment regarding trial funds and where necessary, the time limit for such payment should be defined. The Sponsor may authorize the CRO to pay related trial funds. The Sponsor or the CRO should pay the funds, including initiation fee and settlement fee, in strict accordance with the contract.

2. Provision of trial-related supplies: The parties should negotiate the reasonable and necessary supplies to be provided by the Sponsor based on the needs outlined in the clinical trial protocol, including but not limited to drugs, equipment, materials and consumables; the investigational products should be prepared, packaged, labeled and coded according to relevant requirements of GCP and GMP - Annex on Investigational Products.

3. Protection of personal information: The Sponsor should take appropriate measures to safeguard the confidentiality and security of all personal information (including personal information of subjects, Investigator, and other study personnel) obtained during the study in accordance with applicable laws, regulations and informed consent documents. The processing of personal information should abide by relevant provisions of the *Personal Information Protection Law of the People's Republic of China*.

4. Use of biological samples: The Sponsor, the clinical trial institution and other related parties undertake to comply with the *Regulations on Management of Human Genetic Resources of the People's Republic of China*, the *Rules for the Implementation of Regulations on Management of Human Genetic Resources* and other relevant laws and regulations, and to carry out relevant work in accordance with the national administrative licensing decision or filing pertaining to human genetic resources. The Sponsor, the clinical trial institution and other related parties may only use the corresponding biological samples in the

manner permitted in the study protocol, informed consent form, and human genetic resource management procedure (including administrative licensing decision or filing).

5. Management and control of the quality of clinical trial data and safety reporting: The Sponsor should designate monitors and remain accountable for their conduct to ensure that they can perform their duties and monitor the quality of the trial, with frequency of monitoring aligned with the risk assessment results. If necessary, independent audits may be organized to ensure quality. Monitors should attach importance to the communication with the Investigator/clinical institution. The Sponsor should report adverse drug reactions within the prescribed time limit in accordance with applicable laws and regulations; establish a clinical trial quality management system; and dispatch relevant personnel to participate in the inspection conducted by the regulatory authority(ies).

6. Segregation of rights and responsibilities between the Sponsor and the CRO: The CRO, contracted by the Sponsor to perform clinical trial-related activities, bears the legal and contractual responsibilities for the authenticity, integrity and standardization of clinical trial data as well as the direct legal responsibilities for relevant reports and data generated in connection therewith. Where a CRO signs a clinical trial contract with a clinical trial institution, the CRO is required to provide an authorization letter from the Sponsor permitting the CRO to undertake clinical trial-related business. The ultimate responsibility for the quality and reliability of clinical trial data always resides with the Sponsor. When a Sponsor transfers all or any of the Sponsor's clinical trial-related duties and functions to a CRO, the obligations of the Institution and Investigator under the contract and the law remain unchanged.

II. Responsibilities of the Investigator

This section focuses on the responsibilities to be performed and rights to be exercised by the Investigator, including his/her rights and responsibilities in relation to the clinical trial institution, the study team, etc. As mentioned earlier, the Investigator mentioned herein is the principal investigator in the clinical trial institution, referred to as the Investigator. Same as above, this section is based on the description in GCP, including China's GCP (July 1, 2020) and ICH E6 (R2) Good Clinical Practice, and is drawn up with reference to relevant contents of the Guangdong Consensus on Drug Clinical Trial Management.

The Investigator, who is responsible for the specific conduct of the clinical trial, must ensure that the trial is conducted in compliance with GCP and that the trial data are accurate, complete, standardized and traceable, while assuming the direct legal responsibility for the authenticity, integrity and standardization of the clinical trial data. The clinical trial institution, serving as the direct manager of the drug clinical trial, is responsible for the management and supervision of the authenticity, integrity and standardization of clinical trial data. The clinical trial contract must explicitly outline the requirements for the Investigator, which include conducting the clinical trial in a compliant manner in accordance with laws and regulations, relevant normative documents and guidelines, the trial protocol and its amendments, the approval and requirements of the Ethics Committee, the clinical trial contract, etc. and fulfilling the Investigator's responsibilities and obligations associated with the aforesaid work; likewise, the contract should grant the Investigator relevant rights necessary to complete these tasks. Instead of unnecessarily restating the relevant provisions of China's GCP, the clinical trial contract should specify its requirements based on the important procedures and common issues identified during the actual conduct of the clinical trial.

The CRC, a member of the study team authorized by the Investigator to participate in the conduct of the clinical trial, assists the Investigator in handling non-medical judgment and treatment affairs related to the clinical trial. Operating under the direction of both the clinical trial institution and the Investigator, the CRC provides coordination services as per the Investigator's written authorization, instructions and requirements while remaining under the supervision and control of the clinical trial institution and the Investigator. The CRC may either be a staff member of the clinical trial institution or an external individual contracted for this role. In China, there are cases where the clinical trial institutions engage CRCs from the SMO, with the service fees being paid to the SMO. As such, the clinical trial institution and the Investigator should pay attention to the provisions on the division of responsibilities and rights in the contract with the SMO.

This Consensus will address key issues such as the Investigator's documentation of the medical records and data generated from the study, protection of personal information, delegation and change of the Investigator's responsibilities, and management of the CRC:

1. Documentation of the medical records and data generated from the study: The key output of a clinical trial is clinical trial data. The quality of clinical trial data is related to the quality of the clinical trial, and is closely associated with the safety and rights of subjects. The Investigator, as the person responsible for the conduct of the clinical trial, the quality of the clinical trial, as well as the rights and safety of subjects at a trial site, should ensure that all clinical trial data obtained from source documents and records of the clinical trial are accurate, complete, readable and timely. Source data should be attributable, legible, contemporaneous, original, accurate, complete, consistent and enduring. Modifications to source data should be made with markups that does not obscure the source data, and the reason for these modifications should be documented. The Investigator should complete and modify the case report form in accordance with the instructions provided by the Sponsor to ensure that the data in the case report form and other reports are authentic, accurate, complete, clear, timely and traceable. The clinical trial institution should develop relevant management systems (e.g., intra-institutional quality control management system) to enhance the quality of the clinical trial (including data quality).

2. Protection of personal information: The Institution and the Investigator should take appropriate measures to safeguard the confidentiality and security of all personal information (including personal information of subjects, the Sponsor, etc.) obtained during the study in accordance with applicable laws, regulations and informed consent documents. The processing of personal information should abide by relevant provisions of the *Personal Information Protection Law of the People's Republic of China*.

3. Delegation and change of the Investigator's responsibilities: As the on-site leader of the clinical trial, the Investigator is responsible for the overall supervision and conduct of the clinical trial. This includes providing personnel, materials, and informational resources appropriate to the clinical trial, reasonably delegating the Investigator's responsibilities, supervising all members of the study team in the implementation of the trial protocol, and taking measures to manage the quality of the clinical trial. The Investigator's responsibilities and his/her delegation and division of responsibilities to the members of the study team should be stipulated and described in the clinical trial contract or the Delegation of Responsibilities (DOR) Log signed by the Investigator.

In the event that the Investigator needs to delegate part of his/her responsibilities to other investigators (collectively "Physicians in the Study Team") or to qualified personnel, the delegation should not exempt, affect, or reduce the Investigator's responsibilities and rights, but rather the Investigator is still required to fulfill his/her obligations and commitment under the clinical trial contract, including but not limited to the full performance of the Investigator's responsibilities and the supervision of the conduct of the clinical trial.

Where the Investigator is unable to continue in this role during the conduct of the clinical trial, the Institution and the Investigator ("Original Investigator") shall cooperate in good faith to promptly identify a suitably qualified and competent individual acceptable to the Sponsor to serve as the Investigator ("Successor Investigator") and ensure that all necessary procedures related to the change of the Investigator (e.g., approval by the Ethics Committee and informed consent) are properly completed.

The Original Investigator will be required to continue to perform the Investigator's responsibilities in accordance with the terms and conditions of the clinical trial contract until all matters related to the change of the Investigator are completed. If the Original Investigator is unable to cooperate in terms of the aforesaid matters, then the Institution and the Sponsor may jointly identify a Successor Investigator without the consent of the Original Investigator and enter into a contract with the Successor Investigator to define the responsibilities of the Successor Investigator and terminate the Original Investigator's responsibilities under the clinical trial. It should be noted that a change of the Investigator does not affect, reduce, or exempt an Institution from its responsibilities and obligations under a clinical trial contract.

4. Investigator's management of the CRC: The CRC, a member of the study team authorized by the Investigator to participate in the conduct of the clinical trial, should provide coordination services as per the Investigator's written authorization, instructions and requirements while remaining under the supervision and control of the clinical trial institution and the Investigator. Given multiple forms of management of clinical trial institutions in China, such as clinical trials involving SMO/CRC services, it is recommended in this Consensus:

- Where the clinical trial institution is the party engaging CRC services, the use of CRC services may also be described in the clinical trial contract ("Contract I") by and between the clinical trial institution and the Sponsor (or its contracted CRO), including but not limited to the use, authorization and management of the CRC by the clinical trial institution and the Investigator. When the clinical trial institution and the SMO enter into a bipartite CRC service contract ("Contract II"), they shall specify the designation of the CRC, the responsibilities and obligations of all parties concerned, payment, etc. The CRC service fee should be provided by the Sponsor (or its contracted CRO) to the clinical trial institution as agreed upon in "Contract I" between the Sponsor (or its contracted CRO) and the clinical trial institution; the clinical trial institution should then pay the CRC service fee directly to the SMO as agreed upon in the "Contract II" that it enters into with the SMO;

- If the clinical trial institution intends that the Sponsor (or its contracted CRO) pays the SMO service fee to the SMO on its behalf, a tripartite agreement (contract) may be signed between the clinical trial institution, the Sponsor (or its contracted CRO), and the SMO, specifying the designation of the CRC, the responsibilities and obligations of all parties concerned, payment, etc. as needed. The clinical trial institution, as the party engaging CRC services, should manage the CRC and shoulder appropriate responsibilities. The Sponsor (or its contracted CRO) is solely responsible for bearing the CRC service fee, and such CRC service fee may be paid to the SMO by the Sponsor (or its contracted CRO) pursuant to the CRC service contract or a contract between the Sponsor (or its contracted CRO) and the SMO, provided that CRC service contents should be confirmed by the clinical trial institution.

Moreover, it is recommended that the National Medical Products Administration (NMPA) issue relevant legal and regulatory documents to grant legal and regulatory protection for the Investigator's management of the CRC to facilitate the sound development of the SMO industry.

III. Insurance and Injury Compensation

Participating in a clinical trial provides subjects with access to new therapeutic drugs or regimens, but in the process of scientific exploration, there may be risks to subjects even if the clinical trial is conducted in compliance with the relevant ethical requirements and other laws and regulations. In order to protect the rights of subjects and to reduce the risks to subjects, GCP stipulates the responsibilities of the Sponsor, clinical trial institution and the Investigator in the event of trial-related personal injuries to subjects. While the provisions of GCP are required to be followed in principle, there are no clear provisions on practical issues such as how the insurance terms should be specifically agreed upon and how the responsibilities of the Sponsor should be defined. In this regard, the Sponsor, Institution and Investigator may engage in further discussions to refine and agree upon on these aspects in accordance with the provisions of GCP that should be followed in principle. These issues, frequently debated by both parties, constitute a significant portion of ethics review, some of which need to be defined in the clinical trial contract.

Below are the common issues listed based on the above provisions of GCP and feedbacks from some clinical trial institutions and Sponsors:

1. What type of insurance policy the Sponsor can offer

Pursuant to Article 39 (1) of China's GCP, "The Sponsor shall provide the Investigator and the clinical trial institution with legal and economic insurance or guarantee related to the clinical trial". The requirements of GCP essentially mandate that the Sponsor provide assurance for liability coverage related to injury compensation. However, there are currently no insurance companies in China that offer clinical trial insurances with the subjects as the insured. In fact, most available insurance policies in the Chinese market do not cover the trial institution/ Investigator/subject as the insured. The common type of insurance that Sponsors procure for clinical trials is "Drug Clinical Trial Liability Insurance", in which Sponsors are typically the insured. This type of insurance also serves as a mechanism to ensure the Sponsor's solvency.

As a result, there are differences and discussions among Institutions regarding what insurances the Sponsors should provide, how to define the process of insurance claims and compensation, whether the Sponsors can provide alternative security measures, etc. For example, some Institutions require Sponsors to provide proof of insurance coverage for subjects, while others require Sponsors to insure Investigators. The main reason why these needs cannot be satisfied is that what insurances the Sponsors can provide depends on the insurance types that are available from the insurance companies. In addition, some of the security methods or processes proposed by the Institutions may introduce legal, compliance, financial and tax risks or may be challenging to implement in practice, thereby leading to further discussions between Sponsors and Institutions on these topics.

2. Scope of compensation or indemnification

Pursuant to Article 39 (2) of China's GCP, "The Sponsor shall bear diagnosis and treatment costs arising from clinical trial-related injuries to or death of a subject as well as the corresponding compensation. The Sponsor and the Investigator shall pay the compensation or indemnification to the subject in a timely manner."

The description of "clinical trial-related" in this section is rather vague. It should be further clarified that the Sponsor is liable for compensation only if "the injury is caused by the investigational product or the study procedures approved by the Ethics Committee", and that injuries caused by the Institution or study personnel, or by the subjects themselves (including but not limited to the injury caused by disease progression), or by other third parties should be excluded. Therefore, Sponsors and Institutions often need to engage in further discussions to clearly define the circumstances under which Sponsors should be responsible for compensation.

Currently, discussions between Sponsors and Institutions primarily center on practical issues related to the insurance and injury compensation. Each Sponsor or Institution has its own distinct approach to addressing these issues. Some agree on relevant terms in the master contract, while others make specific agreements as attachments to the contract. Additionally, some Sponsors and Institutions jointly develop relevant procedures and sign memorandums of understanding to find practical solutions to these issues.

To this end, the recommendations with respect to the following key issues are made in this Consensus:

Firstly, a consensus should be reached on what type of insurance policy the Sponsor will offer

The common type of insurance that Sponsors procure for clinical trials is "Drug Clinical Trial Liability Insurance". The key information of the insurance contract is reflected in the insurance certificate issued by the insurance company, and the Sponsor verifies the insurance coverage by providing this certificate.

Sponsors purchase clinical trial liability insurance for the conduct of the clinical trial, and the coverage of the insurance should include personal injuries or deaths caused by the investigational product used in the clinical trial or the clinical trial procedures approved by the Ethics Committee. The injury caused by the Institution or study personnel, or by the subjects themselves (including but not limited to disease progression), or by other parties should be excluded.

From the perspective of insurance relationship, the tool of "insurance" indirectly protects the legitimate rights of the subjects. The amount insured is more based on the Sponsor's considerations on costs and risks. For Sponsors with strong self-solvency, there should be no mandatory requirement regarding the amount insured. However, Sponsors should compensate the subjects in accordance with GCP, laws and regulations. If the insurance payout is insufficient to cover the compensation to which subjects are entitled under GCP, laws and regulations, it is recommended that the contract include a provision stating that the Sponsor will be responsible for any shortfall. Compensation can either be directly provided to the subjects or their families by the insurance company, or the Sponsor can first compensate the subjects or their families and then settle the claim with the insurance company. In either case, it is important to adhere to the relevant requirements for protecting the subjects' personal information.

Secondly, a consensus should be reached on circumstances under which the Sponsor should be liable for injury compensation

Based on the provisions of GCP, the *Civil Code of the People's Republic of China* and other related laws and regulations, the Sponsor is liable for injury compensation only if the injury is caused by the investigational product or the study procedures approved by the Ethics Committee, and that the injury caused by the Institution or study personnel, or by the subjects themselves (including but not limited to the injury caused by disease progression), or by other third parties should be excluded.

IV. Intellectual Property

The *Regulations on Management of Human Genetic Resources revised* and published in 2019 and the *Rules for the Implementation of the Regulations on Management of Human Genetic Resources* published in 2023, which are of great significance for the management of human genetic resources in China, also address issues related to intellectual property. In the practical management of human genetic resources, the scope of application of and specific requirements for "patent sharing" remain unclear, raising concerns for both the Sponsor and the Institution. This issue should be raised for attention and for further research. It is important to note that the intellectual property that is subject to the sharing requirements as outlined in the Regulations on Management of Human Genetic Resources pertains only to patent rights, while other categories of results and intellectual property are not required for sharing.

In order to improve work efficiency and operability, the following are recommended in this Consensus regarding the contents of intellectual property in the contracts of relevant cooperative study, especially the ownership of intellectual property generated from the study as well as the issues concerning publication (the following are not contractual terms):

1. With regard to a registrational study, the achievements/results of the study (including data, technical information, inventions, discoveries, developments, improvements, enhancements, software, know-how, methods, techniques, formulas, etc.) and the intellectual property thereto shall, in principle, be owned by the Sponsor provided that there is no breach of any law or regulation. In the event that any mandatory provision in a law or regulation provides otherwise, such mandatory provision shall prevail or both parties shall negotiate on the ownership.

2. The Sponsor may use, license, or assign the achievements for any purposes without violating any laws or regulations, confidentiality obligations, or relevant contractual terms. The Institution and the Investigator may also publish the study results that they obtain in a clinical trial for non-profit purposes, such as relevant scientific and research purposes, and in accordance with the clinical trial contract (subject to the prior review requirement as expressed in Item 4).

3. In respect of the publication related to an international scientific and research collaboration (regardless of the purpose), the Sponsor and the Institution shall follow the standards and guidelines related to the publication of clinical trial results, such as the *Declaration of Helsinki*, the *Good Publication Practice* (see www.ismpp.org), and the *Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals* formulated by the International Committee of Medical Journal Editors (ICMJE), etc., and publication is encouraged. The Sponsor will strive to work together with the Investigator to submit papers on the main results of the overall study population to peer-reviewed journals in due course.

4. Where the Institution and the Investigator intend to publish any results from a clinical trial, they shall provide the manuscript to the Sponsor for review prior to (the specific time requirements may be negotiated by the parties, e.g., at least 60 days in advance) submitting the contents to be published to a publisher or a third party. The Sponsor shall have the right to request the Institution and the Investigator to remove, or delay the publication of, any confidential information and/or any information that may potentially be used in any patent application. The parties may discuss on authorship of the publication, which are subject to ICMJE's criteria for authorship, and it is the responsibility of the authors to draft and complete the required disclosures in accordance with relevant provisions of ICMJE.

V. The consensus reached is as follows

(I) Main content of the contract

As a recommendation, the core content of a drug clinical trial contract or framework may include and not limited to the following:

1. The name, address, and contact information of the Sponsor and its agent, the clinical trial institution, and the principal investigator;

2. The responsibilities to be fulfilled and the rights to be exercised by the Sponsor, the clinical trial institution and the principal investigator, respectively;

3. Dispute resolution: How to resolve disputes that may arise in the performance of the contract, and specify the arbitration institution and place of arbitration selected for litigation if arbitration is needed;

4. General principles of ownership of intellectual property, authorship and publication of articles (if applicable);

5. Specific agreements on clinical trial (when there is a framework contract and a single contract under the framework, this part can be included in the single contract under the framework), which can include:

- The name of the clinical trial, the detailed description of the contracted study, requirements for conducting the clinical trial, the supply, ownership, use and return of the trial-related materials, instruments and equipment or the disposal after the completion of the trial, and the archiving agreement on the raw data and original documents of the clinical trial;

- The number of valid subjects scheduled to complete or expected to complete the study;

- The effective and expiry dates of the clinical trial contract, and the definition and explanation of some clauses that will remain in force after the completion of the contracted study;

- The main components of the fund for clinical trials, calculation method, payment term (schedule of installment payment), process, necessary invoicing instructions, etc.;

- Specific agreements on the ownership of intellectual property and the publication of articles;

6. Others.

(II) Responsibilities of the Sponsor

1. Payment of trial funds: The Sponsor bears the corresponding trial funds as detailed in the attachment regarding trial funds and where necessary, the time limit for such payment should be defined. The Sponsor may authorize the CRO to pay related trial funds. The Sponsor or the CRO should pay the funds, including initiation fee and settlement fee, in strict accordance with the contract.

2. Provision of trial-related supplies: The parties should negotiate the reasonable and necessary supplies to be provided by the Sponsor based on the needs outlined in the clinical trial protocol, including but not limited to drugs, equipment, materials and consumables; the investigational products should be prepared, packaged, labeled and coded according to relevant requirements of GCP and GMP - Annex on Investigational Products.

3. Protection of personal information: The Sponsor should take appropriate measures to safeguard the confidentiality and security of all personal information (including personal information of subjects, Investigator, and other study personnel) obtained during the study in accordance with applicable laws, regulations and informed consent documents. The processing of personal information should abide by relevant provisions of the *Personal Information Protection Law of the People's Republic of China*.

4. Use of biological samples: The Sponsor, the clinical trial institution and other related parties undertake to comply with the *Regulations on Management of Human Genetic Resources of the People's Republic of China*, the *Rules for the Implementation of Regulations on Management of Human Genetic Resources* and other relevant laws and regulations, and to carry out relevant work in accordance with the national administrative licensing decision or filing pertaining to human genetic resources. The Sponsor, the clinical trial institution and other related parties may only use the corresponding biological samples in the manner permitted in the study protocol, informed consent form, and human genetic resource management procedure (including administrative licensing decision or filing).

5. Management and control of the quality of clinical trial data and safety reporting: The Sponsor should designate inspectors and remain accountable for their conduct to ensure that they fulfill their responsibilities in monitoring the quality of the trial, with frequency of monitoring aligned with the risk assessment results. If necessary, independent audits may be organized to ensure quality. Inspectors should attach importance to the communication with the Investigator/clinical institution. The Sponsor should report adverse drug reactions within the prescribed time limit in accordance with applicable laws and regulations; establish a clinical trial quality management system; and dispatch relevant personnel to participate in the inspection conducted by the drug regulatory authority.

6. Segregation of rights and responsibilities between the Sponsor and the CRO: The CRO, contracted by the Sponsor to perform clinical trial-related activities, bears the legal and contractual responsibilities for the authenticity, integrity and standardization of clinical trial data as well as the direct legal liabilities for relevant reports and data generated in connection therewith. Where a CRO signs a clinical trial contract with a clinical trial institution, the CRO is required to provide an authorization letter from the Sponsor permitting the CRO to undertake clinical trial-related business. The Sponsor remains ultimately responsible for the quality and reliability of clinical trial data. When a Sponsor delegates all or part of the work and tasks associated with its clinical trial to a CRO, the obligations of the research institution and Investigator under the contract and the law remain unchanged.

(III) Responsibilities of the Investigator

1. Documentation of the medical records and data generated from the study: The key output of a clinical trial is clinical trial data. The quality of clinical trial data is related to the quality of the clinical trial, and is closely associated with the safety and rights of subjects. The Investigator, as the person responsible for the conduct of the clinical trial, the quality of the clinical trial, as well as the rights and safety of subjects at a trial site, should ensure that all clinical trial data obtained from source documents and records of the clinical trial are accurate, complete, readable and timely. Source data should be attributable, legible, contemporaneous, original, accurate, complete, consistent and enduring. Modifications to source data should be made with markups that does not obscure the source data, and the reason for these modifications should be documented. The Investigator should complete and modify the case report form in accordance with the instructions provided by the Sponsor to ensure that the

data in the case report form and other reports are authentic, accurate, complete, clear, timely and traceable. The clinical trial institution should develop relevant management systems (e.g., intra-institutional quality control management system) to enhance the quality of the clinical trial (including data quality).

2. Protection of personal information: The Institution and the Investigator should take appropriate measures to safeguard the confidentiality and security of all personal information (including personal information of subjects, the Sponsor, etc.) obtained during the study in accordance with applicable laws, regulations and informed consent documents. The processing of personal information should abide by relevant provisions of the *Personal Information Protection Law of the People's Republic of China*.

3. Delegation and change of the Investigator's responsibilities: As the on-site leader of the clinical trial, the Investigator is responsible for the overall supervision and conduct of the clinical trial. This includes providing personnel, materials, and informational resources appropriate to the clinical trial, reasonably delegating the Investigator's responsibilities, supervising all members of the study team in the implementation of the trial protocol, and taking measures to manage the quality of the clinical trial. The Investigator's responsibilities and his/her delegation and division of responsibilities to the members of the study team should be stipulated and described in the clinical trial contract or the Delegation of Responsibilities (DOR) Log signed by the Investigator.

In the event that the Investigator needs to delegate part of his/her responsibilities to other investigators (collectively "Physicians in the Study Team") or to qualified personnel, the delegation should not exempt, affect, or reduce the Investigator's responsibilities and rights, but rather the Investigator is still required to fulfill his/her obligations and commitment under the clinical trial contract, including but not limited to the full performance of the Investigator's responsibilities and the supervision of the conduct of the clinical trial.

Where the Investigator is unable to continue in this role during the conduct of the clinical trial, the Institution and the Investigator ("Original Investigator") shall cooperate in good faith to promptly identify a suitably qualified and competent individual acceptable to the Sponsor to serve as the Investigator ("Successor Investigator") and ensure that all necessary procedures related to the change of the Investigator (e.g., approval by the Ethics Committee and informed consent) are properly completed. The Original Investigator will be required to continue to perform the Investigator's responsibilities in accordance with the terms and conditions of the clinical trial contract until all matters related to the change of the Investigator are completed. If the Original Investigator is unable to cooperate in terms of the aforesaid matters, then the Institution and the Sponsor may jointly identify a Successor Investigator without the consent of the Original Investigator and enter into a contract with the Successor Investigator to define the responsibilities of the Successor Investigator and terminate the Original Investigator's responsibilities under the clinical trial. It should be noted that a change of the Investigator does not affect, reduce, or exempt a Institution from its responsibilities and obligations under a clinical trial contract.

4. Investigator's management of the CRC: The CRC, a member of the study team authorized by the Investigator to participate in the conduct of the clinical trial, should provide coordination services as per the Investigator's written authorization, instructions and requirements while remaining under the supervision and control of the clinical trial institution and the Investigator. Given multiple forms of management of clinical trial institutions in China, such as clinical trials involving SMO/CRC services, it is recommended in this Consensus:

- Where the clinical trial institution is the party engaging CRC services, the use of CRC services may also be described in the clinical trial contract ("Contract I") by and between the clinical trial institution and the

Sponsor (or its contracted CRO), including but not limited to the use, authorization and management of the CRC by the clinical trial institution and the Investigator. When the clinical trial institution and the SMO enter into a bipartite CRC service contract ("Contract II"), they shall specify the designation of the CRC, the responsibilities and obligations of all parties concerned, payment, etc. The CRC service fee should be provided by the Sponsor (or its contracted CRO) to the clinical trial institution as agreed upon in "Contract I" between the Sponsor (or its contracted CRO) and the clinical trial institution; the clinical trial institution should then pay the CRC service fee directly to the SMO as agreed upon in the "Contract II" that it enters into with the SMO;

- If the clinical trial institution intends that the Sponsor (or its contracted CRO) pays the SMO service fee to the SMO on its behalf, a tripartite agreement (contract) may be signed between the clinical trial institution, the Sponsor (or its contracted CRO), and the SMO, specifying the designation of the CRC, the responsibilities and obligations of all parties concerned, payment, etc. as needed. The clinical trial institution, as the party engaging CRC services, should manage the CRC and shoulder appropriate responsibilities. The Sponsor (or its contracted CRO) is solely responsible for bearing the CRC service fee, and such CRC service fee may be paid to the SMO by the Sponsor (or its contracted CRO) pursuant to the CRC service contract or a contract between the Sponsor (or its contracted CRO) and the SMO, provided that CRC service contents should be confirmed by the clinical trial institution.

Moreover, it is recommended that the National Medical Products Administration (NMPA) issue relevant legal and regulatory documents to grant legal and regulatory protection for the Investigator's management of the CRC to facilitate the sound development of the SMO industry.

(IV) Insurance and injury compensation

1. A consensus should be reached on what type of insurance policy the Sponsor will offer: The common type of insurance that Sponsors procure for clinical trials is "Drug Clinical Trial Liability Insurance". The key information of the insurance contract is reflected in the insurance certificate issued by the insurance company, and the Sponsor verifies the insurance coverage by providing this certificate.

Sponsors purchase clinical trial liability insurance for the conduct of the clinical trial, and the coverage of the insurance should include personal injuries or deaths caused by the investigational product used in the clinical trial or the clinical trial procedures approved by the Ethics Committee. The injury caused by the Institution or study personnel, or by the subjects themselves (including but not limited to disease progression), or by other parties should be excluded.

From the perspective of insurance relationship, the tool of "insurance" indirectly protects the legitimate rights of the subjects. The amount insured is more based on the Sponsor's considerations on costs and risks. For Sponsors with strong self-solvency, there should be no mandatory requirement regarding the amount insured. However, Sponsors should compensate the subjects in accordance with GCP, laws and regulations. If the insurance payout is insufficient to cover the compensation to which subjects are entitled under GCP, laws and regulations, it is recommended that the contract include a provision stating that the Sponsor will be responsible for any shortfall. Compensation can either be directly provided to the subjects or their families by the insurance company, or the Sponsor can first compensate the subjects or their families and then settle the claim with the insurance company. In either case, it is important to adhere to the relevant requirements for protecting the subjects' personal information.

2. A consensus should be reached on circumstances under which the Sponsor should be liable for injury compensation: Based on the provisions of GCP, the *Civil Code of the People's Republic of China* and other related laws and regulations, the Sponsor is liable for injury compensation only if the injury is caused by the investigational product or the study procedures approved by the Ethics Committee, and that the injury caused by the Institution or study personnel, or by the subjects themselves (including but not limited to the injury caused by disease progression), or by other third parties should be excluded.

(V) Intellectual property

1. With regard to a registrational study, the achievements/results of the study (including data, technical information, inventions, discoveries, developments, improvements, enhancements, software, know-how, methods, techniques, formulas, etc.) and the intellectual property thereto shall, in principle, be owned by the Sponsor provided that there is no breach of any law or regulation. In the event that any mandatory provision in a law or regulation provides otherwise, such mandatory provision shall prevail or both parties shall negotiate on the ownership.

2. The Sponsor may use, license, or assign the achievements for any purposes without violating any laws or regulations, confidentiality obligations, or relevant contractual terms. The Institution and the Investigator may also publish the study results that they obtain from a clinical trial for non-profit purposes, such as relevant scientific and research purposes, and in accordance with the clinical trial contract (subject to the prior review requirement as expressed in Item 4).

3. In respect of the publication related to an international scientific and research collaboration (regardless of the purpose), the Sponsor and the Institution shall follow the standards and guidelines related to the publication of clinical trial results, such as the *Declaration of Helsinki*, the *Good Publication Practice* (see www.ismpp.org), and the *Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals* formulated by the International Committee of Medical Journal Editors (ICMJE), etc., and publication is encouraged. The Sponsor will strive to work together with the Investigator to submit papers on the main results of the overall study population to peer-reviewed journals in due course.

4. Where the Institution and the Investigator intend to publish any results from a clinical trial, they shall provide the manuscript to the Sponsor for review prior to (the specific time requirements may be negotiated by the parties, e.g., at least 60 days in advance) submitting the contents to be published to a publisher or a third party. The Sponsor shall have the right to request the Institution and the Investigators to remove, or delay the publication of, any confidential information and/or information that may potentially be used in any patent application. The parties may discuss on authorship of the publication, which are subject to ICMJE's criteria for authorship, and it is the responsibility of the authors to draft and complete the required disclosures in accordance with relevant provisions of ICMJE.