CLINICAL TRIAL AGREEMENT

(Signed by three parties - Sponsored by an Principle Investigator)

This Agreement is signed by the following parties:

Party A: CHANG GUNG MEDICAL FOUNDATION (TAIPEI, LINKOU, KAOHSIUNG, CHIAYI, YUNLIN, KEELUNG, TAOYUAN, TUCHENG) CHANG GUNG MEMORIAL HOSPITAL【Please fill in according to the signatory hospital area】

Party B: 　　　　　　　 Doctor (Principle Investigator)

Party C:

Whereas Party A and Party B plan to implement Party C’s product【Name of Product】(hereafter referred as the「Medicine」) at a clinical trial(hereafter referred as「this Trial」, the terms and conditions are hereby as follows:

Article 1 Content of contract

Whereas Party C is a (Pharmaceuticals, medical materials or others) pharmaceuticals company that specialized in the research, development, manufacturing and sale of medicines for human use and Party B intends to carry out 【Name of the Protocol】at Party A’s medical institution, Party B is the clinical experiment’s sponsor and principle investigator, with the responsibilities of the 『Delegator of the trial: Sponsor and administrator of the trial shall assume the delegator’s obligations and responsibilities in accordance with Good Manufacturing Practice and relevant laws and regulations』, which shall be jointly assumed by both Party A and Party B, and Party C shall provide sponsored medicines and part of the implementation funds.

Party A and Party B agree to implement this experiment according to the Experiment Plan (【Name of the Protocol】; see Protocol in Appendix 1) and not to conduct any extra research. Any revision in relation to this experiment shall be carried out only after approved by the Institutional Review Board Committee. In case of any addition, deletion, or modification of the Experiment Plan, Party A and Party B shall inform Party C through prior written notification.

The Agreement IRB Original Case Number:

The three parties’ employees promise that they never have and will not get any unfair benefits, obtain or reserve any business , business interest, public and official functions or activities or take other improper actions related this trial.

Article 2 Provision of performing funds and medicines (medical devices, materials or other products)

Party C agrees to provide medicines (or medical devices) for this Trial; see Appendix 2 for medicines and expenses.

The clinical experiment’s medicines (or medical devices) are only for the use of Party A and relevant personnel (including co-investigators) in implementing the Trial on Human Subjects according to the Project Plan and may not be used for any other purposes.

Market listed instruments and equipment are acceptable to be donated or borrowed by the experiment delegator and shall be numbered by the site and included in Party A’s fixed asset management. Unlisted instruments and equipment may not be donated or borrowed by the experiment delegator and shall be handled in accordance with the site’s borrowing rules. Furthermore, the experiment delegator shall be responsible for regular maintenance, repair and expenses in relation to the medicinal materials, as well as for presenting repair records to the site for review.

If the sponsoring funding of Party C is paid in New Taiwan Dollar, please remit the sum to Hua Nan Commercial Bank Minsheng Branch according to the remittance account and method announced on the website of this HOSPITAL; if it is not paid in New Taiwan Dollar, Institution only takes US Dollar as the collection currency, collection information are as follows:【Please adjust the receiving information according to the actual sending bank】

Beneficiary bank: Yuan Ta Bank LTD

Branch: International Business Dept.

Account name: CHANG GUNG MEDICAL FOUNDATION LINKOU CHANG GUNG MEMORIAL HOSPITAL

Bank account: 0200102121815

Article 3 Acknowledgement and assistance of the Contract

Party A and Party B shall assume corresponding responsibilities and obligations as this Experiment’s delegator. Party B shall personally supervise this Trial to ensure it is performed in strict accordance with the Protocol, relevant laws and regulations of the ROC Ministry of Health and Welfare and the latest edition of the Declaration of Helsinki and Good Manufacturing Practice.

Party A and Party B shall be responsible for planning and managing this Trial, included without limitation to applying for and obtaining approval from the Institutional Review Board Committee, obtaining an Informed Consent Form, preparing and maintaining the Protocol ’s principal investigator manual, data, statements, etc. In the event of any Adverse Effector Serious Adverse Drug Reactions that occurred in relation to this Trial, Party A and Party B shall report such incidence to the ROC Ministry of Health and Welfare in strict accordance with relevant laws and regulations. If Party A and Party B are informed of any serious adverse drug reactions (as stipulated in Article 4 of the Notification Methods on Serious Adverse Drug Reactions), both of them shall notify Party C’s contact person (Name: ; Tel: ; Fax: ) after being informed.

Party A and Party B agree that Party C, without violates its duty of confidentiality, may inquire into entrusted site involved in service processing in relation to this Trial. Party C shall inform Party B day(s) prior to doing so, and Party A and Party B shall assist in providing detailed explanations and relevant materials and shall agree that Party C may designate its personnel, within normal working days, to have access to the Trial execution site of Party A and Party B to determine the actual Trial performance conditions after notification from Party C day(s) before. It is noted that assistant Trial personnel designated by Party C shall comply with Party A’s clinical Trial regulations, and if not, Party A has the right to inform Party C to replace such personnel.

Article 4 Trial Result allocation and right

Both Party A and Party C have their own inventions or technologies under individual ownership, which shall not be influenced by this Contract.

In the event of any invention, discovery (whether patentable or not), innovation, creation, inspiration, concept or report formulated or developed by Party A , Party B or a co-investigator during the plan process that is related with the Trial medicines or Party C’s confidential information (such as those defined under the Contract), including but not limited to the usage, intake, design of manufacturing or method of Trial medicines or derivatives, they shall immediately be disclosed to Party C.

【The ownership of intellectual property rights shall be specified in one of the following contents. If the second allocation proportion is involved, the agreement shall be reviewed by the Center of Industry-Academia Collaboration】

Any results resulting from the implementation of this experiment, including but not limited to intellectual property rights, such as technical data, right to apply for a patent, patent, copyright and business secret, shall be owned by Party A.

According to the proportion of contributions made by both parties to "this research and development", the ownership of intellectual property shall be based on the principle of Party A ＿＿% and Party C ＿＿%; the application for intellectual property shall also be made by both parties as the joint applicants, and the cost-sharing ratio shall be based on the principle of the ownership ratio of intellectual property. The said fees include application fee, addition and correction fee or response fee, certificate fee, annual fee, office handling fee and other relevant fees payable according to law.

Article 5 Academic publications (AAHRPP 1.8 D)

Party A has the right to publish the clinical Trial’s result, sustainable academic research, and data and outcomes in relation to the clinical trial obtained under the purpose of providing medical care to Human Subject(s) of the clinical trial. The authors’ ranking methodology and contents (including scientific conclusions and professional judgments) in Party A’s academic publications shall be determined at discretion, with Party C’s assisted projects and contents attached. Outcomes or data obtained from the clinical trial that are ready to be published by Party A and Party B (including a co-investigator) at any academic journal, seminar, press conference or other public occasion shall be submitted to Party C for review day(s) before the academic journal publication or day(s) before the convening of a seminar or press conference, and Party C has the right to require Party A and Party B (including Co-investigator) to revise the material with respect to the following conditions:

1. To ensure the correction of an academic journal, seminar or press conference;

2. To ensure Party C’s confidential information is not mishandled or leaked;

3. To safeguard Party C’s intellectual property rights;

4. To together present other relevant supplementary information.

If Party C holds that the clinical trial ’s results may involve and have intellectual property rights as stipulated in Article 4, it has the right to require Party A and Party B (including a co-investigator) in writing to not publish such results within day(s) after it received such results to be published or until all patent application documents in relation to the protocol have been prepared, so as to protect the right of patent application, and Party A and Party B (including a co-investigator) shall not refuse without due causes.

Copyrights of academic papers in relation to the protocol that is published in academic journals shall belong to both Party A and Party B.

Article 6 Confidential information

All relevant confidential information initially possessed and disclosed by any party of this Agreement to other parties for the purpose of implementing the protocol, including but not limited to the principal investigator’s data, project plans, reports, messages, figures, prescriptions, processes, etc. (hereinafter referred to as the Confidential Information) are perceived as assets of the discloser party.

The aforesaid confidential information can exclude: (A) Information individually possessed and certified by each party in written documents before the signing of the experiment plan or disclosure; (B) Information independently developed and obtained by each party; (C) Information obtained by each party from a legal third person via due process, or knowledge or data already known by the public when disclosed.

Article 7 Confidentiality clauses

Party A, Party B and Party C agree to take good care of and try to safeguard and keep all confidential information and other relevant data they learned or held in relation to use of the protocol (including this Agreement). Furthermore, parties agree not to disclose the aforesaid confidential information and other relevant data to any third party without the other parties’ consents in writing.

Parties acknowledge and agree that all confidential information and other relevant data in relation to use of the Protocol shall only be used for lawful purposes as stipulated in thus Agreement and disclosed only to need-to-know personnel (including a co-investigator) to implement the clinical trial; such personnel shall also assume the confidentiality obligations set forth hereinabove.

Parties acknowledge and agree not to during, upon the expiry of or at the termination of this Agreement, and unless otherwise authorized by this Agreement, disclose or deliver confidential information to any third party due to any cooperative relationship, but this does not apply to disclosure or delivery required by law.

Parties acknowledge that during, upon the expiration of and at the termination of this Agreement, and unless otherwise authorized by laws or competent authority, they shall never disclose patients’ names, case numbers and other data in relation to patients’ real identities, states of illness, etc.

Parties acknowledge to during, upon the expiration of and at the termination of this Agreement, destroy or return other parties’ confidential information.

Any party may require another party to present a written pledge to declare and guarantee that all confidential information that it held in relation to the other parties has been destroyed.

Article 8 Compensation for damage

Party C shall ensure that all medicines (medical devices, materials or other products) provided are in accordance with *Good Manufacturing Practices* ,or other quality and safety required by applicable laws and regulations.

In the event that any subject suffers from any damage due to the performance of the clinical trial, Party A and Party B shall assume responsibility for compensation.

Article 9 Prevention of damage occurrence

Before the clinical trial, Party C shall provide Party A with medicines’ (medical devicesor materials’) toxicities, pharmacological actions and other relevant data. After reviewed by Party A and approved by the human subject(s), the trial shall be implemented on the basis of the symptom evaluation results of the human subject(s) and health management principles.

Party B shall ensure each of the Informed Consent Forms is approved by the Institutional Review Board Committee in writing, and from every human subject in written form. Furthermore, Party B shall keep an original copy of each Informed Consent Form signed by the human subject(s).

During the trial , in the case that Party A and Party B (including a co-investigator) find that patients are suffering from adverse effects and are unable to continue the trial, or may be exposed to adverse effects, they shall immediately stop the trial and inform Party C.

In the case that Party C finds that the medicines (or materials) applied in the trial have serious adverse effects that once happened in another hospital during the trial period, it shall immediately inform Party A and Party B.

Party C will use Biological Samples only in ways permitted by the informed consent document under which they were obtained, which shall not be used for other purposes. In case of the breach of the Agreement, Party C should immediately put an end to the use of Biological Samples in breach of the Agreement, and compensate to Party A for all damages and expenses incurred from the handling (whether successful or not) of all legal proceedings (including any reasonable legal and expert charges and expenses).

Article 10 TERMINATION

Termination Events. Termination or suspension of this Agreement will be triggered by the earlier of any of the following events.

a. Study Completion. This Agreement will terminate when the Study is complete, which means the conclusion of all Protocol-required activities for all enrolled subjects.

b. Early Termination of Study. This Agreement will terminate if the Study is terminated early as described below.

(1)Termination of Study Upon Notice. Part A or Part B may terminate the trial for any reason upon 30 days’ written notice to Part C.

(2)Immediate Termination of trial by Part A or Part B. Part A or Part B may terminate the trial immediately upon written notice to Part C for causes that include failure to enroll human subjects at a rate sufficient to achieve trial performance goals; circumstances that in Principal Investigator’s opinion pose risks to the health or well-being of human Subjects; or regulatory agency actions relating to the trial or the Investigational Drug; or Termination under the request of the responsible IRB / REC.

Article 11 Termination and Change

In the case that this Agreement is unable to continue due to any party, except for the immediate termination due to possible damage to human subject(s) after notification, the party shall inform the other parties one month before in written form, and this Agreement will be terminated after approved by the other parties; the same process shall be used for any amendments that occur.

In the event that any party violates this Agreement, unless this Agreement stipulated otherwise, the other parties have the right to terminate this Agreement if the defaulting party still does not perform its obligations under this Agreement after being reminded by the other contracted parties, and the default party shall be liable for damages.

Article 12 Force Majeure

If a party is unable to perform this Agreement due to fire, flood, typhoon, rainstorm, earthquake, war and like occasions (hereafter referred as「Events of Force Majeure」under the Agreement ), such party can be exempted from assuming all liabilities of compensation; said party shall also, during the Events of Force Majeure period, try its best to perform or regain its ability to perform obligations under the Agreement within reasonable limits.

Article 13 Regulations and compliance

Parties shall comply with clinical trial’s ethical principles, *Regulations for Good Clinical Practice,Regulations for Drug Safety Monitoring ,* *Regulations on Good Clinical Practice for Medical Devices* and other applicable laws and regulations of ROC during the trial period.

Article 14 Declaration and guarantee

Party A and Party B declare and guarantee that all personnel during the period for implementing this protocol have relevant qualifications, permits, licenses, certificates and conditions as prescribed by relevant ROC laws and regulations. Party A additionally declares and guarantees that all personnel for implementing this protocol are fully aware of and comply with Party A’s obligations under this Agreement, including but not limited to covenants in Article 4 (Trial Result allocation and right), Article 5 (Academic publications), Article 6 (Confidential information), Article 7 (Confidentiality clauses), etc.

Party C shall inform Party A of any relevant data (including security data and new therapies) in writing during the trial period.

Party C guarantees that all medicines(Medical devices, materials or other products), packages, labels and data referred to in section2 of this Article are real and do not infringe others’ patent, trademark, copyrights, trade secrets or any other rights and interests.

Article 15 USE OF NAME AND COMPENSATION

Unless required by decrees or prior written consent of Party A, Party C shall not use the name or alias of Party A or Party B in any advertising or sales promotion material or in any statement related to pharmaceuticals of the clinical trial, neither shall it express or imply any commercial product or service approved by Party A or Party B. Without prior written consent of Party C, Party A or Party B shall not be use names of Party C and its any employee in any advertisement.

In case of the breach of the provision of section 1, Party C should immediately withdraw the relevant advertisement, sales promotion material or statement and make corrections, and compensate to Institution for all damages and expenses incurred from the handling (whether successful or not) of all legal proceedings (including any reasonable legal and expert charges and expenses), as well as additional punitive liquidated damages of NT$ 5,000,000 by the piece (for example, advertising material is counted by the “sheet”, and advertisement is counted by the “number of times”). *《The following can be added to Article 15section2 depends on the type of the trial: Food, food of special nutrients, cosmetics and commodities that can be purchased directly by the public through open trade (e.g., internet, physical store, TV shopping, etc.)》*

Article 16 Miscellaneous Clause

1. Parties hereto may revise or supplement through negotiation matters not mentioned herein according to laws, practices and the principle of good faith.

2. All disputes arising from the performance of this Agreement should be settled through friendly negotiation, and if there is no agreement upon the negotiation or any party refuses to coordinate, the dispute shall then be submitted to the Part A’s local courts as the court of first instance where the Agreement is reached for settlement, during which ROC laws shall govern.

3. The Attachment and Protocol shall be parts of this Agreement and invalid in the case of any discrepancy with this Agreement.

4. This Agreement is made in triplicate, each of which shall be deemed equally authentic, and each party shall hold one copy.

Party A: CHANG GUNG MEDICAL FOUNDATION (TAIPEI, LINKOU, KAOHSIUNG, CHIAYI, YUNLIN, KEELUNG, TAOYUAN, TUCHENG) CHANG GUNG MEMORIAL HOSPITAL 【Please fill in according to the contracted district】

Director:

Address: Tel:

Party B: Clinical Trial Principal Investigator

Address: Tel:

Party C: Legal Representative:

Address: Tel:

Date: (the Republic of China calendar)

Appendix 2 – Budget

|  |  |  |
| --- | --- | --- |
| In the \_\_\_\_\_\_ Year  (List of sponsored items and amount, please compile funding of each year) | | |
| Item | Funding Budget | Explanation  (The following are common sponsored funding items. Please amend according to the actual sponsored items) |
| Staff Fee (A) |  | 1. X(S)**M**RP research：Limited to compilation of the fee of the Principal Investigator, if no fee of the Principal Investigator is compiled, “Statement that no fee of the Principal Investigator is charged” should be attached. 2. X(S)**P**RP research：Principal Investigator initiated (included partial sponsorship from sponsors) research shall not be allocated the fee of the Principal Investigator, and “Statement that no fee of the Principal Investigator is charged” should be attached. If the research nurse or research assistant personnel expenses are sponsored by a sponsor and appointed by the PI, they may be allocated here and paid. |
| Fee of consumable materials and medicines (E) |  | Taking Human Subject-related expenses as the principle, such as registration fees of subjects, expenses related to outpatient service, test/examination fees, treatment fees, related consumables for treatment (e.g. dressing), hospitalization expenses, nutrition fees, traffic/accommodation allowance of subjects and caregivers, medical service fees (e.g. image interpretation/analysis fee, technical service fee, etc. to be compiled according to charging standards formulated by various departments of this Hospital and incorporated into incomes of this Hospital and then allocated to individuals according to their performance in each department), health education fee, charges for diagnosis and treatment by doctors, and handling and storage costs of human subjects’ samples (funding of which is to be compiled according to charging standards of this Hospital), etc.The standard of various clinical trial test/examination fees: health insurance payment items are priced at 1.5 times the premium, and health insurance non-payment items are priced at the hospital's own expense price plus 1.5 times. |
| Instrument and equipment fee (F) |  | Procurement of clinical trial supplies, equipment, instruments and maintenance fees. |
| Other fee of Trial (Z) |  | (1)Compilation according to charging standards of this Hospital: Expenses of information system support, biostatistics support, etc.; if an application needs to be submitted to the tissue bank for samples in the research, sample application review fee (NT$ 2,000) per application per case needs to be compiled.  (2)Actual payment according to the amount of expenses:  A.Study related office consumables: Seal engraving fee, stationery fee, photocopying fee, photocopying paper, postal and telecommunications fee, related consumables of MFP/fax machine, storage cabinet of documents related to the research, etc.  B.Study related equipment or consumables: Experimental consumables or reagents, blood drawing peripheral consumables (e.g. sterile cotton ball, gauze, cotton swab, injection syringe, blood sampling scalp needle, medical tape, etc.), study instrument calibration fee, glucose meter/blood pressure meter/oximeter/ear thermometer/thermometer/centrifuge and related consumables, refrigerator, cooler bag, light-avoiding medicine box, goggles, alcohol pad, gloves, research locker, zipper bag, etc.  C.Computer peripheral consumables and maintenance: Tablet computer, computer and computer peripheral equipment fees, scanner, DVD/CD-RW, information software, USB, battery, CD, etc.  D.Study related training: Clinical trial related training and certification examination registration fees, such as BLS course, GCP course, etc.  E.Study-related travel expenses: Sponsoring targets shall be limited to be Principal Investigator and experiment team members, and the contract shall specify the sponsored items (such as travelling expense, accommodation expense, meal charge, etc.) and sponsorship amount. If not specified, “Management Measures on Business Trips” of this Hospital shall be followed.  F.Others: Clinical trial liability insurance premium, document storage fee, internet access fee, remittance charge, IRB review fees for XPRP researches, etc. |
| Management fee(K) |  | For total funding less than NT$ 1 million, 15% of the total paid-in sum is allocated according to the account in the current year [management fee = total funding ÷0.85×0.15]; for total funding more than NT$ 1 million, 5% is allocated as management fee [management fee for the part in excess of NT$ 1 million = (total funding-1 million) ÷0.95×0.05]; the allocation of NT$ 10,000 from the annual planned management fee shall be the lower limit (including without the aforementioned sponsoring funding compiled (Items A, E, F, Z)) in the current year. |
| Fee of researchers employed by this Hospital (Q) |  | They refer to the personnel costs of the research assistant and research nurse appointed by the Clinical Trial Center under the entrustment of the Sponsor. After the Sponsor compiles the funding budget of these costs, the reasonableness of which shall be reviewed by the Clinical Trial Center. If there is no need to appoint a research assistant and research nurse to assist in the implementation of the scheme, the Principal Investigator’s statement on having not appointed a research assistant / research nurse shall be attached. |
| Non-working hours attendance allowance for pharmacists in our hospital (U) |  | Refers to the subsidy fee for the trial sponsor to assign the designated pharmacist of this hospital to perform the distribution and management of clinical trial drugs during non-working hours (such as temporary demand on night and holiday) due to medication needs. The attendance allowance for the attending pharmacist is compiled by the sponsor (NT$5,000/per time, no more than 4 hours each time) and transportation allowance (NT$1,000/per time, one round trip is calculated as the unit of calculation) |
| Trial Drug management Fee(S) |  | □A basic setting fee of NT$ 15,000will be charged for the first year, and will be charged annually according to storage conditions at different temperatures. If there are more than two storage methods at the same time, the one with higher cost will be taken as the basis of pricing:  □Room temperature NT$ 26,000, □Refrigeration NT$ 31,000, □Freezing NT$ 38,000.  Note: For this item, Drug Management Fee Assessment Form should be attached, which is to be passed on by the Clinical Trial Center to the specific pharmacist for the experiment in the Hospital for review. |
| Initial fee of trail (J) |  | For applicable drug clinical trial, Phase I or II of drug clinical trial: NT$ 100,000 per case; Phase III or IV: NT$ 50,000 per case. The judgement basis of these costs shall be based on the Experiment Categories and Planned Phases submitted to IRB of this Hospital. In the case of a drug clinical trial case in Phase II-III , it shall be charged according to the Phase II standard.  □Non-drug clinical trial case: No trial initial fee is charged.  □Drug clinical trial case: □Phase I/II/II-III: NT$ 100,000, □Phase III/IV: NT$ 50,000. |
| Total  in \_\_year |  |  |