

AGREEMENT FOR CONDUCTING THE CLINICAL TRIAL _____

(protocol code, Foundation code number)

Madrid, on the ____ of _____ of _____

GATHERED

First party, Mr./Ms. _____ (name of the legal representative of the **SPONSOR**), N.I.F. number _____, acting on behalf of _____ (full name of SPONSORING organization – pharmaceutical laboratory, scientific society, legal entity), (**THE SPONSOR**, from now on), domiciled at _____ (full **SPONSOR'S** address) _____ from (town and zip code), and C.I.F. number _____, authorized as per power of attorney issued at _____, dated _____, and notarized by Mr./Ms. _____.

Second party, **Mr.**....., with N.I.F. number, acting on behalf of the **FOUNDATION FOR BIOMEDICAL RESEARCH FROM THE HOSPITAL** (**THE FOUNDATION**, from now on), domiciled at....., from Madrid - España, with C.I.F. number....., authorized as per power of attorney issued at Madrid, dated, and notarized by Mr./Ms.from Madrid.

D.acting on behalf of the **Hospital**(**HOSPITAL**, from now on), in property and accordance with the agreements between the **FOUNDATION** and the **HOSPITAL**

Third party, Mr./Ms. _____ (name of **Principal Investigator**), with N.I.F. number _____, acting on his/her own behalf (**PRINCIPAL INVESTIGATOR**, from now on) domiciled at, for notification purposes, at the Service of _____ of Hospital _____ (full name of the center), (**HOSPITAL**, from now on), located at _____ (full address of the center), from _____ (town and zip code), with C.I.F. number _____.

All parties (from now on, **the parties**) acknowledge that they have the required capacity to bind themselves by the present Agreement.

THEY STATE

That the **SPONSOR** is interested in conducting the **CLINICAL TRIAL** described in the first clause of the Agreement.

That the **FOUNDATION** (every **FOUNDATION** shall include here a specific paragraph on the ruling and accrediting norm, and on the agreements with the Hospital).

That the **FOUNDATION** and the “Instituto Madrileño de la Salud”, at present called “Servicio Madrileño de Salud” subscribed, with date June, 1st 2004, an agreement on the relationships between both institutions and it is established in article 3.6., that the **FOUNDATION** will sign and manage the clinical trial contracts which will be held in this **HOSPITAL**.

Based on the above, the parties decide to formalize this Agreement, according to the following:

CLAUSES

1. FIRST.- PURPOSE

1.1. The purpose of this Contract is to conduct a **TRIAL** titled “_____” (**TRIAL**, from now on), protocol code “_____” (**PROTOCOL**, from now on), to be mainly conducted at the **HOSPITAL** dependencies, identified in the expository of the present Agreement, under the leadership and responsibility of Dr. _____ as **PRINCIPAL INVESTIGATOR** of the trial. The **TRIAL** will be implemented according to the content specified by the **PROTOCOL**, identical version and dated _____ as that approved by the CEIC _____ (CEIC information –name, center-), under CEIC approval report reference (reference CEIC data), dated on _____.

2. SECOND.- START AND DURATION

2.1. The **TRIAL** will not be initiated unless the mandatory permission of the Spanish Agency for Drugs and Health Products (“Agencia Española de Medicamentos y Productos Sanitarios”, **AEMPS**, from now on) has been issued. The parties commit themselves to make sure that the **TRIAL** is conducted as specified by the **PROTOCOL**, and specifically, not to start the **TRIAL** without the permission of the **AEMPS**.

2.2. The estimated duration of the **TRIAL** is _____ months from the date of the **AEMPS** permission, as indicated in the protocol. In case of competitive recruitment, the number of the recruited subjects may differ from the number originally planned.

3. THIRD.- APPLICABLE NORM

3.1. Parties agree, at all times, to respect and comply with current legislation applicable at the time of signature of this Agreement and during its validity, as well

as to expressly comply with principles and ethical norms, particularly, the following:

- 3.1.1. Law 29/2006, dated July 26, on Warranties and Rational Use of Drugs and Sanitary Products.
- 3.1.2. Royal Decree 223/2004, dated February 6th, regulating clinical trials using drugs (**RD 223/2004**, from now on)
- 3.1.3. Decree 39/1994, dated April 28, for the control of competencies on clinical trials using drugs at the Madrid Community.
- 3.1.4. Order SCO 256/2007, dated February 5th, establishing detailed principles and guidelines of good clinical practice, and requirements to authorize drug manufacturing or imports for research on human subjects.

4. FOURTH.- DUTIES OF CONTRACTING PARTIES

4.1. The contracting parties are bound to fully implement all clauses of this contract, according to its provisions of those of the PROTOCOL. Each party shall comply with its obligations, as per the normative indicated in the third Clause. For each party, obligations, duties and functions under RD/2004 are considered as bonding content in the current Agreement, so any violation will be considered as non-compliance of the current Agreement.

4.2. Parties are committed to:

4.2.1. Collaborating in the TRIAL follow-up visits conducted by: (i) CEIC, (ii) the monitors and auditors acting on behalf of the SPONSOR, and (iii) the competent authorities when conducting inspection interventions. There shall be at least a one week notice prior to these visits (unless agreed otherwise among the parties). Technical and organizational steps will be taken during these follow-up, monitoring and audit visits to ensure maximum compliance with norms to protect personal data.

4.2.2. Comply with internal HOSPITAL and FOUNDATION regulations, on the part of the INVESTIGATOR, SPONSOR, monitors and auditors, as well compliance with the development guidelines for the TRIAL established by the CEIC responsible for its monitoring.

4.2.3. Not issuing agreements or pacts related to the implementation of the TRIAL that might result in exceptions or contradictions with its content. Therefore, each Party states that, as of this date, none of them are part of any agreement or pact that might contradict its content. Specifically, by virtue of this Clause, the Parties shall accept that there will be no agreement to provide compensation of any kind to the PRINCIPAL INVESTIGATOR, or any of his/her collaborators other than those stated in this Agreement. Expenditures for meetings to organize and supervise the implementation of the TRIAL are excluded, as well as those to analyze or disseminate the results (scientific presentations or publications).

- 4.3. In addition to the obligations stated in the applicable norms, the SPONSOR is bound to provide constant support to the PRINCIPAL INVESTIGATOR and to provide him/her and CEIC with any new relevant information related to the drug under research.
- 4.4. The FOUNDATION is bound to the financial management of the present TRIAL. The FOUNDATION shall receive the payments from the SPONSOR, and will distribute them according to Annex I.
- 4.5. The **PRINCIPAL INVESTIGATOR** agrees to safeguard the patient identification codes. The **SPONSOR and PRINCIPAL INVESTIGATOR** agree to maintain the essential documents of the TRIAL during the time period and according to the conditions set forth by current legislation.
- 4.6. It is the **PRINCIPAL INVESTIGATOR'S** responsibility to select the members of the research team and the support staff for the **TRIAL**. They can either be individuals, trading entities, or organizations of a different nature, with adequate material and human resources for its implementation.

FIFTH.- ECONOMIC ASPECTS

- 5.1. The cost of this TRIAL has been initially budgeted at _____ EUROS (_____ €) (TRIAL budget, from now on). This cost has been determined by applying a cost of _____ EUROS (_____ €) per subject to be evaluated, as established by the Economic Memorandum of the **TRIAL** (Annex 1), which specifies all economic aspects.
- 5.2. The sum to be provided by the **SPONSOR** during the implementation of the **TRIAL** will be set according to the specifications of Annex 1, and shall be paid to the **FOUNDATION** as detailed below:
- 5.2.1. _____ % of the **TRIAL** budget to be paid upon signature of this contract.
- 5.2.2. The remainder of the **TRIAL** budget shall be paid, at least each semester, as detailed in the table of cost per visit and recruited patient, included as Annex 1, until the total cost of the budget is paid off. The **SPONSOR** and the **PRINCIPAL INVESTIGATOR** will report to the **FOUNDATION** on a quarterly basis.
- 5.2.3. These instalments will be considered as partial payments to the account, subject to the liquidation of final total expenses of the **TRIAL**.
- 5.3. The final contribution of the **SPONSOR** for the implementation of the **TRIAL** shall be determined by actual activities implemented while conducting the **TRIAL** (**Final cost**, from now on). Final cost will be estimated as follows:
- 5.3.1. Within a maximum period of three (3) months, from the completion of the **TRIAL** at the **HOSPITAL**, the **SPONSOR** and the **PRINCIPAL INVESTIGATOR** shall report in writing to the **FOUNDATION** the total

number of (i) recruited and evaluated subjects, (ii) actual number of visits, (iii) resulting incidences, as well as any tests, analysis, examination, consultation, or hospital stay of special nature that might have occurred, whether or not included in the Economic Memorandum (Annex 1).

5.3.2. As soon as the information mentioned below had been communicated, the **FOUNDATION** will calculate and notify to the parties the final cost of the **TRIAL**, as well as the remaining amounts to be paid by each of them, if applicable. This settlement of the Final Cost will determine the amounts owed by each party, which must be paid by who ever results to be creditors in the period of one (1) month with no need of subsequent requirement.

5.4. All payments will be made upon the presentation of an invoice; the corresponding IVA will be added as per current legislation at the time of payment, under the **SPONSOR's** name. The payment will be made through a bank transfer to:

Name: Fundación para la Investigación Biomédica del Hospital
Banking Entity :
Account number:
IBAN.:
SWIFT.

5.5. Once payments are made by the **SPONSOR** to the **FOUNDATION** they will be under the responsibility of the **FOUNDATION**. It shall be liable for making payments to the researchers or to the trial subjects.

SIXTH.- INSURANCE AND LIABILITY

6.1. The **SPONSOR** has a civil liability policy that meets all requirements under RD 223/2004. This policy, number _____, has been issued by the insurance company _____, and covers any damages arising from the participation of subjects in the **TRIAL** under this Agreement. Policy is in force, as long as the premiums paid by the **SPONSOR** are up to date. The coverage of this policy explicitly includes the **PRINCIPAL INVESTIGATOR** and his/her collaborators, the **HOSPITAL**, and the **FOUNDATION**, (copy of the policy or certificate is attached).

(On an exceptional basis, a different clause may replace this one in case the **SPONSOR** provides a financial warranty, instead of a civil liability policy).

SEVENTH.- CONFIDENTIALITY ASSURANCE AND PROTECTION OF PERSONAL DATA

7.1. To comply with all requirements under current legislation, the parties agree to take all necessary steps within their means to ensure the confidentiality of the information collected for the implementation of the **TRIAL**, as well as the personal data of participants in the trial. Exceptions are: (i) Public domain information, (ii) information previously known by the **PRINCIPAL INVESTIGATOR** or the **FOUNDATION** at the moment of disclosure, or (iii) mandatory disclosure of information enforced by law.

- 7.2. All parties, insofar as they access and deal with personal data from the **TRIAL** participants, have to take all necessary steps to protect this data and prevent access by a third unauthorized party. The parties are bound to the utmost strict observance of what is stated in law 15/1999, dated December 13, on Personal Data Protection, law 8/2001, dated July 13 on Personal Data Protection at the Madrid Community, and law 41/2002, dated November 12, which regulates patient autonomy.

EIGHTH.- DRUGS UNDER RESEARCH

- 8.1. The **SPONSOR** will provide drugs under research free of charge, including comparison drugs and those used as placebo, as per RD 223/2204 guidelines.

(As an exception, this could be substituted by a clause stating the agreement with the **HOSPITAL** for other means to supply research drugs). *(This paragraph will replace the previous one in academic CT).*

- 8.2. The drug under research will be supplied through the **HOSPITAL** Pharmacy Service and will be administered in a controlled manner, as specified by the **PROTOCOL** guidelines.
- 8.3. The drug under research shall not be available to researchers unless a favourable CEIC report and the mandatory authorization of the AEMPS have been secured.

NINTH.- CONTRACT MODIFICATION, TERMINATION, OR SUSPENSION

- 9.1. Any modification to the provisions of this Agreement shall be done in writing, signed by all Parties and attached as an *addendum*. In any case, the modification shall include that which is stated in article 25 of RD 223/2004.
- 9.2. The **TRIAL** can be discontinued or suspended by any of the Parties under any of the conditions included in article 26 of the RD 223/2004, as well as under the following circumstances:
- 9.2.1. Non compliance of essential obligations undertaken by any of the parties.
 - 9.2.2. Non compliance or defective compliance of the remaining obligations undertaken by any of the Parties, as long as such non compliance has not been remedied within fifteen (15) days after giving written notification
 - 9.2.3. Written mutual agreement among the parties.
- 9.3. Discontinuation or suspension of **TRIAL** implementation shall allow the dissolution of the Agreement by the Party that has not breached the obligations of the Agreement.
- 9.4. Upon completion of the **TRIAL**, the Parties shall ensure the participants safety, as well as the continuity of the treatment and compliance with current legislation on subject matter.

TENTH.- RESULTS AND PUBLICATIONS

- 10.1. All **TRIAL** data and results, as well as resulting studies and patent rights, are property of the **SPONSOR**, and the Parties are bound to comply with relevant legislation. This does not preclude the **PRINCIPAL INVESTIGATOR** and the **FOUNDATION** from using the results in their professional activities.
- 10.2. As per provisions of RD 223/2004, once the **TRIAL** is finished, the **SPONSOR** is bound to publish the results, whether positive or negative, in scientific media accessible to the public.
- 10.3. If the **SPONSOR** has not published the **TRIAL** final results, the **PRINCIPAL INVESTIGATOR** can disseminate the data, discoveries or inventions through journals or scientific publications, making reference to the **SPONSOR**, at least. This shall be conducted according to following criteria: Trials on non-marketed products: during the first year, once authorized and marketed in any country; Trials conducted after product has been marketed, during the following year after the completion of the Trial, except when there is a commitment to publish the results in a medical journal submitted to peer review, or if there is an infringement to national law. The **SPONSOR** shall receive for his/her review, a copy of the text proposed for publication and/or dissemination, at least forty-five (45) days before it is sent to a scientific journal and at least twenty (20) days before it is summarized as an abstract. In any case, the **PRINCIPAL INVESTIGATOR** can only use this data subject to prior written authorization on purpose from the **SPONSOR** is issued.

ELEVENTH.- GOVERNING LAW

- 11.1. To resolve any dispute concerning the application or interpretation of the provisions of this Agreement, the parties submit to the jurisdiction of the courts and tribunals in the city of the Madrid Community where the Hospital is located, expressly renouncing to their rights to any other jurisdiction that they might be subjected to.
- 11.2. Should a copy of this Agreement become available in any other language or tongue, the Spanish version shall prevail.

In Witness Whereof, as proof of consent, all Parties sign this document in triplicate for this sole purpose

SPONSOR

FOUNDATION and HOSPITAL PRINCIPAL INVESTIGATOR
