**AGREEMENT BETWEEN THE LA PAZ UNIVERSITY HOSPITAL FOUNDATION FOR BIOMEDICAL RESEARCH, …………..………….. (INVESTIGATOR) AND ………………………… (SPONSOR) FOR THE CONDUCT OF THE CLINICAL TRIAL "………………………………………………………………..…………………………..……...."**

**STUDY CODE:**

**HULP CODE:**

**CLASSIFICATION:** (EPA-SP; EPA-AS; EPA-OD; EPA-LA; NO EPA, OTROS)

In Madrid, on ……………….. 2018

**BEING ASSEMBLED**

**(\*) Set according to specific situation of the parties**

On the one party, Mr./Mrs........................................., with Tax Identity Number .................. on behalf and in representation of .............................with registered address in ………………………………………….. and with CIF/VAT NUMBER/ID .................. (hereinafter the **SPONSOR**),

On the other party, Mr./Mrs......................................., with Tax Identity Number .................. on behalf and in representation of ..................................with registered address in ………………………………………….. and with CIF/VAT NUMBER/ID .................. (hereinafter the **CRO**),

On the other party, Mr.Mrs. .....................................…(name of the legal representative of the**CRO**) with Tax Identity Number .................. acting as legal representative of..............................…(name of the**CRO**), with registered address in .....................................................… (full address of the **CRO**) and with CIF/ VAT NUMBER/ID .......................(hereinafter the **CRO**), acting on behalf and in representation of the**SPONSOR**…………..................… (full name of the sponsoring entity), authorised to execute this document by virtue of a deed of power of attorney duly registered with the Companies Register of .....................…, authorised by the Notary Public Mr/Mrs. ........................…, of the Notary Association of ..................… on ................…This is without prejudice of the Sponsor’s responsibility under **RD 1090/2015;**

On the other party, Mrs Ana Coloma Zapatero, with Tax Identity Number 29151547-J, acting on behalf and in representation of the **LA PAZ UNIVERSITY HOSPITAL FOUNDATION FOR BIOMEDICAL RESEARCH**, (hereinafter **FOUNDATION**), with registered address Paseo de la Castellana, 261 in Madrid (28046), with VAT number G83727057, duly authorised to execute the present document by virtue of the power of attorney authorised in Madrid on 15 January 2010 by the Notary Public of Madrid Mrs Carmen Boulet Alonso, with number 48 of her record

On the other party,Mr. Rafael Pérez-SantamarinaFeijóo, acting on behalf and in representation of **LA PAZ UNIVERSITY HOSPITAL** (hereinafter **HOSPITAL**), by virtue of the agreements between the **FOUNDATION** and the **HOSPITAL**;

And on another party, Mr/Mrs. .....................................*,* with Tax Identity Number ........................., acting on his/her own behalf and representation (hereinafter **PRINCIPAL INVESTIGATOR**), with domicile for notification purposes the .................................. Service of the **HOSPITAL** with address at Paseo de la Castellana, 261 in Madrid (28046).

The Parties mutually acknowledge their capacity to enter into, and the binding force of, this Agreement (hereinafter **the Parties**),

**THEY STATE**

**1.** That according to that available in the current Agreement signed June 17, 2009, between **SERMAS** and **FIBHULP**, it is the responsibility of **FIBHULP**, among other functions, to manage observational studies carried out at **LA PAZ UNIVERSITY HOSPITAL.**

**2.** That similarly, byvirtue of the agreement signed between **LA PAZ UNIVERSITY HOSPITAL** and **FIBHULP** for the development of clinical trials, the hiring and execution of clinical trials to be performed at **LA PAZ UNIVERSITY HOSPITAL** is the responsibility of **FIBHULP.**

**3.** That in said Agreement, it is established that it is incumbent upon the **SPONSOR** of the study and the **PRESIDENT OF THE FOUNDATION**, or the person delegated, to sign the contract in which the economic aspects related to the observational study to be performed at the **HOSPITAL** are reflected.

**4.** That the **SPONSOR** is interested in contracting **FIBHULP** to conduct the observational study titled: **"……………………………………….………...………."**(hereafter called **STUDY**) under the direction of **……………………………………...(INVESTIGATOR),** of the **……………………** Department of **LA PAZ UNIVERSITY HOSPITAL.**

**5.** Said study will be performed in the clinical and healthcare parts in the facilities of **LA PAZ UNIVERSITY HOSPITAL** according to the protocol kept on file in the **CREC** and according to current legal regulations:

- **Royal Decree 577/2013,** in which the pharmacovigilance of medications for human use is regulated;

- **Order SAS/3470/2009,** which publishes guidelines on post-authorisation observational studies for drugs for human use and applicable legislation of the Autonomous Community of Madrid;

- **Royal Decree01/2015, of 24 July**, approving therevised text of the Acta approving guarantees and rational use of medicines and health products;

- **Royal Decree 1345/2007** of 11 October, regulating the authorisation and registration procedures and the dispensing conditions for industrially manufactured medicines for human use;

- **Law 1/1998 of March 2**, Foundations of the Community of Madrid. According to Article 23, employers may contract with the Foundation, either on its own behalf or on that of a third party, prior authorisation of the Protectorate of Foundations.

- **Organic Law 15/99** of 13 December on the protection of personal data and **Act 41/2002, of 14 November**, governing the Basic Aspects of Patients’ Autonomy.

**- Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016** on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing **Directive 95/46/EC (General Data Protection Regulation)**

- The Parties agree that the **STUDY** shall be conducted under the **Principles of the Helsinki Declaration** and according to the **International Conference of Harmonisation (ICH) Guideline for Good Clinical Practice**; they shall comply also with the applicable deontological principles and the international and local anti-bribery and anti-corruption laws, in particular those adopted under the **OECD Convention of 21 November 1997, the Foreign Corrupt Practices** Act and any other that may be applicable to the Parties of the Agreement.

**6.** That the **SPONSOR** has obtained permission fromthe Spanish Agency for Drugs and Health Products (hereinafter **AEMPS**), **“Date of Approval by the AEMPS”,** approval from the Clinical Trials Ethics Committee **(CREC)** of the Hospital **“Name of Hospital whose CREC has given approval and City”** on **“Date of Approval by the referred CREC”** and by the Autonomous Community of Madrid **“Date of Approval of the A.C.M”** and obtained the Consent of HULP Management on **“Date of Consent of HULP Management”.**

Now, therefore, the Parties express their desireto execute this Agreement according to the following:

**cLAUSES**

**ONE.- OBJECT AND DURATION**

**1.1.** The **SPONSOR** contracts **FIBHULP** to perform the study previously cited, which will be performed primarily in the facilities of **LA PAZ UNIVERSITY HOSPITAL** under the management of the **PRINCIPAL INVESTIGATOR** according to the regulations specified in the protocol.

**1.2.** The estimated duration of the research will be **……. Months.**

**1.3.** The Centre and the researcher are considered independent contractors, and at no time during the performance of the study can they be considered employees of the sponsor.

**1.4.** The study will be conducted complying strictly with its protocol, and if the sponsor should make any modifications to this protocol, they commit to communicating the changes and, if necessary, to submit them for prior approval/verification by the Ethics Committee for Clinical Research (**CREC**) of the Centre.

**TWO.- DUTIES OF THE PARTIES**

**2.1.** The parties undertake to collaborate and keep each other informed concerning the Study in order to ensure its success.

**2.2.** The Parties undertake to cooperate with the monitoring visits of the Study that are performed by:

▪ The **CREC**;

▪ The monitors and auditors acting on request of the **SPONSOR**;

▪ The competent authorities when these carry out inspection visits. A minimum notice period of one week will be providedfor such visits except where an agreement exists between the parties stipulating a different time period. Throughout the follow-up, monitoring, and audit visits, those technical and organisational measures will be implemented that guarantee maximum respect for regulations governing the protection of personal data.

**2.3.** The **INVESTIGATOR**, **SPONSOR**, monitors, and auditors undertake to observe the internal regulations of the **HOSPITAL** and the **FOUNDATION**, along with any indications made by the **CREC** responsible for monitoring the study concerning the development of same.

**2.4. FIBHULP** will have the resources needed to guarantee that the **RESEARCHER** complies with current legislation in terms of Observational studies post-authorisation, subject to the ethical norms regulated, as well as ways to facilitate the conducting of audits on the part of the Study Monitor, ……………………..….. **(Name of Study Monitor)**, or those designated by the competent Authority.

The Monitors will act, in all cases, subject strictly to the Protocol and will only have access to the parts of documentation and clinical history of the included patients if, and only if, the Principal Investigator or some member of the research team is present, to ensure that they will have access only to the data strictly necessary to check the correct performance of the study, guaranteeing the confidentiality of the data during the study. In case of a substitution, the Sponsor will report the identity of the newly designated monitor to the Centre.

**2.5.** The Principal Investigator, through the Foundation, will select and hire the members of the research team and the support staff for the study, and staff whowill act independently and without any employment link whatsoever with the Foundation, except in those cases in which some of the members of said team are already on staff at **FIBHULP**. The team can be formed by actual people as well as by mercantile entities or those of another nature,whichincludes material and human means appropriate for the execution of the work.

In the case of researchers and staff not officially hired by **FIBHULP** and/or **HULP**, the amount that the Foundation agrees to with each of them will be paid upon presentation of the corresponding invoices for professional honoraria in their name, in which the VAT must be included and legally must have effect.

**THREE.- FINANCIAL ASPECTS**

**3.1.** The **SPONSOR** will pay the **LA PAZ UNIVERSITY HOSPITAL FOUNDATION FOR BIOMEDICAL RESEARCH** the total amount the study requires plus corresponding VAT upon reception of invoice(s), according to the conditions and terms established as follows:

|  |  |
| --- | --- |
| **ENTITY IN CHARGE OF FINANCIAL ASPECTS (Invoicing Details)** | |
| **NAME** |  |
| **VAT NUMBER/ TAX ID No** |  |
| **REGISTERED ADDRESS** |  |

**(\*)** In order that the Foundation can issue invoices to the detailed costs in this Study Budget, the Sponsor/CRO shall communicate in writing to the FIBHULP at least twice a year the total amount for visits have been made, detailing the breakdown of each one of these visits, including the amounts of actually performed visits, tests, procedures, etc.To do this, the Sponsor/CRO shall forward this information in a mail to **ensayosclinicos@idipaz.es**

The **CRO**, as the **SPONSOR**’slegal representative, is authorised to carry out payments on behalf of the **SPONSOR**, and that the **CRO**’s signature is not required for the amendment/change of all other aspects of the Agreement in which the **CRO** is not directly involved.

**3.2.** The Sponsor will make periodic semestral payments, starting from the beginning of the study, of the amounts corresponding to work completed until that time.

**3.3.** The payments will be made by bank transfer to **FIBHULP**:

|  |  |
| --- | --- |
| **BENEFICIARY** | Fundación para la Investigación Biomédica  del Hospital Universitario La Paz |
| **CIF/ VAT NUMBER/ ID** | ESG83727057 |
| **BANKING ENTITY** | La Caixa  C/ Hermanos García Noblejas 18 (Madrid) |
| **IBAN** | ES47 2100 4065 1322 0009 2143 |
| **SWIFT** | CAIXE SBB |

**3.4.** So that the prior can be performed to good ends, the **SPONSOR** is required to present a detailed account of the follow-up of the study to the Ethics Committee and to the Foundation by visits conducted and patients included, with trimestral periodicity.

All economic aspects related to the study will be reflected in the economic account that accompanies this contract (Appendix I). However, the details of the amount predicted to be paid by the SPONSOR to FIBHULP for the study areindicated as follows:

1. The amount of **€1,500** management fee upon the signature of this contract shall be paid the same;
2. The amount of **………….. Euros** plus VAT per evaluable patient**(80% of the total per patient)**;i.e., whohave their data properly recorded in the corresponding sheet in order to meet the following expenses of **FIBHULP** directly related to the trial: compensation for the activity of the research team as well as the activity of the study support staff; purchases of devices and equipment and other expenses of the Research Unit. The prediction of the inclusion of **……….. patients.**

No payment whatsoever will be made for those patients included and treated who have significantly violated the Protocol. All those patients who have been excluded after the randomisation for adverse events and that require evolutionary follow-up will be paid in full.

Incomplete patients will be paid for according to the work performed with the breakdown of visits shown in **APPENDIX I.**

1. For expenses related to the functioning of the Foundation for management of the study, the Sponsor will pay the amountof **……… Euros** plus VAT **(20% of the total per patient).**

**FOUR.- EXCLUSIVITY**

**4.1.** The **SPONSOR** states that no agreements have been issued nor shall be made other than this contract with the **PRINCIPAL INVESTIGATOR** and his or her collaborators from which additional financial remuneration or payment in kind may result.

**4.2.** This clause excludes expenses for meetings held for the organisation of the Study and those support that the **SPONSOR** might have in future for the reporting the findings in scientific meetings and publications.

**FIVE.- CONFIDENTIALITY ASSURANCE AND PROTECTION OF PERSONAL DATA**

**5.1. FIBHULP** will make available the recourses necessary to ensure that the **RESEARCHER** treats the documentation, information, results, and study-related data according to their confidential and secret character, maintaining restricted circulation of said information and ensuring that this obligation is complied with by all persons that must have access to it, in accordance with that agreed in this commitment.

**5.2.** With regard to the obligations of the study sponsor, when personal data of the researchers and/or patients is stored, appropriate measures must be taken to protect them and prevent access to them by unauthorised third parties according to the**Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016** on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing **Directive 95/46/EC (General Data Protection Regulation)**, **Organic Law 15/99 of December 13** for the Protection of Data of a Personal Nature and **Royal Decree 1720/2007 of December 21,** in line with the regulations forits implementation and in **Law 41/2002** on patient autonomy and rights to information and clinical documentation of 15 November 2002. Such legislation will be applicable to the personal data contained in this agreement.

**5.3.** If the Researcher or the Centredoes not have an adequate place to store the information during the time required by law for this kind of observational study, the Sponsor commits to facilitate said storage of documentation in an appropriate place for its custody.

**SIX.- RESULTS AND PUBLICATIONS**

**6.1. FIBHULP** recognises the ownership of the **SPONSOR** of the data and the results derived from the observational study named in this contract.This does not preclude the right of the **PRINCIPAL INVESTIGATOR** and of the **FOUNDATION** to use the results in their respective professional activities.

**6.2.** The **SPONSOR** undertakes to publish the results, whether positive ornegative, of this study in scientific media accessible to the public. In any case, the publication of the study, as agreed by both parties, will be made in scientific publications, always mentioning the Ethics Committee for Clinical Research (**CREC**) and the competent authorities of the Autonomous Communities that have approved the observational study, as well as the source of funding.

**SEVEN.- CORRUPT PRACTICES**

**7.1.** The anti-corruption policy provides that the members of the staff of ……………………………. (**SPONSOR**) and of any third party acting for the account or on behalf of the **SPONSOR** shall not have any personal interest or commitment that mightconflict with or limit their capacity to comply in an ethically adequate manner with their respective obligations under this Agreement. Said policy provides also that any activities performed in connection with this Agreement shall comply in all respects with the ethical standards and principles above and anyapplicable laws. ……………………………. (**SPONSOR**) considers that an ethical, transparent behaviour is of the essence and applies a zero-tolerance policy to any and all corrupt practices.

**7.2.** The members of the staff of …………………………… (**SPONSOR**) and of any third party acting on behalf of the **SPONSOR** shall not initiate any contact or authorise directly or indirectly payments of any type to any of the parties participating in the **CLINICAL TRIAL** with the aim of securing an unfair advantage or to unduly influence any decision. The term ‘Payment’ shall include payments or commitments to pay any money or anything of value, or the offer of any other good or service.

**7.3.** The **FOUNDATION** shall keep a register of any economic transaction arising from this Agreement and shall make available to ………………… **(SPONSOR),** upon the latter’s request in writing, any documents required to verify due compliance with the commitments acquired within this instrument.

**EIGHT.- DRUGS UNDER RESEARCH**

**8.1**. The **SPONSOR** shall provide, free of cost, the drugs under research, including comparison drugs and those used as placebo necessary for thestudy.

**8.2**. The drug under research shall be supplied through the **HOSPITALPHARMACY SERVICE** and shall be administered in a controlled manner, as specified by the **PROTOCOL** guidelines.

**8.3.** The drugs under research shall not be available to researchers unless a favourable **CREC** report and the mandatory authorisations have been obtained.

**NINE.- CHANGES TO OR CANCELLATION OF THE STUDY**

The Study can be modified or cancelled at the request of one or both parties or by mutual agreement in the following circumstances:

**▪ 9.1.-** Impossibility of including a minimum number of patients to allow the final evaluation of the observational study in a reasonable amount of time;

**▪ 9.2.-** Acts of god;

**▪ 9.3.-** If an intermediate analysis of the existing data suggests it;

**▪ 9.4.-** By decision of the EMA.

Amendments to the terms of the Agreement shall be in writing duly signed by the Parties and as an **addendum** thereto.

In case the observational study is suspended, the **SPONSOR** will pay to **FIBHULP** the amount corresponding to the work completed.

**TEN.- JURISDICTION**

In order to resolve any discrepancy that mightarise in the application or interpretation of that established in the present agreement, both parties agree to submit themselves to the jurisdiction of the Courts and Tribunals of Madrid for any matter derived from the present contract.

Should a copy of this Agreement become available in any other language, the Spanish version shall prevail.

And in order to state the legal effects, as a show of agreement, all parties sign the present document, in triplicate and for one purpose.

For the **SPONSOR**, For the **CRO**

Mr. /Mrs ………………….. Mr./ Mrs ………………………

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## For the FOUNDATION

Fdo.: Doña Ana Coloma Zapatero

## For the HOSPITAL

D. Rafael Pérez-SantamarinaFeijóo

Fort the **PRINCIPAL INVESTIGATOR**

Mr./Mrs ………………………

#### APPENDIX 1.- STUDY BUDGET

**PROTOCOL CODE:**

**STUDY TITLE:**

**▪ SUMMARY OF THE STUDY BUDGET**

|  |  |
| --- | --- |
| **ESTIMATED NUMBER OF PATIENTS TO RECRUIT** |  |
| **PAYMENT COMPLETE AND EVALUABLE PATIENT** | **€** |
| **TOTAL COST OF STUDY** | **€** |

**▪ BREAKDOWN FOR VISITS**

|  |  |  |  |
| --- | --- | --- | --- |
| **DESCRIPTION** | **NUMBER OF VISITS** | **COST PER VISIT** | **TOTAL WITHOUT EXTRAORDINARY COSTS** |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |
| **TOTAL COST PER SUBJECT** |  | **€** | **€** |

|  |  |  |  |
| --- | --- | --- | --- |
| **ADDITIONAL TESTS** | **UNITS** | **PAYMENT€** | **TOTAL €** |
|  |  |  |  |
|  |  |  |  |

**(\*) ADDITIONAL TESTS carried out for this type of patient in usual care**

|  |  |  |  |
| --- | --- | --- | --- |
| **EXTRAORDINARY DIRECT COSTS** | **UNITS** | **COST** | **TOTAL €** |
|  |  |  |  |
|  |  |  |  |

**(\*) ADDITIONAL TESTS that have an extra cost for the Hospital and are performed outside of usual care**

**1.1   FOUNDATION**

FIBHULP may designate this quantity to address the expenditures directly related to the trial: compensation for the research team’s activity and the study support staff’s activity; purchasing equipment and other expenditures of the Research Unit.

**1.2   CONTRACT MANAGEMENT**

The **SPONSOR** shall pay the Foundation **€1500** for Administrative and Contract Management Expenses on signing the agreement.

**APPENDIX\_2: LIST OF INVESTIGATORS (with DNI)**