ANEXO I

TEXTO ORIGINAL COMPLETO

AGREEMENT TO CONDUCT CLINICAL TRIALS WITH MEDICINAL PRODUCTS

Title: A RANDOMIZED, OPEN-LABEL, MULTICENTER, CONTROLLED STUDY TO ASSESS SAFETY AND EFFICACY OF ELAD® IN SUBJECTS WITH ACUTE ALCOHOLIC HEPATITIS (AAH) AND FAILURE PER THE LILLE SCORE

Protocol Code:

EUDRACT No:

In ___, on April M _ 2015,

BY AND BETWEEN

Of the first part _____, acting as **Managing Director of the Integrated Health Organisation** _____ and on behalf of the said Organisation with registered address at _____and CIF (Fiscal Identification No.) _____(hereinafter Site)

And of the second part, _____ acting as Scientific Director of the _____ **(hereinafter** XXX**),** and on behalf of the said Organisation with registered address at _____ and CIF (Fiscal Identification No.) _____ under the powers of attorney bestowed by public deed, granted in her favour by the said entity and executed before _____, Notary in _____, on 10 March 2014 under number _____ of his official records

Of the third part, _____ on behalf of _____ (hereinafter **"Sponsor"**), with registered address at _____ and US Fiscal Identification No. _____ with legal capacity to sign this agreement.

And of the fourth part, Ms _____, with NIF (Fiscal Identification No.) _____ and with address, for notification purposes, at the Site's Digestive Unit/Service. Acting on her own behalf, as Principal Investigator, (hereinafter also referred as **"Principal Investigator"**).

All parties mutually recognise each other's full capacity to execute this document.

II. Declare

1. Whereas the Sponsor is interested in conducting a clinical trial with medicinal products, as identified in the heading of this agreement, with the aims and objectives as follows: to assess the safety and tolerance of the product _____ with respect to the global survival in population with severe acute alcoholic hepatitis for whom the corticoids treatment has failed.
2. Whereas the Principal Investigator, having reached an agreement with the Sponsor, wishes to exercise the functions assigned to the Principal Investigator of the clinical trial under current regulations.
3. Whereas the Association XXX Institute, has as its foundational goals: to promote the biomedical and epidemiological research of public health and health services; to scientifically base the programmes and policies of the sanitary system and to enhance preferably the translational research, understood as the research aimed to accelerate the transfer of scientific knowledge to the clinical practice, based on international recommendations, within the territorial area of Bizkaia, by virtue of the collaboration agreements with _____ in which the management of the R+D that is developed in this area is commended to it.
4. Whereas the Site is prepared to develop the trial as regards the provision of health services and material aspects necessary for its implementation under the conditions agreed by the Sponsor and XXX.

Therefore, and pursuant to the foregoing, the parties enter into this Agreement to conduct the clinical trial (hereinafter also referred to as the **"Agreement"**), based on the following

III. Clauses

1. Purpose

1.1. The purpose of this Agreement is the development, for and on behalf of the Sponsor, of the clinical trial with medicinal products identified as "A Randomized, Open-Label, Multicenter, Controlled Study to Assess Safety and Efficacy of ELAD® in Subjects with Acute Alcoholic Hepatitis (AAH) AND Failure per the Lille Score with code

(hereinafter the **"Trial"**), which will be conducted at the Site, under the direction and responsibility of the Principal Investigator and coordinated and managed by BioCruces.

1.2. The estimated number of patients to be included in this Site is four (4) patients.

1.3. The Sponsor bestows the obligation on the Principal Investigator to recruit the required patients to enable the clinical trial to be correctly performed. The patients who will submit to the Trial are to be selected according to the criteria and time limits specified in the Protocol without prejudice to any extension by the parties of the initially envisaged term.

2. Terms of performance.

2.1. Protocol and Good Clinical Practice (GCP).

2.1.1. The Trial shall be conducted in accordance with the conditions and requirements of the Protocol, attached as Annex I (hereinafter, the **"Protocol"**), complying with current applicable legislation at any time, in particular Royal Decree 223/2004, of 6 February, on clinical trials with medicinal products (hereinafter, **"RD 223/2004"**), the GCP standards and the ethical principles regulating the performance of clinical trials with medicinal products in human beings.

2.1.2. The parties will comply with the provisions of the Protocol, including the amendments or modifications, in accordance with the provisions of Article 25 of Royal Decree 223/2004.

2.2. Start and Duration of the Trial

2.2.1. The start of the Trial will depend upon obtaining: the authorisation of the *Agencia Española de Medicamentos y Productos Sanitarios* (Spanish Drug and Healthcare Products Agency) (hereinafter AEMPS), the ruling of the Clinical Research Ethics Committee acting as the reference committee and/or the favourable report by the Clinical Research Ethics Committee (hereinafter CREC), agreement from the Site's management and the signing of this agreement by all parties.

2.2.2. The Trial duration is as indicated in the Protocol, approximately 60 months per patient, counting from the patient's enrolment date, on the condition that, previously to the authorization of the AEMPS, the favorable report of the CEIC has been obtained, and the present contract is signed by all parties. The parties of this Agreement shall consider the Study to be complete and concluded at all sites at such time as all data is collected from all sites, entered into a database, all queries resolved and the database is locked.

2.2.3. The Trial schedule for the Site is attached as Annex II.

2.2.4. The Sponsor undertakes to inform the Site, CREC and XXX as soon as possible after obtaining authorisation from AEMPS.

2.3. Amendments.

2.3.1. Any amendment to the Protocol must be by mutual written agreement between the Sponsor and the Principal Investigator, and notified to the CREC and AEMPS to obtain their approval, as well as the approval of the Site and XXX. If it is considered as an important modification or amendment, an assessment will be made as to whether it is necessary to adapt the Agreement and/or the annexes thereto, by addenda.

2.3.2. Any change of persons participating in the Trial must first be communicated to the Sponsor, CREC and XXX for their approval.

2.4. Legal ethical regulations.

The Trial is to be conducted according to the current regulations applicable at any time. Upon the signing of this Agreement the following regulations are applicable:

2.4.1. Law 29/2006, of 26 July, on Guarantees and Rational Use of Medicines and Healthcare Products.

2.4.2. Decree 3/2005 (Basque Country), of 11 January, establishing the *Comité Ético de Investigación Clínica de la Comunidad Autónoma del País Vasco* (Basque Country Autonomous Community Clinical Research Ethics Committee).

2.4.3. RD 223/2004.

2.4.4. Law 41/2002 of 14 November, basic regulation governing patient autonomy and the rights and obligations attached to clinical information and documentation.

2.4.5. Royal Decree 1015/2009 of 19 June, regulating the availability of medicinal products in special situations.

2.4.6. Royal Decree 1716/2011 of 18 November, establishing the basic requirements for authorisation and operation of Biobanks in biomedical research and treatment of biological samples of human origin, and regulating the operation and organisation of the National Register of Biobanks for Biomedical Research.

2.4.7. Organic Law 15/1999 of 13 December 1999, on Personal Data Protection and Royal Decree 1720/2007 of 21 December, approving the regulation implementing the said Organic Law.

2.4.8. It is of mutual agreement to conduct the Trial in accordance with the Principles contained in the Declaration of Helsinki and in accordance with the ICH

(International Conference of Harmonization) Guidelines for Good Clinical Practice (GCP)

2.5. Informed Consent.

2.5.1. The Trial will be conducted with the utmost respect for patients' rights. The patients will be clearly and precisely informed of the purpose of the Trial and the possible consequences to their health, according to the provisions of Articles 3, 4, 5 and 6 of RD 223/2004. In particular, strict compliance with the obligations to obtain informed consent (Article 7 of RD 223/2004) and the obligations applicable under regulations guaranteeing patient safety is necessary.

2.6. Access.

2.6.1. The CREC shall have access at any time to the Trial documentation necessary to monitor the clinical trials as established in the regulations, especially the informed consent of the patients participating in the Trial.

2.6.2. The relevant Health Authority, the CREC and the monitors and/or the auditors appointed by the Sponsor may have access to the clinical documentation and information at the Site regarding the subjects involved in the Trial, in order to verify the accuracy and reliability of the information on such subjects provided by the Principal Investigator. The designated monitors and/or the auditors shall work in accordance with the provisions of Articles 35 and 36 of Royal Decree 223/2004. The Principal Investigator shall ensure that the monitors, auditors or CROs respect the regulations on confidentiality regarding any information about the study subjects.

2.6.3. The Site will also allow the CREC and relevant health authority inspectors to access such data.

2.7. Publication of results.

2.7.1. The Sponsor is obliged to publish the results of the Trial, whether positive or negative, in scientific media. The Sponsor shall be responsible for producing the final or partial reports, as well as providing them to the appropriate parties. For this purpose, the Principal Investigator will provide the Sponsor with the medical data obtained during the Trial as stipulated in the Protocol in order to issue the

final report signed by the Principal Investigator, in accordance with paragraph k) of Article 35 and paragraph h) of Article 37 of RD 223/2004.

The Trial results may not be published by XXX the Principal Investigator or the Site until the Trial is completely finalised, and prior authorisation to that effect is issued by the Sponsor. For this purpose, a copy of the proposed publication shall be sent to the Sponsor for review at least sixty (60) days prior to its submission for publication. Once it is received by the Sponsor, the Sponsor will have a term of thirty (30) days in order to review the copy of the proposed publication and give its reply to it. If in this period of time, the Sponsor gives no reply, the proposed publication shall be considered approved. Likewise, the Sponsor may request an additional term of up to sixty (60) days in order to guarantee the appropriate protection of the data, results, discoveries, inventions, as well as all the industrial and intellectual rights over them, including the know-how, performed, obtained or developed during the Trial.

2.7.2. The lack of authorisation to publish the results will not prevent XXX the Principal Investigator or the Site from using the results in their professional non-commercial and educational activities.

2.7.3. If the Sponsor has not published the final results of the Trial (understood as the overall results in the case of multicenter trials) within twenty-four (24) months after having received the final report, the Principal Investigator may disseminate those results for professional purposes, and in scientific journals and publications. However, the Sponsor must receive for review, a copy of the proposed publication, at least sixty (60) days prior to its submission for publication, in order for the Sponsor to be able to suggest, if applicable, any modifications which should be included aimed at removing commercial, technical or scientific information which is confidential in nature. Likewise, the Sponsor may request an additional term of up to sixty (60) days in order to guarantee the appropriate protection of the data, results, discoveries, inventions, as well as all the industrial and intellectual rights over them, including the know-how, performed, obtained or developed during the Trial.

2.7.4. When the results are presented at meetings or published in scientific journals in all cases the authorship or inventorship rights to appear as such shall be respected. In addition, reference will be made to the Site where the Trial has

been performed, as well as to the Sponsor who funded the Trial. A copy of the publication or the presentation containing the results must be sent to the CREC.

2.7.5. The participation of the Principal Investigator or his collaborators as authors in multicentre publications will be determined in accordance with the Sponsor's policies and generally accepted authorship standards.

2.7.6. If the Trial was multicentre, then the results will not be published until six (6) months have elapsed as from the first multicentre publication.

2.8. Confidentiality and data protection

2.8.1. The parties to the Agreement undertake to preserve the confidentiality and privacy of the information, results and data relating to the study, including, without limitation, all information related to ____ System and its components, they will maintain restricted circulation of the said information and will be responsible for the fulfilment of this obligation by all persons who rightly have access to the said information in accordance with this Agreement.

The Site and the Principal Investigator will be responsible for the fulfilment of the confidentiality obligations set out in this provision by those Trial participants, as defined in Clause 3.1.3 and 3.1.4, who must have access to the confidential information.

The following information shall be exempt from these confidentiality obligations: (i) when it was already known by the receiving party at the time of disclosure by the disclosing party (ii) it is or becomes part of public domain by any means other than a wrongful act or omission by the receiving party (iii) disclosure is specifically required by law or by an order of a court or tribunal or the administration.

The confidentiality obligations set forth in this section 2.8.1 shall remain in force for a term of 10 years from the date of completion of this Trial.

2.8.2. The Site, the Principal Investigator and the monitors and/or auditors appointed by the Sponsor guarantee that the personal data of the subjects included in the study will be processed in accordance with the provisions of Law 15/1999 of 13 December on Personal Data Protection and the implementing regulations, Law 2/2004 of 25 February on Publicly Owned and Created Personal Data Files of the Basque Data Protection Agency as well as Law 41/2002 of 14 November, basic

regulation governing patient autonomy and the rights and obligations attached to clinical information and documentation. In particular they shall ensure that any personal data of patients communicated to the Sponsor, is previously disassociated, to ensure that the information obtained cannot be associated to an identified or identifiable individual.

2.8.3. XXX undertakes to ensure that the persons or entities hired to perform the said Trial respect the data protection regulations.

3. Participants

3.1. Participants

3.1.1. Sponsor

Contact details:

Organisation: Viral Therapies Inc.

Address: 15010, Avenue of Science, suite 200, San Diego (California), Estados Unidos

Contact person: Michael Stephens

Phone:

Email: mstephens@viraltherapies.com

3.1.2. Principal Investigator:

The Principal Investigator will care for and ensure that all the Trial participants and especially the collaborators will fully comply with this Agreement and its annexes, having been sufficiently informed of the same.

3.1.3. Collaborators

3.1.3.1. The Principal Investigator is responsible for proposing the members of the Research Team and the Trial support team. The following have been proposed by the Principal Investigator as the collaborative investigators:

- Mr Francisco Javier Bustamante.
- Mr
- Mr
-
-

3.1.3.2 Services collaborators:

_____(Reanimation Service)
_____ (Nursing Service)

3.1.4. Other Staff

3.1.4.1. *XXX* may hire the rest of the professionals, as well as the materials needed to conduct the Trial, according to the requirements indicated by the Principal Investigator, the Site and the Sponsor.

3.1.5. *XXX*

XXX's role includes managing the coordination of tasks, finances and administration to support the Site and the Principal Investigator in conducting the Trial correctly.

3.1.6.Clinical Research Organisation Not applicable

3.1.7.Monitor

The Sponsor has designated Mr _____ as monitor of the Trial (hereinafter, the "**Monitor**") with National Identity Document No. The Promoter will be required to inform BioCruces if the said Monitor is replaced.

El Promotor ha designado como monitor/a del Ensayo a Aram de la Fuente Canel (en adelante, el "**Monitor/a**") con DNI En caso de modificación del monitor/a bastará una notificación del Promotor a _____

4. Trial Site

4.1. The Trial shall be conducted in the Hospital Universitario Cruces.

4.2. The Site shall place at the disposal of the Trial the human resources included in its ordinary activities, such as the necessary material, technical and organisational resources, and will adopt organisational measures, assign personnel and acquire materials as required to ensure the regular and proper management and performance of the Trial.

5. Supply of the medicinal products and any special equipment required to conduct the test

5.1. Product

5.1.1. The Sponsor will provide the Principal Investigator, via the Site's Intensive Care Unit, with the material required for the performance of the Trial. These materials will be provided free of charge and will be administered in a controlled manner, as specified by the Protocol guidelines.

5.1.2. The drugs under research, as well as the necessary equipment to perform the trial, may not be used, sold or provided to any third party without the prior written approval of the Sponsor.

5.1.3. After the Trial, the Sponsor agrees to provide, free of charge, the medicinal products corresponding to the Trial to those patients who were active at the Trial closing date, according to the guidelines applied, and which the Principal Investigator considers are appropriate for their treatment. The Principal Investigator, with the Site's approval, must apply to AEMPS for authorisation to use the medicinal products and the Sponsor should give its consent, according to RD 1015/2009. This commitment will remain in effect until the result are published, or for a maximum of one year after the Trial is completed.

5.1.4. Except in the case indicated above and if upon termination of the Trial there are surplus medicinal products, the Site and the Principal Investigator will return such surplus to the Sponsor, agreeing with the latter the procedure to collect, destroy or transfer the surplus.

5.2. Equipment

The necessary equipment to perform the trial will include the ELAD System, the ELAD cartridges, as well as all the disposable components for the treatment of the subjects randomized to receive _____treatment.

The Sponsor shall deliver the____'s System and the _____'s cartridges to the Site's Intensive Care Unit, where an _____ specialist, appointed by the Sponsor will be waiting

at the Site to take receipt of the shipment.

The Site shall facilitate the access to its premises to ~~a minimum of three ELAD specialists~~ the people specialists in ELAD, who have previously obtained the necessary authorisation required by (hereinafter ELAD specialists), who will be responsible for overseeing and safe running of _____ System at the patient's bedside for the duration of____ treatment. The Site shall also grant access to its premises to the ____specialists at the completion of the Trial in order that they disinfect, dismantle and remove the _____ System from the Site.

If extraordinary equipment is required to carry out the Protocol, it will be purchased and installed by the Sponsor, with authorisation and supervision of the Site and (Annex V). Furthermore, the Sponsor will be liable for any maintenance costs during the study. At the end of the Protocol the extraordinary equipment will be removed by the Sponsor at its cost.

6. Biological samples for the performance of the Trial

6.1. The processing, storage and transfer of the biological samples, in accordance with the assignment by _____ to XXXX dated 3rd April 2009, corresponds to the _____ *para la Investigación* (_____ for Research) - _____ (Biobanco), which is a member of _____. The qualifications, experience and use of standard procedures by Biobanco provide added value to the Trial as they guarantee the quality requirements in the management of biological samples, as well as strict compliance with the legal and ethical requirements of such processes as set out in RD 17 16/2011 of 18 November, which establishes the basic requirements for authorisation and operation of biobanks in biomedical research and for processing human biological samples, and also regulates the operation and organisation of the National Register of _____ for Biomedical Research.

6.2. In accordance with the agreements adopted as indicated above and according to legal, ethical and quality criteria, when the Trial involves the use of biological samples, Biobanco will be the tool used to manage the same according to standard operating procedures.

6.3. The samples shall only be used for the proposed objectives in the Trial's realisation and shall be destroyed at its completion, unless the donor has granted his/her consent for their deposit in the _____ for Research.

7. Economic Aspects of the Trial (Annex III).

7.1. XXXX will invoice the Sponsor for all the expenses incurred in the Trial, except for compensation corresponding to the Research Team and the payments to the patients. The economic aspects are in the financial report attached as Annex III to the agreement, as an inseparable part of the same. They include:

7.1.1. Agreement management costs *(Will be charged by XXXX in the case of a multicenter in the Basque Country and by XXX in the case of a unicenter studio in ____ at the Basque Country level)*

An amount of € 1,500 + VAT has been agreed as payment for the costs of managing the Agreement. This amount will be paid upon receipt of the relevant invoice, prior to the study assessment by the CREC, or during the agreement management process. In multicenter trials there will be one single payment for this concept. The amounts are calculated according to the table published by XXXX. (Table I of Annex III).

7.1.2. The costs of conducting the Trial (will becharged by XXX in both cases).

The amount of (amount of concluded patient) €, plus tax obligations, per concluded patient of the study arm, and (amount for concluded patient) €, plus tax obligations, per concluded patient of the control arm, which include at least the following:

- Extraordinary direct costs, for example expenses that would not have occurred had the patient not participated in the Trial such as additional analytical or radiological controls, additional or specific visits to other specialists, etc. (Tables II and IV of Annex III).
- Compensation of pharmacy costs for its involvement in the receipt, storage and management of the medicinal products, as well as monitoring and supervising the dispensing orders. (Tables II and VI of ANNEX III and ANNEX IV)
- Compensation to _____ for processing, storage and transfer of the samples used in this Clinical Trial (Table V of ANNEX III).
- Compensation to the patients: when appropriate, the Sponsor shall pay the amount budgeted in the financial report to the patients, for the concepts established in RD 223/2004, through the Research Team (Table VII ANNEX III).

Compensation for the dedication of health-care professionals and other structural resources of the Site, stratified by either visits made or patient with follow-up completed (completed patients).

7.1.3. Patient's compensation: when appropriate, the Sponsor shall pay to the patients the amount set forth in the Financial Report, for the concepts set forth in the RD 223/2004, by means of (payment method to be determined) (investigator team, etc.) (Table VII ANNEX III).

7.2. XXX will distribute the revenues as follows:

7.2.1.10% of the Study total will be assigned to XXX to cover the expenses incurred in managing the Study.

7.2.2.Extraordinary costs, compensation for pharmacy and XXXXX costs will be invoiced by XXX and destined to cover the corresponding expenses.

7.2.3.The remaining costs are allocated as follows:

- 30% will be allocated to the research Site to promote the research. (Table III of Annex III).
- 70% will be allocated to the Research Team. (Table III of Annex III).

7.2.4._____ in the case of multicentre trials in the Basque Country and BioCruces in the case of unicentre trials in _____ at the Basque Country level reserve the right to adapt or adjust the distribution of costs and billable amounts when negotiating the agreement. This may be due to the size of the Study, its impact on the Basque Autonomous Health Service, or because it is considered an area of special interest.

7.3. Other economic aspects of the Trial:

7.3.1.According to the requirements of the Trial, and where necessary, the Sponsor should include in the financial report any costs incurred by personnel who are not part of the Site, as well as the expenses for diagnostic and therapeutic procedures performed in other institutions.

7.3.2.The Sponsor may hire XXXX or XXX, for Trial administration, as well as the payment of direct expenses for purchasing equipment, compensation to personnel who are not part of the Site, analyses and additional examinations by other institutions.

7.3.3.Forms of Payment

The calculation of the amount of the Trial that has been conducted for invoicing purposes will be notified quarterly by the Sponsor to XXX on the one hand, and by the Principal Investigator on the other. In this way XXX may compare data and issue the corresponding invoices.

The Sponsor will pay issued invoices within a maximum of thirty (30) days from the date of receipt of each invoice, to the account number designated by the Foundation.

The first payment shall be made at the date of signature of the Agreement and shall correspond to a maximum of 20% of the total expected turnover, in case the trial's duration is less than or equal to 12 months. The first payment shall correspond to a 10% of the total cost when the duration of the trial exceeds 12 months. In case that the during the trial's execution the abovementioned amounts are not exceeded, XXX undertakes to return the over invoicing, always provided that the provisions set forth in clause 11 are respected.

8. Obligations

8.1. The Sponsor shall bear all the obligations corresponding thereto in accordance with Law 29/2006 and Royal Decree 223/2004 and particularly the communication obligations referred to in Article 27 of the said Decree.

8.2. The Sponsor will also be responsible for obtaining all necessary permits, both from the CREC as well as from AEMPS, prior to the start of the Trial.

8.3. The Principal Investigator will conduct the Trial, according to the terms of Article 37 of RD 223/2004.

8.4 The Site will offer its facilities so that the professionals involved in conducting the Trial, especially the Principal Investigator, the Monitor and the other researchers, may comply with their duties.

8.5. The Site shall provide the patients that participate in the Trial with the important information facilitated by the Sponsor. The Site may request the Principal Investigator and the Ethics Committee to carry out these communications with the patients. For the purposes of this clause, "important information" shall be information that may (i) affect the safety or medical care of the subjects that are currently participating in the Trial or that have participated in the Trial in the past; (ii) affect the willingness of the of the subjects to continue participating in the trial; (iii) influence the development of the Trial or (iv) alter the granted authorizations.

~~8.5.~~8.6. The Center will facilitate to the Promoter the necessary authorizations for the specialists in ELAD can access to the facilities of the Center, according to the provisions of clause 5.2 of the contract.

~~8.6.~~8.7. XXX will be responsible for the financial and administrative management of the funds for the development of the Trial.

~~8.7.~~8.8. The Site shall maintain the adequate records relevant to the Trial in compliance with the Protocol, the GCP standards and applicable laws.

9. Ownership and Exploitation of the Results

9.1. All data, results, discoveries, inventions, as well as all industrial or intellectual property rights over the same, including know how, made, obtained or developed during the Trial by the Principal Investigator, the other members of the Research Team, its collaborators and any other person involved in the development of the Trial (hereinafter, the "**Results**") will remain the exclusive property of the Sponsor.

9.2. The Principal Investigator and the Site are obliged to provide the Sponsor with all information regarding the Results, as well as to respect their confidential character, and to collaborate with the Sponsor in as many acts and works as are necessary to enforce the rights over such Results, all without prejudice to the provisions agreed in clause 2.7.

9.3. XXX will include in any agreements entered into with other people or entities necessary for the appropriate performance of the Trial, a clause protecting the rights of the Sponsor in relation to the Results.

9.4. The Sponsor may freely exploit the Results without further obligations than to respect the rights of authorship or inventorship recognised as such.

10. Insurance

10.1. The Sponsor has accredited having taken out a civil responsibility insurance policy with Chubb Insurance Company _____, in accordance with Article 8 of RD 223/2004. The policy number is _____ and complies with the requirements and procedures established in Article 61.3 of Law 29/2006 (art. 61 .3), and such policy is currently in force as the Sponsor is up to date with the payment of the corresponding premiums.

~~10.1.~~10.2. The Promoter will be liable for any obligations of an economic nature that might result from damages caused to the subject of the Essay, even when insurance does not cover entirely damages and be legally responsible (for the same). The foregoing shall not apply when such (above mentioned) damages have been caused by negligent conduct, fraudulent or there has been a breach of its obligations under this Agreement by the Center, BioCruces and/or the Principal Investigator. In this case, the Center, BioCruces and/or the Principal Investigator will remain unharmed to the Promoter of any responsibility that derives from the negligence or from the wilful misconduct.

~~10.2.~~10.3. In any case, the insurance policy must sufficiently cover personal injury (including death), losses and other incidents and accidents that may occur to persons participating in the Clinical Trial, arising from the formulation, administration and action of the investigated product when following the indications of the Protocol.

~~10.3.~~10.4. Likewise, the Site and the Principal Investigator represent and warrant that they have contracted and undertake to maintain in force their respective civil liability insurance policies that are required under the applicable laws in force at any given time.

11. Suspension of the Trial

11.1. The Trial may be suspended, and, in consequence, this Agreement will be terminated, under the following circumstances:

11.1.1. If from the available data it is inferred that it is not safe or justified to continue to administer the Trial medicinal product and/or the comparator product or placebo to patients.

11.1.2. In the event of any breach by any of the Parties of their obligations under this Agreement, if the breach is not remedied by the defaulting party within 30 days from receiving a written communication from the non-breaching party demanding compliance with these obligations.

11.1.3. If compliance with the Protocol is lacking or the data are continuously incomplete or inaccurate.

11.1.4. By mutual written agreement between all contracting parties.

11.1.5. At the sole discretion of the Site, the Principal Investigator or the Sponsor individually considered, with one month prior notice.

11.2. The Trial Sponsor reserves the right to discontinue the inclusion of patients in any of the following cases:

11.2.1. If the Principal Investigator fails to include the agreed number of patients within the assigned time, without justification acceptable to both parties.

11.2.2. If the total number of patients to be included in the Trial is reached by other participating researchers, in the case of multicentre trials.

11.3. The termination of this Agreement and the ongoing Trial will require discussion and coordination to ensure patient safety, continuity of treatment and compliance with current legislation on the issue.

11.4. In any of these cases, a report will be produced and signed by all parties, declaring the reasons for the suspension of the Trial.

11.5. Upon termination or suspension of the Trial, the Principal Investigator, following the instructions of the Sponsor, will return all supplied materials and any unused medicinal products in his possession to the Sponsor. With regard to _____ System, clause 5.2 of this Agreement shall apply.

11.6. In the event of early termination of the Trial, the Sponsor shall pay only the costs that have been incurred up to the date of early termination, except in cases of patients who have to leave the study for adverse effects attributable to or derived from the Trial, and not envisaged in the Protocol. In the case of such patients, for invoicing and payment purposes, the amount due will be calculated as if all visits had been completed.

11.7. In the case of patients who withdraw from the Trial early for other reasons, the amount payable shall be calculated in proportion to the visits made.

12. Miscellaneous

12.1. The failure of a party to exercise any right of this Agreement shall not constitute a waiver to of such right.

12.2. If any provision of this Agreement shall be declared invalid, such provision shall be severed and all remaining provisions shall continue in full force and effect.

12.3. ~~This Agreement~~ The parties may not be assigned or transferred by the Site or the Principal Investigator without the previous written consent of the others parties.~~Sponsor.~~

~~12.4. Notwithstanding the above, the Sponsor may assign or transfer this Agreement, in whole or in part, without the previous consent of the other parties. in favour of a third entity. In this event, the Sponsor shall inform the other parties of such assignment or transfer.~~

13. Governing law and jurisdiction

13.1. The provisions of this Agreement shall be governed by and construed in accordance with the applicable regulations regarding clinical trials and in particular in accordance with the provisions of Royal Decree 223/2004.

13.2. In the case of any dispute concerning the interpretation or fulfilment of this Agreement, the parties submit themselves to the jurisdiction of the courts for ____, namely _____, expressly waiving any other jurisdiction that may apply to them.

And in witness whereof, the Parties sign this document.

For BioCruces: For the SPONSOR:

_____ _____

In acceptance of the terms of this Agreement:

For the Site: Principal Investigator:

_____ _____

ANEXO II

TEXTOS PARALELOS (INGLÉS Y ESPAÑOL)

CONTRACT FOR THE PERFORMANCE OF A CLINIAL TRIAL ENTITLED:

"_____
_____
_____
_____."

(**Protocol Code:** _____)

In Pamplona, (*Date*)

BY AND BETWEEN

Mr./Ms_____, with Tax ID: _____, in his/her capacity as _____, acting for and on behalf of (*THE SPONSOR – FULL NAME*), with corporate domicile in _____ and Tax ID: _____ (hereinafter, the **SPONSOR**), duly authorized for this purpose by virtue of the powers released in _____, on (*date*), before Mr./Ms _____, Notary Public,

on the one part,

and

Mr, José M.ª Roig Aldasoro acting for and in representation of the Miguel Servet Foundation (hereinafter, the **FOUNDATION**), with corporate domicile in C/ Irunlarrea 3, 31008 Pamplona and Tax ID: G31187420, duly empowered for this purpose by virtue of his election by the President of the Council of the **FOUNDATION** on August 30th of 2011.

and

Mr. Víctor Peralta Martín, acting as Director of the Complejo Hospitalario de Navarra, Centre of the Navarre Health Service (Osasunbidea), (hereinafter, the **CENTRE**), located in C/ Irunlarrea 3, 31008 Pamplona and with Tax ID: Q3150004D, duly empowered to enter into this Contract by virtue of Regional Order 78/2013, date July 4th, of the President of the Governing Council of Navarre Health Service.

and

Dr. _____, with Tax ID: _____, acting in his/her own name and right (hereinafter, the **PRINCIPAL INVESTIGATOR**), domiciled for notification purposes at the _____ Service of the **CENTRE**,

and

If applicable, the coordinates of the CRO entity acting in representation of the SPONSOR:

Mr./Ms _____, with Tax ID: _____ in his/her capacity as _____, acting for and on behalf of (*the CRO – FULL NAME*), with corporate domicile in _____ and Tax ID: _____ (hereinafter, the **CRO**), duly authorised for this purpose by virtue of the powers released in _____, on (*date*), before Mr./Ms _____, Notary Public,

on the other part.

The parties hereto mutually recognize their capacity to execute the present Contract (hereinafter, the **PARTIES**).

DECLARE

The FOUNDATION is an organization constituted under the New Jurisdiction by decision of the Navarre Government expressed in Regional Decree 211/1986 of 26 September. By virtue of the provisions of Regional Decree 126/2008 of 22 December, the FOUNDATION presents itself as the entity through which the Regional Health System is to promote biomedical research within the public health system of the Regional Community of Navarre. Its competences include the facilitation of the financing, development and integrated management of the projects, research teams, cooperative groups or other networks in which the researchers of the Navarre Health Service participate.

The SPONSOR is interested in the performance of the clinical trial (hereinafter, the STUDY) described in the first clause of the Contract.

The CENTRE is a health centre pertaining to the Navarre Health Service which also has research within the framework of the Health Sciences as one of its main objectives.

The PRINCIPAL INVESTIGATOR possesses the scientific training and experience in medical care required to assume responsibilities in the performance of the STUDY.

Based on the above considerations, the PARTIES have decided to enter into the present Contract in accordance with the following clauses:

FIRST.- PURPOSE

1.1.- The purpose of the present Contract is the performance of the STUDY entitled**,** "_____ _____", SPONSOR's Protocol Code "_____" (hereinafter, the PROTOCOL), which shall be conducted within the facilities of the CENTRE as specified in the premises of the present Contract under the direction and responsibility of Dr. _____ who shall act as the PRINCIPAL INVESTIGATOR thereof. The STUDY shall be performed in conformity with the specifications of the PROTOCOL subject to the Favourable Opinion of the responsible CEIC _____ .

SECOND.- START, DURATION AND PATIENT ENROLMENT
(Equivaldría a "Conditions of performance en el texto a traducir)

2.1.- The Management of the CENTRE has authorized the performance of the STUDY within its facilities, subject of course to the prevailing applicable State and Autonomous legislation and, in particular, Royal Decree 223/2004 of 6 February, as well as in compliance with the internal regulations established by the CENTRE, always provided that the STUDY has been authorized by the Spanish Agency for Medicines and Health Products (Agencia Española de Medicamentos y Productos Sanitarios-AEMPS) of the Ministry of Health and has received the favourable opinion of the Responsible Ethics Committee for the Clinical Investigation (Comité Ético de Investigación Clínica de Referencia (CEICR).

It remains expressly established that the STUDY may not be initiated nor, as a consequence, patients enrolled, until the existence of the corresponding authorization of the AEMPS of the Ministry of Health as well as of the favourable opinion of the CEICR.

2.2.- The STUDY is planned to be completed on _____ and, in accordance with the PROTOCOL, the CENTRE plans to enrol _____ patients until_____. In the event of competitive enrolment, the number of included patients may vary from the number initially planned.

2.3.- Where a multicentre study is concerned, the SPONSOR reserves the right to discontinue enrolment if the number of patients reaches the total number of bbpatients planned to be included in the STUDY by the various participating investigators.

2.4.- Patient inclusion shall be completed by the date of completion of the present STUDY, unless the inclusion date is extended for justified reasons and/or by mutual agreement of the PARTIES.

THIRD.- APPLICABLE LAW

3.1. At all times the PARTIES shall respect and comply with the applicable prevailing legislation from the date of signature and for the term of validity of the present Contract and shall follow expressly as well all ethical principles and norms such as, in particular:

3.1.1. Law 29/2006 of 26 July on the Guarantees and Rational Use of Medicines and Health Products.
3.1.2. Royal Decree 223/2004 of 6 February governing clinical trials with medicinal products (hereinafter, RD 223/2004).
3.1.3. Organic Law 15/1999 of 13 December on the Protection of Personal Data.
3.1.4. Law 14/2007, of 3rd July, of Biomedical Research.
3.1.5. Directive 2001/20/EC on Good Clinical Practice.
3.1.6. Orden Foral 125/2009 of 29 September of the President of the Governing Council of Navarre Health Service, establishing processes and criteria to conduct clinical research projects under the Department of Health and its agencies autonomous.

FOURTH.- OBLIGATIONS OF THE PARTIES

4.1. The PARTIES shall fulfil their contractual obligations in accordance with the provisions of the present Contract and of the specifications of the PROTOCOL. Each Party shall comply with its own obligations in conformity with and within the meaning of the norms specified in the Third Clause. The obligations, duties and functions provided for in RD 223/2004 shall constitute for each of the PARTIES and for all purposes the binding contents of the present Contract to the extent that the non compliance therewith shall be considered as constituting a default thereunder.

4.2. The obligations of the PARTIES are to:

4.2.1 collaborate in the follow-up visits of the STUDY to be undertaken by: (i) the CEIC, (ii) the monitors and auditors acting for and on behalf of the SPONSOR and (iii) the competent authorities when performing inspection tasks. Such visits shall be notified with at least a one week pre-advice unless the PARTIES have agreed on another timeline. In the course of such follow-up, monitoring and audit visits, the most appropriate technical and organizational means shall be adopted in order to comply with the norms governing the protection of personal data;

4.2.2. observe, on the part of the INVESTIGATOR, the SPONSOR, the monitors and auditors, the internal regulations of the CENTRE as well as the guidelines on the performance of the STUDY provided by the CEIC in charge of the follow-up thereof;

4.2.3. refrain, in relation with the performance of the STUDY, from agreeing on other terms and conditions conflicting with or contradicting those of the present Contract. To this effect, each one of the PARTIES declares that, on the date of signature of the present Contract, it is not part of any agreement or contract conflicting therewith. The PARTIES recognize in particular that, by virtue of the present Clause, the SPONSOR shall not grant nor pay to the PRINCIPAL INVESTIGATOR or to any of his/her collaborators any consideration of any type over and above that provided for in the present Contract. Excepted are the costs of meetings held for the organization and supervision of the performance of the STUDY or costs intended to cover the analysis and dissemination of the results thereof (presentations or scientific publications).

4.3. Before the start of the STUDY, the SPONSOR shall have obtained all the required permissions, authorizations and approvals required for the performance of the STUDY.

4.4. In addition to the obligations provided for in the applicable legislation, the SPONSOR shall provide continuous support to the PRINCIPAL INVESTIGATOR and supply him/her and the CEIC with any relevant new information issuing in respect of the investigational medicinal products.

4.5. The SPONSOR shall communicate as well to the health authorities and to the CEIC of Navarre any unexpected serious adverse event susceptible of issuing

from the treatments under study, whether occurring within or outside of Spain, as well as any occurrence implying a modification or violation of the Protocol.
Finally, the SPONSOR shall notify the AEMPS and the CEIC of Navarre of the completion of the STUDY. Thereafter, the SPONSOR shall submit to the same the final Report on the results of the STUDY as well as the corresponding report in the event of the discontinuation thereof, provided that, in the event that the term of the STUDY exceeds one year, the annual reports and the safety reports shall all be made with the collaboration of the INVESTIGATOR.

4.6. The obligation of the FOUNDATION is the administrative and financial management of the present STUDY and to receive the payments specified in Annex I.

4.7. The CENTRE shall make available the required human, material, technical and organizational means for the performance the STUDY in order to facilitate within its facilities the accomplishment of the functions of the professionals called upon to participate in the performance of the STUDY (in particular, those of the PRINCIPAL INVESIGATOR, the Monitor and the other research personnel).

4.8. The PRINCIPAL INVESTIGATOR shall hold the identification code of the patients into custody. The Monitor of the STUDY shall have access as well to the source documents and other clinical documentation of the patients included in the STUDY at the time of each visit performed subject to the patients having signed an informed consent.

4.9. The SPONSOR and the PRINCIPAL INVESTIGATOR shall keep the source documents for the duration of the STUDY at the conditions established by the prevailing legislation.

4.10. The PRINCIPAL INVESTIGATOR shall care as well for the selection of the members of the research team and of the support personnel of the STUDY which may be composed of individuals, commercial or other types of entities possessing appropriate material and human means for the performance thereof.

FIFTH.- RESEARCH TEAM AND MONITOR

5.1. Together with the PRINCIPAL INVESTIGATOR of the STUDY, members of the research team shall include the following individuals:

Mr./Ms _____ Tax ID: _____
Mr./Ms _____ Tax ID: _____
Mr./Ms _____ Tax ID: _____

5.2. The SPONSOR shall designate the Monitor of the STUDY in accordance with the provisions of Articles 35 and 36 of Royal Decree 223/2004 of 6 February who shall assume the direct monitoring of the performance thereof.

SIXTH.- FINANCIAL ASPECTS

6.1 The cost of the STUDY has been initially budgeted in the amount of € _____ (_____EUROS) (hereinafter, the **Budget of the STUDY**). This amount has been computed based on a cost of € _____ (_____EUROS) per assessable subject in accordance with the specifications of the Budget of the STUDY (Annex I).

6.2 The amounts to be paid by the SPONSOR in the course of the performance of the STUDY shall be determined in accordance with Annex I and shall include all the remunerations provided for therein.

Accordingly, it shall include:

- The remuneration of the PRINCIPAL INVESTIGATOR (25%)
- The remuneration of the Research Team designated by the PRINCIPAL INVESTIGATOR (35%)
- The remuneration of the Pharmacy Service (5%)
- The remuneration of the CENTRE (20%)
- The Management costs of the FOUNDATION (15%)

6.3 If applicable, the remuneration due to personnel foreign to the CENTRE and the costs of diagnostic and therapeutic procedures due to other institutions and entities, if related to the STUDY, shall be taken into consideration.

6.4 The Budget of the STUDY shall be due and payable semi-annually based on the visits made and reviewed during the said semester until the full amount specified in the Budget of the STUDY has been paid.

6.5 Upon making payments, the SPONSOR shall be freed fully of its corresponding financial obligations.

6.6 In studies with zero Budget shall be paid the amount of 500 € for administration of the study to the FOUNDATION, in a single payment at the signing of the contract upon presentation of invoice, which will apply VAT According to the rules applicable on the date.

6.7 All payments shall be made against submission of an invoice in the name of the SPONSOR and subject to the VAT in accordance with the legislation prevailing on the date of issuance thereof. To this effect, _____ (the SPONSOR/the CRO) and the PRINCIPAL INVESTIGATOR shall keep the FOUNDATION informed in order for the latter to be able to issue the corresponding invoices.

Invoicing Data:

- Name: _____
- Address: _____
- Tax ID: _____
- Invoicing Address: _____
- Telephone Contact: _____

SEVENTH.- INSURANCE AND LIABILITIES

7.1. The SPONSOR maintains a civil liability insurance policy complying in all respects with the provisions of RD 223/2004 (Annex III). The said policy, No. _____, has been underwritten with _____ insurance company and covers damages susceptible of issuing from the STUDY. The SPONSOR is up-to-date with the payment of the corresponding premiums.

EIGHTH.- WARRANTIES OF CONFIDENTIALITY AND OF THE PROTECTION OF PERSONAL DATA

8.1. The PARTIES shall take all available measures to warrant the confidentiality of the information made available for and issuing from the performance of the STUDY as well as of the personal data of the subjects included therein, this in order to comply with all the requisites established by the prevailing legislation. Excluded therefrom is information that: (i) is part of the Public Domain, (ii) was known to the PRINCIPAL INVESTIGATOR before being communicated, or (iii) is required to be disclosed by virtue of the law.

8.2. To the extent that they accede to and treat personal data of the subjects in the STUDY, the PARTIES shall take appropriate measures to protect such data and to avoid access thereto by non-authorized third parties. The PARTIES remain strictly bound by the provisions of Organic Law 15/1999 of 13 December on the Protection of Personal Data and of Law 41/2002 of 14 November governing the autonomy of the patient.

NINTH.- INVESTIGATIONAL MEDICINAL PRODUCTS

9.1. The SPONSOR shall supply the investigational medicinal products, including comparative products and placebos, free-of-charge in accordance with the provisions of RD 223/2004.

9.2 The investigational medicinal products shall be supplied through the Pharmacy Service of the CENTRE for controlled dispensation in accordance with the specifications of the Protocol.

9.3 The investigational medicinal products shall not be made available to the PRINCIPAL INVESTIGATOR and the Research Team in the absence of the favourable opinion of the CEIC and of the relevant authorisation of the AEMPS.

TENTH.- AMENDMENT, TERMINATION OR SUSPENSION OF THE CONTRACT

10.1. Any amendment to the present Contract shall be made in writing and signed by the Parties in the form of an *Addendum* thereto. In any event, the amendment shall conform to the provision of Article 25 of RD 223/2004.

10.2. The STUDY may be discontinued in the case of the occurrence of a serious adverse event or of whatever similar circumstance allowing reasonably to discontinue the performance of the STUDY or of any other cause making the perusal thereof impossible or definitely unadvisable.

The Contract may also be terminated or suspended by either of the PARTIES in any of the circumstances foreseen by Article 26 of RD 223/2004 as well as in the following case:

10.2.1. the breach by one of the PARTIES of its essential obligations;

10.2.2. the default or defective observance of the remaining obligations assumed by one PARTY always provided that the defaulting Party has failed to cure the default or defect within fifteen (15) days from the date the other PARTY has requested in writing compliance by the defaulting PARTY;

10.2.3. the written mutual agreement of the PARTIES;

10.2.4. if, based on available data, it appears unsafe or unjustified to pursue the administration of the investigational medicinal products, comparative products or placebos to the patients.

10.3. In case of breach of this Contract and/or the PROTOCOL, the non-defaulting PARTY may terminate this Contract immediately upon written notice to the defaulting PARTY and suspend the performance of the STUDY promptly.

10.4. The PARTIES shall guarantee the safety of the subjects until the completion of the STUDY as well as the pursuance of the treatment in accordance with the prevailing legislation.

10.5. Upon completion or discontinuation of the STUDY, the PRINCIPAL INVESTIGATOR shall return to the SPONSOR all unused prescribed material and investigational medicinal products in its possession.

10.6. In the event of discontinuation of the STUDY, the SPONSOR shall pay only those services effectively performed until the date of discontinuation.

ELEVENTH.- RESULTS AND PUBLICATION

11.1. The intellectual and industrial property rights deriving from the clinical research hereunder shall vest with the SPONSOR without prejudice to the rights recognized to the researchers by law.

In the case of contracts with zero budget, the parties agree that the intellectual property of any outcome from this study will be shared in proportion to the contribution of each to this investigation. Such a co-ownership shall be specified in the instruments protecting such rights. Corresponding property protection costs shall be shared similarly by the PARTIES.

11.2. In conformity with the provisions of RD 223/2004, the SPONSOR shall publish the results, whether positive or negative, once the STUDY has been completed. Such a publication shall be made in scientific media accessible to the public.

11.3. The SPONSOR failing to publish the final results of the STUDY, the PRINCIPAL INVESTIGATOR shall be entitled to divulge such data, discoveries or inventions

for professional purposes in scientific publications and journals with at least a reference to the SPONSOR in accordance with the following criteria:

- Clinical trials with non commercialized products: in the first year following the date of the marketing authorization thereof in any country;

- Clinical trials completed after the marketing thereof: in the year following the completion thereof, unless there is an undertaking to publish the results in a medical journal subject to peer review or a contravention to the national legislation.

The SPONSOR shall be presented with the text to be published or divulged at least forty-five (45) days before the date of submission to the scientific journal and at least twenty (20) days before if an abstract is concerned. In any event, only the PRINCIPAL INVESTIGATOR shall be entitled to use such data subject to the written express prior authorization of the SPONSOR.

11.4. The SPONSOR agrees that the FOUNDATION publishes on the www.navarrabiomed.es, for information purposes, the following data:

• Title
• Phase
• Objective
• Sponsor
• Protocol code
• Condition

TWELFTH.- JURISDICTION

12.1. Any discrepancy in the application or interpretation of the contents of the present Contract shall be submitted to the jurisdiction of the courts and tribunals of Navarre, the PARTIES waiving recourse to the doctrine of conflicts of laws.

12.2. Should a copy of the present Contract be available in another language, the Spanish original shall prevail.

In faith whereof, the Parties have signed the present document in quadruplicate for one sole purpose in Pamplona the __ day of _____ 20__.

Mr. Víctor Peralta Martín
Director of the Centre

Mr/Ms _____
The Sponsor

Mr. José M.ª Roig Aldasoro
Director of the Miguel Servet Foundation

Dr. _____
Principal Investigator *

CONTRATO DE REALIZACIÓN DEL ENSAYO CLÍNICO TITULADO: _____
_____
_____

Código del protocolo:_____

En Pamplona, a____ de _____ de 20__

REUNIDOS

De una parte, D/Dña._____, con N.I.F. nº_____, en su calidad de_____, actuando en nombre y representación de (EL PROMOTOR -NOMBRE COMPLETO-), con domicilio social en _____, y con C.I.F. nº _____ autorizada al efecto, conforme a los poderes expedidos en _____, con fecha___de _____de 20__, ante el notario D/Dña._____.

Y de otra parte:

D. José M.ª Roig Aldasoro, actuando en nombre y representación de la Fundación Miguel Servet (en adelante, **FUNDACIÓN**), con domicilio social en C/ Irunlarrea 3, 31008 de Pamplona y con C.I.F. nº G31187420, autorizado a tal efecto, nombrado por la Presidenta del Patronato de la Fundación Miguel Servet en fecha 30 de agosto de 2011.

D. José Ignacio Yurss Arruga, Director de Atención Primaria de Navarra, de la cual dependen los Centros de Salud de Atención Primaria (en adelante, **CENTRO**), nombrado mediante Orden Foral 68/2011 de 24 de agosto, de la Consejera de Salud.

El/la Dr. _____ con N.I.F. nº_____, actuando en su propio nombre y derecho (en adelante, **INVESTIGADOR PRINCIPAL**), con domicilio, a efectos de notificaciones, en el Centro de Salud _____ situado en C/ _____, de _____.

Si existiera, datos de la entidad que actúa en representación del Promotor:

D/Dña._____, con N.I.F. nº_____, en su calidad de_____, actuando en nombre y representación de (LA CRO -NOMBRE COMPLETO-), con domicilio social en _____, y con C.I.F. nº _____ autorizada al efecto, conforme a los poderes expedidos en _____, con fecha___de _____de 20__, ante el notario D/Dña._____.

Reconociéndose las Partes la capacidad mutua necesaria para obligarse por el presente Contrato (en adelante, **las Partes**)

EXPONEN

Que la FUNDACIÓN es una organización que se constituyó al amparo del Fuero Nuevo, por voluntad del Gobierno de Navarra expresada en el Decreto Foral 211/1986, de 26 de septiembre. Que, en virtud de lo previsto en el Decreto Foral 126/2008, de 22 de diciembre, la Fundación

Miguel Servet se presenta como la entidad a través de la cual el Departamento de Salud va a impulsar la investigación biomédica del sistema sanitario público de la Comunidad Foral de Navarra. Entre sus competencias figura facilitar la financiación, el desarrollo y la gestión integral de los proyectos, grupos de investigación, redes, CIBER, u otros similares en los que participen investigadores del Servicio Navarro de Salud.

Que el PROMOTOR, está interesado en la realización del ENSAYO CLÍNICO (en adelante **ENSAYO**) descrito en la cláusula primera del contrato.

Que el CENTRO, es un centro sanitario perteneciente al Servicio Navarro de Salud que también tiene como uno de sus objetivos principales la investigación en el ámbito de las Ciencias de la Salud.

Que el INVESTIGADOR PRINCIPAL tiene la formación científica y la experiencia en la atención sanitaria requerida para responsabilizarse de la realización del ENSAYO arriba referenciado.

Basándose en lo anteriormente expuesto, deciden formalizar el presente Contrato, de acuerdo a las siguientes estipulaciones:

PRIMERA.- OBJETO

1.1.- El objeto del presente Contrato es la realización del ENSAYO cuyo título es "_____ _____" código de protocolo del Promotor "_____" (en adelante **PROTOCOLO**), que se llevará a cabo en las dependencias del CENTRO identificadas en el Expositivo del presente Contrato, bajo la dirección y responsabilidad del/la Dr/a. _____ que actuará como INVESTIGADOR PRINCIPAL del mismo. El ENSAYO se realizará de acuerdo al contenido especificado en el PROTOCOLO con Dictamen Favorable del CEIC de referencia _____ .

SEGUNDA.- INICIO, DURACIÓN E INCLUSIÓN DE PACIENTES
(Equivaldría a "Conditions of performance en el texto a traducir)

2.1.- La Dirección del Centro ha autorizado la realización del ENSAYO en su sede, en el bien entendido de la estricta sujeción al Ordenamiento legal, estatal y autonómico, que los regula, y en especial al Real Decreto 223/2004, de 6 de febrero y con observancia de las normas de orden interno establecidas en el Centro, siempre que se acredite autorizado por la Agencia Española de Medicamentos y Productos Sanitarios (AEMPS) del Ministerio de Sanidad y evaluado favorablemente por el Comité Ético de Investigación Clínica de Referencia (CEICR).

Queda expresamente establecido que no podrá iniciarse el ENSAYO ni, por consiguiente, reclutar a pacientes hasta tanto no conste acreditada la existencia de la correspondiente autorización de la AEMPS del Ministerio de Sanidad así como la preceptiva evaluación positiva del Comité Ético de Investigación Clínica de Referencia (CEICR) y del CEIC de Navarra.

2.2.- El ENSAYO tiene como fecha prevista de finalización el _____ y prevé incluir en este CENTRO, según protocolo, a _____ pacientes hasta la fecha de _____. En el

caso de reclutamiento competitivo, el número de sujetos reclutados puede variar respecto a lo previsto inicialmente.

2.3.- Cuando se trate de un ensayo multicéntrico, el PROMOTOR se reserva el derecho de interrumpir la inclusión si se alcanza el número total de pacientes que tienen que incluirse en el ENSAYO por los diferentes investigadores que participan en el mismo.

2.4.- A la fecha prevista de finalización del presente ENSAYO deberá haberse completado la inclusión de pacientes, a menos que por motivos justificados y/o común acuerdo entre las partes contratantes, se prorrogara el plazo de inclusión.

TERCERA.- NORMATIVA APLICABLE

3.1. Las Partes se comprometen, en todo momento, a respetar y dar cumplimiento a la legislación vigente aplicable a la firma de este Contrato y durante su vigencia, así como a observar expresamente los principios y normas éticas, en particular, las siguientes:

3.1.1. Ley 10/2013, de 24 de Julio, que modifica a la Ley 29/2006, de 26 de julio, de Garantías y Uso Racional de los Medicamentos y Productos Sanitarios.
3.1.2. Real Decreto 223/2004, de 6 de febrero, por el que se regulan los ensayos clínicos con medicamentos (en adelante, RD 223/2004).
3.1.3. Ley Orgánica 15/1999, de 13 de diciembre, de Protección de Datos de Carácter Personal.
3.1.4. Ley 14/2007, de 3 de julio, de Investigación Biomédica.
3.1.5. Directiva 2001/20/EC de Buena Práctica Clínica.
3.1.6. Orden Foral 125/2009, de 29 de septiembre, de la Consejera de Salud, por la que se establecen los procesos y criterios de actuación a seguir en materia de realización de proyectos de investigación clínica en los centros dependientes del Departamento de Salud y sus organismos autónomos.

CUARTA.- OBLIGACIONES DE LAS PARTES

4.1. Las Partes vienen obligadas a la completa ejecución de las prestaciones previstas en el presente Contrato, de conformidad con lo previsto en el mismo y en el PROTOCOLO. Cada Parte cumplirá con las obligaciones que le son propias de conformidad y a tenor de la normativa señalada en la Cláusula Tercera. Las obligaciones, deberes y funciones previstos en el RD 223/2004 para cada una de las Partes constituyen, a todos los efectos, contenido obligacional en el presente Contrato, de forma que su inobservancia se reputará un incumplimiento del presente Contrato.

4.2. Son obligaciones de las Partes:

4.2.1 Colaborar en las visitas de seguimiento del ENSAYO que se realicen por parte de: (i) el CEIC, (ii) los monitores y auditores que actúen a instancias del PROMOTOR y (iii) las autoridades competentes, cuando realicen actuaciones de inspección. Estas visitas serán comunicadas con una antelación mínima de una semana salvo que exista acuerdo de otro plazo entre las Partes. Durante la realización de dichas visitas de seguimiento, monitorización y auditorias, se adoptarán las medidas de índole técnico u organizativo que garanticen el máximo respeto de la normativa sobre protección de datos de carácter personal.

4.2.2. Observar el INVESTIGADOR, el PROMOTOR, los monitores y auditores las normas de régimen interno del CENTRO, así como las indicaciones que sobre el desarrollo del ENSAYO realice el CEIC responsable de su seguimiento.

4.2.3. No pactar con relación a la realización del ENSAYO acuerdos o términos ajenos que excepcionen este Contrato o que contravengan el mismo. A estos efectos, cada una de las Partes manifiesta que a fecha de este Contrato no son parte en ningún acuerdo o pacto que contravenga el mismo. En particular, en virtud de esta cláusula las Partes aceptan que no podrá acordarse ni pagarse al INVESTIGADOR PRINCIPAL ni a ninguno de sus colaboradores contraprestaciones de cualquier tipo distintas de las previstas en este Contrato. Se excluyen de esta prohibición los gastos para reuniones celebradas con la finalidad de organizar y supervisar la realización del ENSAYO, así como las que pretendan analizar o dar a conocer los resultados del mismo (presentaciones o publicaciones científicas).

4.3. El PROMOTOR habrá obtenido antes del inicio del ensayo, la totalidad de los requisitos, autorizaciones y aprobaciones necesarias para la realización del ensayo clínico.

4.4. Son obligaciones del PROMOTOR, además de las previstas en la normativa aplicable, el dar continuo apoyo al INVESTIGADOR PRINCIPAL y proporcionar a éste y al CEIC cualquier nueva información de relevancia que se suscite sobre el medicamento en investigación.

4.5. El PROMOTOR está obligado a comunicar también, a las autoridades sanitarias y al CEIC de Navarra cualquier acontecimiento adverso, grave e inesperado que pueda estar relacionado con los tratamientos en investigación, ocurridos dentro o fuera de España, así como cualquier incidencia que implique una modificación o violación del protocolo.
Por último, el PROMOTOR notificará a la AEMPS y al CEIC de Navarra la finalización del ensayo. Posteriormente, les remitirá el Informe final sobre los resultados del ensayo así como el informe correspondiente en caso de finalización anticipada; los informes anuales, si el ensayo tuviera una duración superior al año y los informes de seguridad con la colaboración, en todos ellos, del INVESTIGADOR.

4.6. Es obligación de la FUNDACIÓN la gestión administrativa económica del presente ENSAYO, recibiendo los pagos de conformidad con lo previsto en el Anexo I.

4.7. El CENTRO pondrá a disposición para la ejecución del ENSAYO los medios humanos, materiales, técnicos y organizativos necesarios, facilitando en sus instalaciones el cumplimiento de las funciones de los profesionales que deban participar en la ejecución del ensayo (en especial, las del INVESTIGADOR PRINCIPAL, el Monitor y demás personal investigador).

4.8. El INVESTIGADOR PRINCIPAL, se compromete a custodiar los códigos de identificación de los pacientes. El monitor del Ensayo Clínico también accederá a las historias clínicas y demás documentación clínica de los pacientes incluidos en el ensayo clínico, en cada visita que realice, autorización que deberá constar en el consentimiento informado escrito del paciente.

4.9. El PROMOTOR y el INVESTIGADOR PRINCIPAL se comprometen a conservar los documentos esenciales del ENSAYO durante el tiempo y en las condiciones establecidas en la legislación vigente.

4.10. Corresponde igualmente al INVESTIGADOR PRINCIPAL la selección de los miembros del equipo investigador y del personal de apoyo al ENSAYO, que podrá estar formado tanto por personas físicas como por entidades mercantiles o de otra índole, que cuenten con medios materiales y humanos apropiados para la ejecución del mismo.

QUINTA.- EQUIPO INVESTIGADOR Y MONITOR

5.1. Junto al Investigador Principal del ensayo constituyen el equipo de investigación, los investigadores que a continuación se indican:

D. _____ D.N.I. nº _____
D. _____ D.N.I. nº _____
D._____ D.N.I. nº _____

5.2. El Promotor nombrará al Monitor del ensayo clínico, en cumplimiento de lo dispuesto en los artículos 35 y 36 del Real Decreto 223/2004 de 6 de febrero, a quien corresponderá el seguimiento directo de la realización del Ensayo.

SEXTA.- ASPECTOS ECONÓMICOS

6.1 El importe del coste de este ENSAYO se ha presupuestado inicialmente en _____ EUROS (_____€) (en adelante, **Presupuesto de Ensayo**). Este importe se ha determinado aplicando un coste de _____EUROS (_____€) por sujeto evaluable, conforme a lo establecido en la Memoria Económica del ENSAYO (Anexo I).

6.2 El importe que deba abonar el PROMOTOR durante la ejecución del ENSAYO será determinado por aplicación del Anexo I y deberá contemplar todas las remuneraciones del mismo. Incluirá por tanto:

- La compensación para el Investigador principal (25%)
- La compensación para el Grupo Investigador designado por el Investigador principal (35%)
- La compensación al Servicio de Farmacia (5%)
- Compensación al Centro Sanitario (20%)
- Gastos de gestión de la Fundación Miguel Servet (15%)

6.3 En caso de existir, deberán contemplarse la compensaciones que deban realizarse a personal ajeno al Centro y los gastos de procesos diagnósticos y terapéuticos a realizar en otras instituciones y entidades originados por el Ensayo.

6.4 El Presupuesto del Ensayo se abonará semestralmente conforme a las visitas realizadas y revisadas durante dicho semestre hasta el pago íntegro del importe que constituye tal Presupuesto.

6.5 Los pagos realizados por el PROMOTOR serán plenamente liberatorios para primero.

6.6 En estudios con memoria económica cero, se abonará la cantidad de 500€ en concepto de gestión administrativa del estudio a la FUNDACIÓN MIGUEL SERVET, en un único pago a la firma del contrato contra presentación de factura, a la que se le aplicará el IVA de

acuerdo con la normativa aplicable en la fecha de emisión de la misma y a nombre del PROMOTOR.

6.7 Los pagos se harán efectivos en un plazo máximo de 60 días tras la fecha de emisión de la factura.

6.8 Todos los pagos deberán efectuarse contra presentación de factura, a la que se le aplicará el IVA de acuerdo con la normativa aplicable en la fecha de emisión de la misma y a nombre del PROMOTOR. A los citados efectos, _____(el PROMOTOR / la CRO) y el INVESTIGADOR PRINCIPAL mantendrán informado a la FUNDACIÓN para que ésta pueda emitir las facturas correspondientes a cada centro.

Datos de facturación:
- Nombre: _____
- Dirección: _____
- NIF: _____
- Dirección de envío: _____
- Teléfono de contacto: _____

SÉPTIMA.- SEGURO Y RESPONSABILIDADES

7.1. El PROMOTOR tiene suscrita una póliza de seguro de responsabilidad civil que cumple en todos sus aspectos lo establecido en el RD 223/2004 (Anexo III). Dicha póliza, número _____, ha sido concertada con la entidad aseguradora _____, cubre los perjuicios que como consecuencia del ENSAYO objeto de este Contrato pudieran derivarse, y está al corriente de pago de las primas correspondientes a la misma.

OCTAVA.- GARANTÍAS DE CONFIDENCIALIDAD Y PROTECCION DE DATOS DE CARÁCTER PERSONAL

8.1. Las Partes se comprometen a poner todos los medios a su alcance para garantizar la confidencialidad de la información facilitada para la realización del ENSAYO y obtenida durante su realización, así como la de los datos de carácter personal de los sujetos reclutados para el mismo, a fin de cumplir con todos los requisitos establecidos en la normativa vigente. Se exceptuará de este compromiso de confidencialidad aquella información que: (i) sea de dominio público, (ii) fuera conocida previamente por el INVESTIGADOR PRINCIPAL en el momento de ser revelada, o (iii) fuera obligatorio revelar por imperativo legal.

8.2. Todas las Partes, en la medida en que accedan y traten datos de carácter personal de los sujetos del **ENSAYO**, deberán tomar las medidas oportunas para protegerlos y evitar el acceso a los mismos por parte de terceros no autorizados. Las Partes quedan obligadas a la más estricta observancia de lo establecido en la Ley Orgánica de Protección de Datos Personales 15/1999 de 13 de Diciembre, y la Ley 41/2002, de 14 de noviembre, básica reguladora de la autonomía del paciente.

NOVENA.- MEDICAMENTOS EN INVESTIGACIÓN

9.1. El PROMOTOR suministrará gratuitamente los medicamentos en investigación, incluidos los de comparación y placebos, en los términos que se establecen en el RD 223/2004.

9.2 El medicamento en investigación será suministrado a través del Servicio de Farmacia del CENTRO, dispensándose de manera controlada y de conformidad con las directrices del PROTOCOLO.

9.3 No se pondrá a disposición de los investigadores el medicamento en investigación hasta que no cuente con el informe favorable del CEIC y la preceptiva autorización de la AEMPS.

DÉCIMA.- MODIFICACIÓN, CANCELACIÓN O SUSPENSIÓN DEL CONTRATO

10.1. Cualquier modificación a lo previsto en este Contrato deberá realizarse por escrito y firmado por las Partes como *addendum* al mismo. En todo caso, en la modificación se observará lo previsto en el artículo 25 del RD 223/2004.

10.2. El ENSAYO podrá terminarse anticipadamente si se produce un acontecimiento adverso grave o cualquier otra circunstancia similar, que hagan razonable no continuar con la ejecución del ensayo, o cualquier otra que imposibilite o desaconseje la continuación del mismo de forma definitiva.

También podrá ser terminado o suspendido por una de las Partes en cualquiera las situaciones previstas en el artículo 26 del RD 223/2004, así como en los siguientes casos:

10.2.1. Por incumplimiento de las obligaciones esenciales asumidas por alguna de las Partes.

10.2.2. Por incumplimiento o cumplimiento defectuoso de las restantes obligaciones asumidas por otra de las Partes, siempre que tal incumplimiento no sea subsanado en el plazo de quince (15) días a contar desde que la otra Parte le intime por escrito el cumplimiento.

10.2.3. Por mutuo acuerdo entre las Partes, manifestado por escrito.

10.2.4. Si de los datos disponibles se infiere que no es seguro o justificado seguir administrando el fármaco de ensayo y/o el fármaco comparativo o el placebo a los pacientes.

10.3. La terminación o suspensión de la ejecución del ENSAYO permitirá la resolución del Contrato por la Parte que no haya incumplido sus obligaciones contractuales.

10.4. Las Partes garantizarán la seguridad del sujeto en la finalización del ENSAYO, así como la continuidad del tratamiento y el cumplimiento de la normativa legal vigente en la materia.

10.5. A la finalización o suspensión del ensayo, el investigador principal devolverá al PROMOTOR el material suministrado y toda la medicación no utilizada que esté en su poder.

10.6. En caso de finalización anticipada del ensayo, se pagarán por el PROMOTOR del ensayo solamente las prestaciones que hayan sido realizadas hasta la fecha de la finalización anticipada.

UNDÉCIMA.- RESULTADOS Y PUBLICACIONES

11.1. Los derechos de propiedad intelectual e industrial que pudieran derivarse de la evaluación experimental objeto del presente contrato, pertenecen al PROMOTOR, sin perjuicio de los derechos que la ley concede a los/as investigadores/as.

En el caso de contratos con memoria económica cero, las partes acuerdan que la propiedad intelectual e industrial de los resultados derivados del presente estudio sea compartida, en proporción a la aportación de cada una de ellas a la presente investigación. En los instrumentos de protección del conocimiento generado, se hará constar de manera expresa dicha circunstancia de co-titularidad. Los gastos derivados necesarios para la protección de dicha propiedad, serán asumidos por las partes en los mismos términos.

11.2. Conforme a lo establecido en el RD 223/2004, el PROMOTOR se compromete a publicar una vez finalizado el ENSAYO los resultados obtenidos, sean positivos o negativos. Esta publicación tendrá lugar en medios científicos de acceso público.

11.3. Si los resultados finales del ENSAYO no han sido sometidos a publicación por parte del PROMOTOR, el INVESTIGADOR PRINCIPAL podrá dar a conocer con fines profesionales, y en revistas y publicaciones científicas, dichos datos, descubrimientos o invenciones, con mención al menos del PROMOTOR de acuerdo a los siguientes criterios: Ensayos con productos no comercializados: en el primer año después de su autorización y comercialización en cualquier país; Ensayos realizados después de la comercialización: en el año posterior a la finalización del ensayo, a menos que se comprometa la publicación en una revista médica sometida a revisión por pares o contravenga la legislación nacional. El PROMOTOR, deberá recibir para revisión copia del texto propuesto para su publicación y/o divulgación, al menos cuarenta y cinco (45) días antes de la fecha de envío a la revista científica y, al menos, veinte (20) días antes en el caso de que se trate de un resumen. En cualquier caso, el INVESTIGADOR PRINCIPAL sólo podrá utilizar estos datos previa autorización expresa y por escrito del PROMOTOR.

11.4. El PROMOTOR acepta que la FUNDACIÓN publique en la Web www.navarrabiomed.es con fines informativos, los siguientes datos del ENSAYO:

- Título
- Fase
- Objetivo
- Promotor
- Código protocolo
- Enfermedad investigada

DUODÉCIMA.- JURISDICCIÓN

12.1. Para resolver cualquier discrepancia en la aplicación o interpretación de lo establecido en este Contrato, las Partes se someten, con renuncia expresa al fuero que pudiese corresponderles, a jurisdicción de los juzgados y tribunales de Navarra.

12.2. En el caso de disponer de una copia de este Contrato en otra lengua o idioma, prevalecerá la versión en español.

Y para que conste, y en prueba de conformidad, las Partes firman este documento por cuadriplicado, y a un solo efecto en Pamplona a __ de _____ de 20__.

D. José Ignacio Yurss Arruga
Director de Atención Primaria de Navarra

D. _____
El Promotor,

D. José M.ª Roig Aldasoro
Director Fundación Miguel Servet

Dr. _____
Investigador Principal

ANEXO III

EJEMPLOS ADICIONALES

Debido a que en el cuerpo principal del presente trabajo ya se han explicado y ejemplificado los principales problemas del lenguaje jurídico-económico, muchos de los puntos que se van a presentar en el presente anexo solo se van a utilizar para cuantificar el gran número de ejemplos de cada uno de los aspectos mencionados. A su vez, como muchos de estos aspectos cuentan con numerosos ejemplos, solamente se presentarán aquellos cuya ejemplificación se considere importante para demostrar algún punto dentro del texto a traducir y del lenguaje utilizado.

Paralelismos

1. «*in accordance with* **(1)** *the provisions of Law 15/1999 of 13 December on Personal Data Protection and the implementing regulations,* **(2)** *Law 2/2004 of 25 February on Publicly Owned and Created Personal Data Files of the XXX Data Protection Agency as well as* **(3)** *Law 41/2002 of 14 November, basic regulation governing patient autonomy and the rights and obligations attached to clinical information and documentation.*» → conforme a **(1)** las disposiciones de la Ley Orgánica 15/1999, de 13 de diciembre, de Protección de Datos de Carácter Personal y sus Reglamentos de desarrollo, **(2)** la Ley 2/2004, de 25 de febrero, de Ficheros de Datos de Carácter Personal de Titularidad Pública y de Creación de la Agencia Vasca de Protección de Datos, así como **(3)** la Ley 41/2002, de 14 de noviembre, básica reguladora de la autonomía del paciente y de derechos y obligaciones en materia de información y documentación clínica.

Como en el ejemplo anterior, se establecen los diferentes objetos introducidos por un conector (*in accordance with*) y se mantiene un paralelismo para distinguir con claridad cuáles son esos objetos (indicados mediante (1), (2) y (3)).

Aspectos grafémicos

Empleo de mayúsculas

En los siguientes ejemplos se va a mostrar cómo cada una de las partes del contrato, los documentos mencionados y aquellos centros participantes se escriben durante todo el contrato para identificarlos:

- «*The **Trial** may be suspended, and, in consequence, this **Agreement** will be terminated…*»

- …the **Site** and the **Principal Investigator** represent and warrant

Aspectos léxicos

Ámbito jurídico

1. Términos semitécnicos - polisemia

1. «*XXX undertakes to ensure that the persons or entities hired to perform the said Trial respect the data protection **regulations**.*» → *regulation* puede significar tanto regulación como reglamento. En su búsqueda, encontré en textos de la Unión Europea (que constituyen una gran fuente de equivalentes, ya que la mayoría de textos están disponibles en ambos idiomas) que se traduce como reglamento. → XXX se compromete a asegurar que las personas o entidades contratadas para realizar el Ensayo respetan los **reglamentos** de protección de datos.
2. «*Law 41/2002 of 14 November, basic **regulation** governing patient autonomy and the rights and obligations attached to clinical information and documentation.*» → en este fragmento encontramos de nuevo el término *regulation*, sin embargo, en esta ocasión se debe tener cuidado con su traducción, ya que no equivale a reglamento. Es una ley española, por lo que se debe buscar el nombre acuñado y no realizar una traducción propia. En ella vemos como se traduce por: «la Ley 41/2002, de 14 de noviembre, básica **reguladora** de la autonomía del paciente y de derechos y obligaciones en materia de información y documentación clínica.»
3. «*the **provision** of health services and material aspects*» → en contextos jurídicos, «*provision*» suele equivaler a «disposición», sin embargo, en esta ocasión pertenece al ámbito general → **suministro** de servicios y materiales. En el resto de casos encontrados en el texto, se utiliza en su sentido jurídico → «*The parties will comply with the **provisions** of the Protocol*» → Las partes cumplirán las **disposiciones** establecidas en el protocolo.
4. *«according to the **terms** of Article 37 of RD 223/2004.»* → según el Diccionario de Términos Jurídicos de Alcaraz, *term* puede significar tanto «condición» como «término». Este ejemplo es similar al de contrato y acuerdo, existe una mínima diferencia entre ambos términos. En *terms of performance* se traduce por

«condiciones de realización», sin embargo, no es el mismo contexto. Al buscar en *linguee* el conjunto *terms of Article 37,* una de las traducciones pertenece al Boletín Oficial de la Unión Europea y en él directamente omiten *term*, por lo que también he decidido omitirlo: conforme al Artículo 37 del RD 223/2004.

5. «*in the Protocol without prejudice to any extension by the parties of the initially envisaged* ***term****.*» → otro de los significados de *term* es "plazo",
6. «*The Site will offer its facilities so that the professionals involved in conducting the Trial, especially the Principal Investigator, the Monitor and the other researchers, may comply with their* ***duties***.» → *duty* puede significar tanto «obligación» como «labor/función» (refiriéndose al trabajo realizado por el personal de trabajo) → debido a que el lenguaje legal utiliza generalmente los mismos términos para los mismos significados y ya aparece el término *obligations*, es lógico que hable de las funciones de los profesionales mencionados: El Centro pondrá a disposición sus instalaciones de manera que los profesionales involucrados en la realización del Ensayo, en especial el Investigador principal, el Monitor y los demás investigadores, puedan cumplir sus **funciones**.
7. *«The Trial may be suspended, and, in consequence, this Agreement will be* ***terminated****, under the following circumstances…»* → tras la búsqueda de *agreement* en diferentes diccionarios y memorias de traducción, he observado que puede referirse a tres formas de acabar un contrato: "resolución", "rescisión" y "extinción", sin embargo, estos equivalentes no son sinónimos, por lo que se debe consultar el significado concreto de cada uno de ellos. En el Blog de Traducción Jurídica dedican un artículo para hablar de este término y de sus traducciones y dificultades. "Extinción" se refiere "a cualquier causa de extinción", mientras que "la resolución opera por causas sobrevenidas a la firma del contrato" y rescisión "cuando el incumplimiento de una de las partes ocasiona importantes perjuicios a la otra y la ley le concede el derecho a rescindir el contrato". En el texto paralelo encontrado (punto 10.2), lo traducen por "terminado", sin embargo, debido a que en el párrafo en el que aparece el término se introducen todas las causas por las que se podra "finalizar" el contrato, he utilizado "extinción", ya que el término se utiliza en rasgos generales.

2. Términos no especializados – polisemia

- «*and particularly the* ***communication*** *obligations referred to in Article 27 of the said Decree*.» → si no prestamos atención a este sintagma, probablemente lo traduciríamos como "obligaciones de comunicación". Sin embargo, debido a que son un tipo de obligaciones incluidas en un decreto, he decidido buscar dicho decreto para ver cómo se refiere a esas obligaciones. El equivalente es "obligaciones de información".

3. Sinonimia

1. «*Any amendment to the Protocol must be by mutual* ***written agreement*** *between the Sponsor and the Principal Investigator*» → en este contexto, «*agreement*» puede significar «contrato» o «acuerdo». Estos dos términos son prácticamente equivalentes, sin embargo, tal y como establece Álvarez (1999:17), "para que haya sinonimia absoluta, tienen que ser permutables en todos los contextos". Aunque podríamos decir que son dos sinónimos completamente equivalentes, existe una mínima diferencia entre ellos, que pasa desapercibida entre los legos. Para resolver el problema acudí a un experto, que me explicó que en esta ocasión el equivalente se obtiene por contexto: no se llevan a cabo contratos dentro de contratos, sino que "Cualquier enmienda del Protocolo se realizará mediante un **acuerdo** escrito entre el Promotor y el Investigador principal".

Aspectos morfológicos y sintáctivos

1. Preposiciones sufijadas

- *«The Sponsor shall bear all the obligations corresponding* ***thereto*** *in accordance with Law 29/2006 ....»* → En esta ocasión, la preposición arcaica *thereto* se refiere al mismo contrato en el que aparece, por lo que en español se debe explicitar → El Promotor debe cargar con todas las obligaciones correspondientes **al contrato**, conforme a la Ley 29/2006….

2. Locuciones preposicionales complejas

En este apartado se va cuantificar el número de veces que aparece la locución preposicional *In accordance with.* Aparece un total de 8 veces, contando el ejemplo introducido en la parte principal del trabajo, lo que establece la importancia de este tipo de preposiciones en el lenguaje jurídico:

1. «*The parties will comply with the provisions of the Protocol, including the amendments or modifications,* ***in accordance with*** *the provisions of Article 25 of Royal Decree 223/2004.*»
2. « *…all information related to the XXX System and its components, they will maintain restricted circulation of the said information and will be responsible for the fulfillment of this obligation by all persons who rightly have access to the said information* ***in accordance with*** *this Agreement.*»
3. «*…the study will be processed* ***in accordance with*** *the provisions of Law 15/1999 of 13 December on Personal Data Protection and the implementing regulations…*»
4. « The Sponsor shall bear all the obligations corresponding thereto **in accordance with** Law 29/2006…»
5. «*The Sponsor has accredited having taken out a civil responsibility insurance policy with Chubb Insurance Company of XXXX,* ***in accordance with*** *Article 8 of RD 223/2004.*»
6. « *The provisions of this Agreement shall be governed by and construed* ***in accordance with*** *the applicable regulations regarding clinical trials and in particular i****n accordance with*** *the provisions of Royal Decree 223/2004.*»

3. Uso de tiempos futuros

La importancia del arcaísmo *shall* para expresar obligación dentro de los contratos queda reflejada en el número de apariciones dentro de la parte del contrato seleccionada para su traducción:

- *«The confidentiality obligations set forth in this section 2.8.1* ***shall remain*** *in force…»* → Las obligaciones de confidencialidad establecidas en este punto **permanecerán** en vigor…

- *«…the Sponsor **shall pay** the amount budgeted in the financial report…»* → …el Promotor **abonará** la cuantía presupuestada en el informe financiero…
- *«…the Sponsor **shall pay** to the patients the amount set forth in the Financial Report…»* → el Promotor **pagará** a los pacientes la cuantía establecida en el informe financiero

Estos son algunos de los numerosos ejemplos que se utiliza dicho verbo modal.

3. Subordinación

a) *«The purpose of this Agreement is the development, for and on behalf of the Sponsor, of the clinical trial with medicinal products **identified as "A Randomized, Open-Label, Multicenter, Controlled Study To Assess Safety And Efficacy Of Xxx In Subjects With Acute Alcoholic Hepatitis (AAH) And Failure Per The Lille Score with code____" (hereinafter the "Trial"), which will be conducted at the Site, under the direction and responsibility of the Principal Investigator and coordinated and managed by____.»***

Al igual que en los dos primeros ejemplos, la oración subordinada se introduce mediante un verbo acabado en *–ed.* Y también vemos otra oración subordinada introducida por "*which*" → con esta alta subordinación se quiere establecer que el objeto del contrato es el desarrollo de ese contrato específico, que se identifica por ese nombre y que se va a realizar en ese centro y no de otro:

- El objeto de este Contrato es la realización, por parte del Promotor y en su nombre, del ensayo clínico con productos médicos **identificado como "Un estudio abierto, controlado, multicéntrico y aleatorio para evaluar la seguridad y eficacia del producto XXX en sujetos con hepatitis aguda alcohólica (HAA) y su suspensión mediante elzpuntaje de Lille con código___" (de aquí en adelante el "Ensayo"), que se realizará en el Centro, según la dirección y responsabilidad del Investigador principal y estará coordinado y dirigido por____.**

*b) In any case, the insurance policy must sufficiently cover personal injury (including death), losses and other incidents and accidents **that** may occur to persons **participating** in the Clinical Trial, **arising** from the*

formulation, administration and action of the investigated product ***<u>when</u>*** *following the indications of the Protocol.* → este ejemplo de uno de los más representativos de la subordinación múltiple presente en los textos legales. Tenemos cuatro oraciones subordinadas: una adverbial temporal (*when*) y tres adjetivas (*that, participating* y *arising*). Las subordinadas introducidas por *that* y *arising* modifican a «*personal injury, losses and other incidents and accidents*», *participating* modifica a *«persons»* y la oración introducida por *when* modifica a «*formulation, administration and action of the investigated product*». Una vez identificadas las relaciones entre oraciones, debemos establecer las concordancias en español para mostrar esas relaciones:

- En cualquier situación, la póliza de seguro tiene que cubrir, de forma suficiente, las lesiones personales (incluido el fallecimiento), las pérdidas y otros incidentes y accidentes **<u>que puedan ocurrirles</u>** a las personas **<u>que participan</u>** en el Ensayo clínico, **<u>que surjan</u>** de la composición, administración y acción del medicamento investigado **<u>al seguir</u>** las indicaciones del Protocolo.

4. Coordinación y subordinación múltiple

a) *«The Promoter will (1) be liable for any obligations of an economic nature* ***<u>that</u>*** *might result from damages caused to the subject of the Essay,* ***<u>even when</u>*** *insurance does not cover entirely damages* ***<u>and</u>*** *(2) be legally responsible (for the same).»*

En el presente ejemplo podemos ver como el conjunto *obligations of an economic nature* está modificado por una oración subordinada adjetiva introducida por *that* (que) y a su vez, la oración subordinada adverbial concesiva introducida por "*even when*" (incluso cuando) modifica a todo lo anterior. De esta manera se expresa una objeción que no impide el cumplimiento de lo expuesto en la oración principal. Además de las subordinadas, tenemos la conjunción *and* que introduce una oración coordinada con la primera, de manera que el promotor será (1) responsable de…. y (2) legalmente responsable de lo mismo. Se han indicado mediante (1) y (2) las oraciones principales coordinadas:

- El Promotor (1) será responsable de todas las obligaciones de naturaleza económica **que** puedan surgir de los daños causados a los sujetos del Ensayo, **incluso si** el seguro no cubre todos los daños y (2) será legalmente responsable de los mismos.

b) *«Likewise, the Site **and** the Principal Investigator represent **and** warrant **that** they have contracted **and** undertake to maintain in force their respective civil liability insurance policies **that** is required under the applicable laws in force at any given time.»* →

Esta oración representa claramente la gran coordinación utilizada en los contratos para añadir elementos dentro de una misma oración, de manera que se especifique al máximo toda la información necesaria para regular la situación mostrada en el contrato. En la última subordinada introducida por *that*, para evitar el uso de la pasiva en español, se ha realizado una realizado una transposición de verbo a adjetivo (required – requerido).

- Del mismo modo, el Centro **y** el Investigador principal declaran **y** garantizan **que** han contratado **y que** se comprometen a mantener en vigor su póliza de seguro de responsabilidad civil, **requerido** según las leyes aplicables en vigor en cualquier momento. →

Otros problemas de traducción

Erratas en el TO

a) «*a multicenter trials in the Basque Country*» → hay una discordancia de género entre el artículo y el sustantivo, por lo que debemos tomar la decisión de si han añadido la "s" o la "a" por error. Por contexto, debido a que el contrato regula un solo ensayo, había tomado la decisión de traducirlo en singular. → un ensayo multicéntrico en el País Vasco. Sin embargo, tras avanzar en la traducción del texto, más adelante se vuelve a hacer referencia a lo mismo y utiliza el plural, por lo que finalmente he cambiado ambas por «ensayos multicéntricos».

b) «The amount of (amount of concluded patient) €, plus tax obligations, per concluded patient of the study arm, ~~and (amount for concluded patient) €, plus tax obligations, per concluded patient of the control arm~~, which include at

least the following:» → en este párrafo se produce una repetición que no tiene ningún sentido, por lo que en el TM he decidido eliminar la repetición.

c) «I*n case that ~~the~~ during the trial's execution…*» → se ha introducido un «*the*» que no tiene ningún sentido en la oración.

d) *«The center will facilitate to the ~~Promoter~~ Sponso»r* → dentro del contrato hay una sección en la que se incluyen todas las partes participantes en él y *promotor* no aparece. La conclusión a la que se ha llegado es que se han confundido y querían mencionar *Sponsor*, que es el término que se utiliza durante el resto del contrato.

e) *«requirements and procedures established in Article 61.3 of Law 29/2006 ~~(art. 61.3)~~ »* → repetición del artículo donde se encuentran los requisitos y procedimientos.

ANEXO IV

GLOSARIO

Debido a la numerosidad de términos encontrados en el texto a traducir, se han creado tres tablas para diferenciar la procedencia de los distintos términos:

1. Términos del lenguaje legal
2. Términos del lenguaje económico
3. Términos del lenguaje biomédico

Glosario términos jurídicos

Addenda	adenda	http://www.oxforddictionaries.com/translate/english-spanish/addendum?q=addenda
Agreement	Acuerdo /Contrato	http://www.oxforddictionaries.com/translate/english-spanish/agreement
Amendment	Enmiendas	http://www.oxforddictionaries.com/translate/english-spanish/amendment
Applicable law	Ley aplicable	http://www.linguee.es/espanol-ingles/search?query=applicable+law&source=auto
Article	Artículo	Diccionario de términos jurídicos (Alcaraz & Hugues)
Clauses	Estipulaciones	Diccionario de términos jurídicos (Alcazaz & Hugues) Texto paralelo del Anexo 2 (página 85)
Conditions and requirements	Condiciones y requisitos	http://geoparquepirineos.com/contenidos.php?niv=1&cla=_2OA1CEG09&cla2=_2OB01K3NA&cla3=&tip=2&idi=1
Confidentiality and data protection	Confidencialidad y protección de datos	http://www.linguee.es/espanol-ingles/search?source=auto&query=Confidentiality+and+data+protection Texto paralelo del Anexo 2 (página 86)
Confidentiality obligations	Obligaciones de confidencialidad	http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:C:2006:279:0002:0008:ES:PDF → (página 6, artículo 9)

Court	Tribunal	Diccionario de términos jurídicos (Alcaraz & Hugues)
Defaulting party	Parte incumplidora	http://www.linguee.es/espanol-ingles/search?source=auto&query=non+breaching+party
Disclosing party	Parte divulgadora	http://www.linguee.es/espanol-ingles/search?source=auto&query=disclosing+party
Duties	Funciones	Diccionario de términos jurídicos (Alcaraz & Hugues)
Fulfillment	Cumplimiento	Diccionario de términos jurídicos (Alcaraz y Hugues) http://unesdoc.unesco.org/images/0018/001808/180878s.pdf → Anexo II, pág 5, artículo 12 del enlace)
In force	En vigor	https://documents-dds-ny.un.org/doc/UNDOC/GEN/G05/105/08/PDF/G0510508.pdf?OpenElement → (página 2)
Jurisdiction	jurisdicción	Diccionario de términos jurídicos (Alcaraz & Hugues)
Law	Ley	http://www.oxforddictionaries.com/translate/english-spanish/law
Legal capacity	Capacidad jurídica	http://iate.europa.eu/SearchByQuery.do?method=searchDetail&lilId=839800&langId=&query=legal%20capacity&sourceLanguage=en&domain=0&matching=&start=0&next=1&targetLanguages=es
Legislation	Legislación	Diccionario de términos jurídicos (Alcaraz y Hugues) http://iate.europa.eu/SearchByQuery.do?method=searchDetail&lilId=1226041&langId=&query=legislation&sourceLanguage=en&domain=0&matching=&start=0&next=1&targetLa

		nguages=es
Modifications	Modificaciones	http://www.linguee.es/espanol-ingles/search?query=modification+of+a+contract&source=auto
Non – breaching party	parte cumplidora	http://www.linguee.es/espanol-ingles/search?source=auto&query=defaulting+party
Obligation	Obligación	Texto paralelo del Anexo 2 (página 86)
Parties	Partes	Texto paralelo del Anexo 2 (página 84)
Provisions	Disposiciones	http://iate.europa.eu/SearchByQuery.do?method=searchDetail&lilId=792838&langId=&query=provision&sourceLanguage=en&domain=0&matching=&start=0&next=1&targetLanguages=es
Purpose	Objeto	Texto paralelo del Anexo 2 (página 85)
Receiving party	Parte destinataria	http://www.linguee.es/espanol-ingles/search?source=auto&query=receiving+party
Regulations	Reglamento	http://iate.europa.eu/SearchByQuery.do?method=searchDetail&lilId=797196&langId=&query=regulation&sourceLanguage=en&domain=0&matching=&start=0&next=1&targetLanguages=es
Royal Decree	Real Decreto	https://www.boe.es/diario_boe/txt.php?id=BOE-A-2004-2316
Sole discretion	Única discreción	http://www.linguee.es/espanol-ingles/search?source=auto&query=sole+discretion
Suspension	Suspensión	Diccionario de términos jurídicos (Alcaraz & Hugues)
Terminate	Extinguir / terminar	Diccionario de términos jurídicos (Alcaraz & Hugues) → extinguir
Tribunal	Juzgado	Diccionario de términos jurídicos (Alcaraz &

		Hugues)
Written agreement	Acuerdo escrito	http://www.linguee.es/espanol-ingles/search?source=auto&query=written+agreement Texto paralelo del Anexo 2 (página 90, punto 10.2.3)

Glosario términos económicos

Administrative management	Gestión administrativa	http://iate.europa.eu/SearchByQuery.do?method=searchDetail&lilId=320023&langId=&query=Administrative%20management&sourceLanguage=en&domain=0&matching=&start=0&next=1&targetLanguages=es
Amount	Cuantía	http://www.wordreference.com/es/en/translation.asp?spen=cuantia
Budgeted	Presupuestado/a	
Civil responsibility insurance policy	seguro de responsabilidad civil	Texto paralelo del Anexo 2. (página 89, punto 7.1) http://www.linguee.es/espanol-ingles/search?source=auto&query=civil+responsibility+insurance+policy
Compensation	Compensación/ remuneración	http://www.wordreference.com/es/translation.asp?tranword=Compensation Texto paralelo del Anexo 2 (página 88, punto 6.2)
Costs	Costes	http://www.wordreference.com/es/translation.asp?tranword=costs
Direct expenses	Gastos directos	http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:1998:060:0001:0029:ES:PDF → (página 15)
Expenses	Gastos	http://www.wordreference.com/es/translation.asp?tranword=expenses
Extraordinary direct costs	Costes directos extraordinarios	http://www.linguee.es/espanol-ingles/search?source=auto&query=Extraordinary+direct+costs
Financial management	gestión financiera	http://iate.europa.eu/SearchByQuery.do?method=searchDetail&lilId=1078011&langId=&q

		uery=financial%20management&sourceLanguage=en&domain=0&matching=&start=0&next=1&targetLanguages=es
Financial report	Memoria económica	Texto paralelo del Anexo 2 (página 88, punto 11.1)
Insurance company	Compañía de seguros/ aseguradora	http://www.linguee.es/espanol-ingles/search?source=auto&query=insurance+company
Invoice	Facturas / facturar	http://www.wordreference.com/es/translation.asp?tranword=invoice
Over invoicing	sobrefacturación	http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2004:023:0001:0013:ES:PDF → (pág 4)
Payment	Pago	http://www.oxforddictionaries.com/translate/english-spanish/payment
Quarterly	trimestralmente	http://iate.europa.eu/SearchByQuery.do?method=searchDetail&lilId=1364540&langId=&query=quarterly&sourceLanguage=en&domain=0&matching=&start=0&next=1&targetLanguages=es
Revenues	Ingresos	http://www.oxforddictionaries.com/translate/english-spanish/revenue?q=revenues
Single payment	Pago único	http://iate.europa.eu/SearchByQuery.do?method=searchDetail&lilId=930432&langId=&query=single%20payment&sourceLanguage=en&domain=0&matching=&start=0&next=1&targetLanguages=es
Tax obligations	Obligación tributaria	http://www.linguee.es/espanol-ingles/search?source=auto&query=tax+obligation
Total expected turnover	Facturación total prevista	http://context.reverso.net/traduccion/ingles-espanol/total+turnover

Glosario términos biomédicos

Acute alcoholic hepatitis (AAH)	Hepatitis alcoholica aguda (HAA)	http://www.acronymfinder.com/Acute-Alcoholic-Hepatatis-(disease)-(AAH).html http://www.linguee.es/ingles-espanol/traduccion/acute+alcoholic+hepatitis.html
AEMPS	AEMPS	http://www.acronymfinder.com/Agencia-Espa%C3%B1ola-de-Medicamentos-y-Productos-Sanitarios-(Spanish)-(AEMPS).html
Clinical trial	Ensayo clínico	http://context.reverso.net/traduccion/ingles-espanol/clinical+trial
Corticoids	corticoides	http://www.wordreference.com/es/translation.asp?tranword=corticoids
CREC	CEIC	http://www.hospitalcruces.com/alDiaNoticiasDetalle.asp?lng=es&id=140
Ethics committee	Comité de ética	http://www.europarl.europa.eu/sides/getDoc.do?pubRef=-//EP//TEXT+CRE+20050309+ITEMS+DOC+XML+V0//ES&language=ES
Integrated Health Organisation	Organización sanitaria integrada	http://www.osakidetza.euskadi.eus/r85-ckcent11/es/contenidos/informacion/acceso_obb/es_def/index.shtml
Lille score	Puntaje de lille	Diccionario Crítico de Dudas de F. Navarro y en http://www.intramed.net/contenidover.asp?contenidoID=60799 → texto paralelo sobre la hepatitis alcohólica aguda
Managing Director	Director general	http://context.reverso.net/traduccion/ingles-espanol/managing+director
Medicinal products	Medicamentos / productos	http://www.europarl.europa.eu/sides/getDoc.do?pubRef=-

	medicinales	//EP//TEXT+CRE+20021022+ITEMS+DOC+XML+V0//ES&language=ES
Multicenter study	Estudio multicéntrico	Texto paralelo del Anexo 2 (página 83, punto 2.3) Y en http://www.linguee.es/espanol-ingles/search?source=auto&query=multicenter+study
Protocol and Good Clinical Practice (GCP)	Protocolo y Buena Práctica Clínica (BPC)	Texto paralelo del Anexo 2 (página 86,punto 3.1.5) http://www.acronymfinder.com/Good-Clinical-Practice-(GCP).html http://iate.europa.eu/SearchByQuery.do?method=searchDetail&lilId=1226337&langId=&query=good%20clinical%20practice&sourceLanguage=en&domain=0&matching=&start=0&next=1&targetLanguages=es
Research Team	Equipo de investigación	http://iate.europa.eu/SearchByQuery.do?method=searchDetail&lilId=1260693&langId=&query=Research%20Team&sourceLanguage=en&domain=0&matching=&start=0&next=1&targetLanguages=es
Severe acute alcoholic hepatitis	Hepatitis alcoholiga aguda grave	http://emedicine.medscape.com/article/170539-treatment http://www.smschile.cl/portal/documentos/Libro_resumen_congrrso_2011.pdf → (página 13)
Specialist	especialista	http://www.wordreference.com/es/translation.asp?tranword=specialist
Translational research	Investigación traslacional	http://iate.europa.eu/SearchByQuery.do?method=searchDetail&lilId=926769&langId=&query=translational%20research&sourceLanguage=en&domain=0&matching=&start=0&next

		=1&targetLanguages=es
Unicentre trials	Ensayos unicéntricos	http://www.linguee.es/espanol-ingles/search?query=unicenter+trials&source=auto

Muchos términos se han encontrado en textos paralelos, por lo que se mostrarán en el Anexo 2 (página 74).