Decision No. Δ3(α) οικ. 36809

**Amending and supplementing Joint Ministerial Decision Γ5α/59676/2016 (Government Gazette B 4131) of the Ministers of Economy & Development and Health “Provisions regarding the implementation of Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC”**

**THE MINISTERS**

**OF ECONOMY & DEVELOPMENT AND HEALTH**

Having regard to:

1. the provisions of Article 1 paragraphs 1, 2 and 3 and Article 3 of Law 1338/1983 “Implementation of Community law” (GG A 34), as amended by Article 6 of Law 1440/1984 “Participation of Greece in the capital, reserves and provisions of the European Investment Bank, the capital of the European Coal and Steel Community and the Euratom Supply Agency”, and of Article 65 of Law 1892/1990 (GG A 101);
2. the provisions of Article 14 paragraph 4 and Article 2 paragraphs 1 and 2 of Law 1316/1983 (GG A 3), as currently in force;
3. Regulation (EU) No. 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products intended for human use, and repealing Directive 2001/20/EC;
4. Joint Ministerial Decision Γ5α/59676/2016 of the Ministers of Economy & Development and Health “Provisions regarding the implementation of Regulation (EC) No. 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products intended for human use, and repealing Directive 2001/20/EC” (GG B 4131);
5. Article 4 of Law 4523/2018 (GG A 41) “Provisions on the manufacturing of finished cannabis-based medicinal products, and other provisions";
6. Directive 2001/83/EC on the Community code relating to medicinal products for human use, as amended by Directives 2002/98/EC, 2004/27/EC, 2004/24/EC, 2010/84/EC and 2011/62/EU;
7. Decision ΔΥΓ3α/32221 “Harmonisation of Greek legislation with the relevant European Union legislation regarding the manufacturing and marketing of medicinal products for human use in compliance with Directive 2001/83/EC on the Community code relating to medicinal products for human use (OJ L 311/28.11.2001), as currently in force and as amended by Directive 2011/62/EU on the prevention of the entry of falsified medicinal products into the legal supply chain (OJ L 174/1.7.2011)” (GG B 1049), as amended by Joint Ministerial Decision ΔΥΓ3α/Γ.Π.οικ. 90023/27.9.2013 (GG B 2485) “Amending and supplementing Joint Ministerial Decision ΔΥΓ3α/Γ.Π. 32221/29.4.2013 harmonising Greek legislation with the relevant European Union legislation […] i line with Directive 2012/26/EU amending Directive 2001/83/EC on pharmacovigilance” (OJ L 299/27.10.2012)”;
8. Article 90 of Presidential Decree 63/2005 “Codification of legislation on government and government bodies” (GG A 98);
9. Presidential Decree 121/2017 “Statute of the Ministry of Health”, as currently in force;
10. Presidential Decree 73/2015 “Appointment of Vice-President of the Government, Ministers, Alternate Ministers and Deputy Ministers” (GG A 116);
11. Presidential Decree 125/2016 “Appointment of Vice-President of the Government, Ministers, Alternate Ministers and Deputy Ministers” (GG A 210);
12. Presidential Decree 22/2018 “Appointment of Vice-President of the Government, Ministers, Alternate Ministers and Deputy Ministers” (GG A 37);
13. Presidential Decree 123/2016 “Reconstitution and renaming of the Ministry of Administrative Reform and e-Government, re-constitution of the Ministry of Tourism, establishment of a Ministry of Immigration Policy and a Ministry of Digital Policy, Telecommunications and Information, renaming of the Ministry of Interior and Administrative Reconstruction, Economy, Development, Tourism and Infrastructure, Transportation and Networks” (GG A 208);
14. the fact that the provisions of the present Decision do not imply any burden on the state budget or the budgets of the entities refereed to herein, in accordance to Document No. B2(a), B1(a)13521/19.2.2019 of the General Directorate of Financial Services of the Ministry of Health;

WE DECIDE:

1. To amend and supplement Joint Ministerial Decision Γ5α/59676/2016 (GG Β 4131) of the Ministers of Economy & Development and Health “Provisions regarding the implementation of Regulation (EU) No. 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/ EC” by inserting Articles 26 to 33, with a view to harmonising, simplifying and rationalising clinical trial procedures, as follows:

“Article 26

Signature of the agreement

1. With a view to simplifying and speeding up the process of signing the agreement envisaged in Article 5 hereof between the sponsor, the principal investigator, the legal representative of the healthcare institution (private or public hospital) and the ELKE/ELKEA account manager for public hospitals, a Standard Quadripartite Agreement shall apply, along with the templates for “Acceptance of project management”, “Project team members” and “Project budget”, as per Annexes I, II, III and IV attached hereto. Any further terms and conditions or clarifications added by the Sponsor to the Standard Agreement shall be included in an annex attached thereto.

2. Once the clinical trial has been authorised by the National Organisation of Medicines (EOF), the principal investigator shall submit to the hospital’s administration a dossier containing: (a) an agreement signed by the sponsor and the Principal Investigator along with all its annexes in four (4) equally authentic counterparts; (b) EOF’s authorisation; (c) the clinical trial protocol summary in the Greek language; (d) the insurance contract; and (e) the templates for “Acceptance of the project management”, “Investigator team” and “Project budget”.

3. Within ten (10) working days of the submission of the dossier to the hospital’s administration, the agreement shall be signed by the legal representative of the hospital.

4. The aforementioned agreement along with the entire dossier shall be promptly forwarded to the ELKA/ELKAE manager and shall be signed within ten (10) working days of the date of its signature by the hospital.

5. Any modification of agreements with the hospital and financial management agencies shall be permitted after the commencement of the clinical trial, and the procedures, supporting documents and time frames laid down in this Decision shall apply.

6. Within three months of the publication hereof, a web address shall be set up for all the bodies and agencies involved in the authorisation and management of clinical trials, in order to enable the electronic submission of forms and supporting documents by the sponsors.

7. Any delay in signing the agreement as described above shall give rise to the disciplinary and administrative sanctions referred to in Article 5 hereof.

Article 27

Costs of hospitalisation and laboratory and diagnostic tests

1. The costs of laboratory and diagnostic tests and other procedures performed within the hospital, as arising in respect of each patient due to his/her participation in the clinical trial, shall be borne by the Sponsor.

2. The costs of hospitalisation, laboratory and diagnostic tests and any pharmaceutical care and other procedures performed within the hospital and due to health complications of clinical trial subjects as a result of their participation in the clinical trial shall be borne by the Sponsor.

3. As from the signature of the agreement, each clinical trial shall be assigned a unique identifier, which is the Clinical Trial Reference Code applying to all procedures performed within each hospital in the context of the clinical trial.

4. The costs referred to in paragraphs 1 and 2 of this article for each clinical trial according to the Clinical Test Reference Code shall be determined by the hospital’s financial services on the basis of the official price lists as established by relevant Ministerial Decisions, and the relevant tax document shall be issued to the Sponsor.

5. Τhe above amounts shall be paid by the Sponsor directly to the hospital.

Article 28

Financial management of the clinical trial

1. Charges at a flat rate of five per cent (5%) in favour of the financial management agency and fifteen per cent (15%) in favour of the hospital shall be withheld from the investigators’ remuneration as indicated in the project budget.

2. The financial management of a clinical trial conducted at NHS healthcare structures, military hospitals and private-law hospitals (Onassio Cardiac Surgery Centre and Papageorgiou Thessaloniki General Hospital) shall be carried out through the Special Account of Research and Development Funds (ΕLKEA) of the relevant Healthcare Region.

3. The financial management of a clinical trial conducted at NHS healthcare structures with the participation of university faculty member researchers, at university hospitals or at private hospitals led by a university faculty member as Principal Investigator shall exclusively be carried out through the ELKE account.

4. The aforementioned charges to be withheld in favour of the hospital for the conduct of the clinical trial, as well as the remuneration of investigators, shall be paid through the respective financial management agency within thirty days of the deposit of the amount by the Sponsor.

5. The Sponsor shall make stepwise payments, according to the payment schedule specified in the agreement signed.

Article 29

Low-intervention clinical trials

For the conduct of a low-intervention clinical trial as defined in paragraph 3 of Article 2 of Regulation (EU) No 536/2014, the provisions hereof and of this Chapter shall apply.

Article 30

Non-commercial clinical trials

In non-commercial clinical trials, where the sponsor is a hospital or a university, the investigational medicinal product may be reimbursed by the Main Insurance Funds, and the provisions of Articles 2 and 3 shall not apply.

Article 31

Disciplinary provisions

1. Without prejudice to the provision of the following paragraph, in the event of unjustified delays in the above procedure or misconduct, the Minister of Health, as senior disciplinary authority, shall impose on the Governors of the hospitals and Heads of Healthcare Regions the sanctions of reprimand and a fine equal up to one month’s salary and, for recurring misconduct, the sanction of removal from office.

2. The disciplinary review of Directors of Military Hospitals and the NIMTS hospital shall be subject to the applicable provisions for the respective category of staff.

CHAPTER V

NON-INTERVENTIONAL STUDIES

Article 32

Procedure for authorisation and acceptance of a non-interventional study

1. Before a non-interventional study can be conducted in Greece, the Sponsor shall submit to the Committee for Non-Interventional Studies (CNIS) a dossier containing the application for authorisation of a non-interventional study, the study protocol, the patient’s informed consent form, as well as a draft agreement as specified in the following article, signed by the sponsor and the Principal Investigator with all its annexes in four (4) equally authentic counterparts. All of these documents shall be submitted in the Greek language.

2. After reviewing the dossier and, provided that the relevant fees have been paid, the Committee shall, within one month, deliver a reasoned opinion on whether the requirements of paragraph 1 of Article 4 of Law 4523/2018 for the conduct of a non-interventional study have been met, and shall promptly notify the sponsor thereof.

3. Following a positive opinion from the Committee, the Principal Investigator shall promptly submit a copy of the dossier along with the Committee’s opinion to the secretariat of the relevant Scientific Board for acceptance of the non-interventional study by the Scientific Board as well as by the Governor of the hospital or the Head of the Healthcare Region, as provided for in paragraph 3 of Article 4 of Law 4523/2018.

4. Any objections to the conduct of a non-interventional study and to the content of the dossier shall be communicated by the Scientific Board to the CNIS and to the sponsor within thirty days of the submission of the dossier. Failure by the Scientific Board to respond by this deadline shall be deemed tacit acceptance.

Article 33

Commencement of a non-interventional study

1. With a view to simplifying and speeding up the process of signing the agreement envisaged in paragraph 4 of Article 4 of Law 4523/2018, a Standard Quadripartite Agreement shall apply, along with the templates for “Acceptance of project management”, “Project team members” and “Project budget”, as per Annexes I, II, III and IV attached hereto. Any further terms and conditions or clarifications added by the Sponsor to the Standard Agreement shall be included in an annex attached thereto.

2. Within ten (10) working days of the acceptance of the non-interventional study by the relevant Scientific Board, the agreement shall be signed by the legal representative of the hospital/primary healthcare unit.

3. The aforementioned agreement along with the entire dossier shall be promptly forwarded to the ELKA/ELKAE account manager and shall be signed within ten (10) working days of the date of its signature at the investigator site level.

4. As from the signing of the agreement, each non-interventional study shall be assigned a unique identifier, which shall be the “Non-Interventional Study Code” applying to all procedures performed at each investigator site in the context of the non-interventional study.

5. In all other respects and unless the provisions of this Chapter state otherwise, the provisions of Articles 26, 27, 28 and 31 hereof shall apply.”

2. To renumber “CHAPTER V” to “CHAPTER VI” and to renumber Articles 26, 27 and 28 to Articles 34, 35 and 36, respectively.

3. As from the publication hereof, Joint Ministerial Decision ΔΥΓ3α/18910/2013 (GG Β 390) “Supplementing Joint Ministerial Decision ΔΥΓ3α/89292/2003 (GG Β 1973) of the harmonisation of Greek legislation with the corresponding EU legislation under Directive 2001/20/EC of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the clinical trials of medicinal products for human use, as amended and currently in force, with a view to harmonising, simplifying and rationalising clinical trial procedures” and any other provision to the contrary shall be repealed.

The present Decision is accompanied by Annexes, which form an integral part hereof.

ANNEXES

I. CLINICAL TRIAL AGREEMENT

II. ACCEPTANCE OF PROJECT MANAGEMENT

III. PROJECT TEAM MEMBERS

IV. PROJECT BUDGET

CLINICAL TRIAL AGREEMENT

Project title: ……………………………………

(hereinafter referred to as “the Trial” and/or “the Clinical Trial”.

Sponsor:

Company representing the Sponsor in Greece:

Product being tested (medicinal product/medical device):

Protocol:

EUdraCT number:

Investigator site:

This agreement is entered into in Athens as of this … day of .[month/year] (hereinafter the “Signature Date”) by and between:

on the one hand, the company ……………………..located at ………………………………………….., Tax Registration No……………. legally represented by …………………….. (hereinafter the “Sponsor/CRO”), specifically authorised to act in Greece as the Sponsor of the Trial for and on behalf of the foreign company ……………………………..; and

on the other hand, Mr/Ms……………………. Physician [insert title]………………. of the ………………….. Department of the ……………… Hospital of………….., resident in ………………………, at ………………St., hereinafter referred to in the Agreement as well as in the Annexes thereof as the “Principal Investigator” and/or “Scientific Supervisor” of the Trial; and

as additional signatories to this agreement, the ………………………. Hospital of………..located in ……………….. at…………………..St., legally represented by its Governor, Mr/Ms ……………………………., hereinafter referred to as the “Hospital”, and the ELKE/ELKEA account manager………… located in ……………………….. at……………….St., legally represented by Mr/Ms ……………….[insert title] hereinafter called “ELKE/ELKEA”.

WHEREAS:

I. The company “………………………..”, which is the Sponsor of the Trial, having for itself and on behalf of the above-mentioned foreign company, all the rights and obligations, as entailed by the status of Sponsor in legal and practical terms under the applicable EU and national legislation, vis-à-vis all competent authorities and bodies, and proceeds to any action required by the law for obtaining authorisation and approval for the lawful conduct of the Clinical Trial, in accordance with the provisions of applicable legislation on clinical trials and good clinical practice in the conduct of clinical trials on medicinal products for human use, as well as in accordance with the ICH Guidelines for Good Clinical Practice.

II. The Sponsor/CRO has requested the Principal Investigator to conduct the Trial and has applied to the Hospital and its staff for approval to hosting the Trial at the Hospital’s facilities; the Trial shall be financed by the Sponsor and shall concern the investigational product (medicinal product or medical device) specified in the approved Clinical Trial Protocol.

III. The Hospital has the authority to approve/accept the conduct of the Trial and has the appropriate equipment to host the Trial at its facilities, and the Principal Investigator states that he/she has agreed to lead the Trial, which shall be conducted at the …………….. Department of the ………………….Hospital of …………………….. within the jurisdiction of the … Healthcare Region.

IV. The parties hereto undertake that the Trial shall be conducted in accordance with: (a) the applicable legislation on clinical trials for medicinal products intended for human use; (b) the authorisations of the conduct of the Trial from the National Ethics Committee (NEC) and from the National Organisation of Medicines (EOF); (c) the terms and conditions specified in the Protocol and in any amendments and/or supplements thereto; (d) the ICH Guidelines for Good Clinical Practice; (e) the Code of Medical Conduct; and (f) the terms and conditions laid down hereinbelow.

V) The financial management of the project will be carried out through the ELKEA account of the ….. Healthcare Region of …………, which has been established in the …… Healthcare Region (…. Healthcare Region) of ……..……….. for the purpose of managing the funds deriving from the implementation of research & development projects, educational and training programmes and provision of scientific and technological services, conduct of special studies, special laboratory tests and analyses, experience exchange programmes as well as other relevant services or activities arising from the financing of relevant scientific proposals by staff of NHS and Social Care Units, which fall within the scope of the research programmes and projects referred to in Article 6 of Law 1514/85, and/or through the Special Account of the University of ………………. (“Special University Account”), which has been established for the purpose of utilising and managing the funds deriving from any source and intended for the recovery of any costs entailed by research & development projects, educational and training programmes and the provision of scientific, technological and artistic services, conduct of special studies, conduct of tests, measurements, laboratory tests and analyses, issuance of opinions, preparation of specifications on behalf of third parties as well as any other relevant services or activities linking education and training with production and performed or provided by the scientific staff of Universities or Technical Universities and with the co-operation of other specialists, in accordance with Article 1, paragraph 2 of Joint Ministerial Decision KA 679/96/22.08.96 (Government Gazette B 826).

VI. The Scientific Board of the Hospital, in line with the relevant decision of the Board of Directors of the Hospital, has already approved: (i) by its Approval of Clinical Trial dated ……………., the conduct of the Clinical Trial at its facilities, in particular the facilities of the ………Department; and (ii) the Patient’s Informed Consent Form issued on [date].

NOW, THEREFORE, in consideration of the premises and the mutual covenants set forth herein, the Parties agree as follows.

1. Conduct of the Trial

1.1 The parties agree that the Protocol and any lawfully approved amendment thereto form an integral part of this Agreement.

1.2 The Principal Investigator agrees to provide his/her professional expertise and knowledge for the conduct of the Trial in accordance with Protocol No. …………. dated ………………. and any lawfully approved amendment thereto and in accordance with the applicable EU and national legislation good clinical practice in the conduct of clinical trials on medicinal products for human use and in accordance with the ICH Guidelines for Good Clinical Practice (hereinafter the “ICH-GCP Guidelines”), and to comply with the deadlines and the terms and conditions laid down in this Agreement.

1.3 If the Principal Investigator ceases to co-operate with the Hospital, he/she shall notify the Sponsor thereof in writing within five (5) days before the end of cooperation. For purposes of continuity in the conduct of the Clinical Trial, the Principal Investigator hereby undertakes to the Sponsor that he/she will remain as Scientific Supervisor of the Clinical Trial until a new Principal Investigator is appointed. The Sponsor shall have the right to appoint any person from among the Hospital’s staff as the new Principal Investigator. The new Principal Investigator shall be required to agree to the terms and provisions of this Agreement. The Sponsor may decide to not appoint a new Principal Investigator and terminate this Agreement in accordance with Article 2.2 hereinbelow, in which case the Hospital shall take action as necessary to implement the Sponsor’s decision.

1.4 The Principal Investigator may appoint other persons as he/she sees fit, to act as co-investigators and contribute to the conduct of the Trial. All co-investigators must be appropriately qualified, appointed in a timely manner with an employment status known to the Sponsor; in this regard, an updated list of all the persons participating in this capacity shall be maintained. Before assuming any obligation or performing any procedure in the context of the Trial, the co-investigator(s) must have obtained all necessary approvals by the authorities (EOF and NEC) in accordance with the relevant provisions. The Principal Investigator shall be solely responsible for managing and overseeing such teams of co-investigators, who shall in all cases be bound by the same terms and conditions as applicable to the Principal Investigator under this Agreement. The Hospital and the Principal Investigator shall be solely responsible for the services provided by their personnel and guarantee that only competent and duly qualified persons shall be involved in the provision of such services.

1.5 The Principal Investigator hereby represents that both he/she and the co-operating physicians have obtained the professional license to practice medicine in Greece provided for by the law [or are trainee medical specialists] and have not committed any disciplinary or criminal offense relating to medical practice. Furthermore, the Principal Investigators represents that both he/she and the co-investigators have read and understood all the contents of the Investigator’s Brochure provided by the Sponsor/CRO, including the potential risks and side effects of the investigational product.

1.6 For the conduct of the Trial, the Sponsor shall supply the Investigational Product (medicinal product or medical device), the trial-related documentation (including Case Report Forms) and, where applicable, shall concede the use of the equipment detailed in Annex A or any equipment as may be required during the conduct of the Trial. The equipment shall be in the sole ownership of the Sponsor if applicable in view of its nature (loan for use) and shall be kept in the same good condition as delivered throughout the duration of the Trial, except for normal wear and tear. The Hospital hereby accepts the aforementioned loan for use and concedes the appropriate facilities for the installation of the equipment. The Principal Investigator shall be responsible and liable for the equipment, including its maintenance (with the exception of consumables) or any risk of loss or damage in connection with the equipment throughout the duration of the Trial. The Sponsor shall not be responsible for replacing the equipment as a result of improper use. Upon the completion or termination of the Trial, the disposal or return of the equipment due to the termination of the loan for use shall be managed in accordance with the Sponsor’s instructions.

1.7 Neither the Hospital nor the Principal Investigator shall use the Investigational Product (medicinal product or medical device), or any trial-related documentation and materials supplied by the Sponsor, or the equipment loaned for use under this agreement, for a purpose other than the conduct of the Trial or in a manner other than in accordance with the terms and conditions of use, as detailed in Annex A hereof. The responsibility for the proper delivery, storage, distribution, use, safekeeping, return and count of the stock of the Investigational Product shall lie with the Hospital and the Principal Investigator. With specific regard to the medicines supplied for the Trial, these shall exclusively be used in accordance with the instructions set out in the Protocol and exclusively for the purposes of the Trial. The instructions provided by the Sponsor regarding their disposal shall be followed. Upon the completion or termination of the Trial, any remaining stocks of medicines shall be disposed of or returned in accordance with the current instructions of the Sponsor and in the manner described in Article 2.4 hereinbelow;

2. Duration and Termination

2.1 The duration of this Agreement shall start on the Signature Date as indicated in the beginning hereof, provided that the relevant authorisations have been granted by EOF and NEC, and shall end on ……….[month] of the year …….., unless earlier terminated in accordance with the provisions hereof. The parties agree that this Agreement may be terminated earlier than that date, if the parties mutually agree that the contractual obligations have been fulfilled, or later than that date, exclusively and only if the deadline for the fulfilment of such obligations has been extended by mutual written agreement of the parties under the terms of this Agreement.

2.2 This Agreement shall be terminated upon the expiry of its period of duration specified above. However, it can also be terminated before the expiry of such period, in the event that the necessary authorisations are not issued by EOF and/or NEC, and at any time (a) following a mutual agreement in writing between the parties, also specifying how to deal with the consequences of such termination; or (b) if either of the parties terminates the agreement by giving a fifteen (15) days’ written notice duly communicated to the other parties; and (c) unilaterally and without reason by the Sponsor, subject to fifteen days’ notice. The termination shall take effect following the lapse of the aforementioned period of notice. This agreement shall be terminated without prejudice to any of the parties, and the contractual obligation of the Sponsor to the Principal Investigator and the Hospital shall be limited to the part of the remuneration that corresponds to actual services rendered and work completed until the effective date of the termination, releasing the Sponsor from the obligation to pay the remainder of the remuneration that has not yet fallen due. If applicable, any excess amount paid as remuneration shall be reimbursed to the Sponsor within thirty (30) days.

2.3 Either party shall have the right to terminate this Agreement in writing with immediate effect and without any loss or penalty and without notice, where there is a serious reason for doing so. Serious reasons include a breach of any of the provisions of this Agreement, all of which are considered to be material, non-compliance with the applicable EU and national legislation governing the conduct of clinical trials and the provision of the services hereby agreed, evidence giving rise to concerns about the safety of trial subjects and necessitating the termination of the Agreement, as well as evidence showing a lack of adequate effectiveness. In these cases, the termination shall be made in writing and shall take effect as soon as it is communicated. If the serious reason arises from the fault of any of the parties, the party not in fault shall have against the party in fault all the rights conferred by the law, including in particular the right to claim any damage it will sustain due to such reason. Upon the communication of the termination, the Principal Investigator agrees to promptly discontinue the Trial, provided that this is medically safe for trial subjects.

2.4 The Hospital and the Principal Investigator shall return to the Sponsor, or destroy in accordance with the Sponsor’s explicit instructions, any unused quantities of the Investigational Product, all documents, materials and equipment supplied by the Sponsor/CRO and all Confidential Information, as defined in Article 7.2 hereinbelow, upon the completion of the Trial or the termination/expiration, in any manner, of this Agreement. This provision shall not apply to documents and records which must be kept by the Principal Investigator and remain at the Investigation Site under the Principal Investigator’s responsibility, as set out in the Protocol and as required by the applicable EU and national legislation.

3. Competent Authorities – Written Informed Consent – Approvals

3.1 Pursuant to the provisions of applicable national and EU legislation, the Principal Investigator shall be responsible for obtaining approval for the Protocol and any amendments thereto, the Patient’s Informed Consent Form, the project budget (fees) and any other documents relating to the Trial, from the Scientific Board and/or Board of Directors of the Hospital before the commencement of the Trial. If the Board of Directors and/or the Scientific Board of the Hospital requires any changes to the Protocol or to the Patient’s Informed Consent Form, such changes shall not be made before the Sponsor is notified and agrees to the changes. The Principal Investigator shall be responsible for the submission of all the necessary documents in order to obtain the necessary authorisations and approvals for the lawful conduct of the Trial in accordance with applicable legislation.

3.2 The Principal Investigator shall also be responsible for obtaining the Patient’s Informed Consent Form signed by or on behalf of each patient participating in the Trial; such form must have been approved by the Sponsor, the Scientific Board and/or the Board of Directors of the Hospital and by the competent authorities and bodies (EOF and NEC). The duly signed Consent Forms shall be kept on record by the Principal Investigator and shall not be transmitted or disclosed to the Sponsor, in accordance with applicable data protection legislation. These records shall be available, upon request, to the competent officials of EOF or of other authorities. When requested to, the Principal Investigator may, in a solemn statement, confirm that the procedure and record-keeping requirements have been complied with for all trial subjects, and shall be liable for any false statement.

3.3 The Sponsor/CRO shall, in co-operation with the Principal Investigator, be responsible for the completion of all the formalities required for obtaining authorisation of the Trial (such as the submission of the clinical trial authorisation application) and for supplying or importing the Investigational Product (The Study Product) and, where required, for obtaining the written approval of the competent authorities and of the National Ethics Committee (NEC) before the commencement of the Trial.

3.4 The Principal Investigator shall act in full compliance with the applicable laws governing the subject-matter of this Agreement.

3.5 In all cases, the Principal Investigator shall obtain a written approval of the Protocol and of the Patient’s Informed Consent Form before the commencement of the Trial. The Sponsor shall permit the delivery of quantities of the Investigational Product only after receiving a copy of the written approval. The Principal Investigator agrees not to include any subject in the trial before obtaining a written positive opinion from the relevant ethics authority and EOF’s explicit authorisation of the Trial. The Hospital and the Principal Investigator shall promptly inform the Sponsor of any audit or inspection by any regulatory authority in relation to the Trial conducted under this Agreement.

4. Reporting of Data and Adverse Events

4.1 The Principal Investigator agrees to regularly report to the Sponsor/CRO all the results of the Trial and other data required by the Protocol (the “Data”) through properly completed (in paper or electronic form) Case Report Forms (CRFs) within …. (…) days after each visit by a patient participating in the Trial to the Investigation Site, with the exception of the startup visit and the Serious Side Effects which must be added within 24 hours. For the avoidance of any doubt, Data shall include, without being limited to, documents, either handwritten or printed, graphs, video and audio material, as well as information included in any file, electronic database or information in electronic form, which are generated or produced in connection with the Trial. The reporting documents must be kept separately as supporting documentation for entries into the ECRF/CRF and shall be retained for fifteen (15) years or more if longer retention periods are required by local or international standards. All identification codes of the trial subjects must be kept in a safe place for fifteen (15) years or more if longer retention periods are required by local or international standards.

4.2 The Principal Investigator also agrees to record and report to the Sponsor promptly, and in any event no later than twenty four (24) hours after becoming aware of any serious adverse reactions, pregnancy or other serious medical cases as these are defined in the Protocol, which may be observed during the conduct of the Trial and affect any trial subject. The Principal Investigator further agrees to follow-up such reports with thorough, written follow-up reports which he/she shall forward to the Sponsor in accordance with the time frames specified by the internal procedures of the Sponsor and by the Protocol, the applicable legislative provisions and regulatory requirements, both during and after the end of the Trial. In addition, the Principal Investigator agrees to provide information directly to EOF, only when so requested by EOF in accordance with applicable legislation.

4.3 The Principal Investigator shall also report to the Local Pharmacovigilance Officer of the Sponsor, within 24 hours of becoming aware of any suspected adverse reactions to the medicinal products of the Sponsor, in accordance with the Sponsor’s internal procedures for the reporting and management of adverse reactions and applicable legislation. The Principal Investigator shall also report any Product Quality Complaint coming to his/her knowledge, within 24 hours of becoming aware thereof, to the Sponsor’s Production Line Manager or Local Pharmacovigilance Officer.

4.4 Furthermore, the Principal Investigator shall report to the Pharmacovigilance Supervisor of the Sponsor within 24 hours of becoming aware thereof, any product quality complaint. A complaint is defined as any visible concern about the potential failure of product to meet any of its specifications after its distribution. More specifically, product quality complaint is defined as any concern regarding the identity, safety, efficacy or performance of the product. Product quality complaints include, without limitation, the following:

• complaints regarding packaging, such as missing or defective content or illegible labelling of lot number or expiry date;

• complaints regarding the physical characteristics of the product, such us change of colour, volume or clearness;

• complaints regarding the presence of particles or sediment, e.g. a reported existence of solid particles or clusters in a fluid which should have been lucid.

4.5 Both the Principal Investigator and the Sponsor/CRO shall be required to regularly update the Hospital, EOF and the NEC on the progress of the Trial and, after the end thereof, submit a detailed report on the results of the Trial.

4.6 The Principal Investigator shall be under the express obligation to retain, after the end of the Trial, all the records that concern and relate to the Trial, for the period specified in the Protocol and required by the applicable EU and Greek legislation, as well as for as long as required in writing by the Sponsor.

4.7 Throughout but also after the end of the Trial, the Principal Investigator shall respond to any query addressed to him/her by the Sponsor, EOF, or the competent authorities in connection with this Agreement, the trial subjects or procedure, subject to prior notification of the Sponsor in each of these cases. In the case of queries addressed to him/her by the media or financial analysts during or after the end of the Trial, the Principal Investigator undertakes to consult and previously inform the Sponsor’s Scientific Supervisor (Medical Director) and, where appropriate in view of the principle of confidentiality and secrecy under this Agreement as well as medical secrecy, refrain from responding.

5. Oversight – Monitoring of the Trial

5.1 During the term of this Agreement, the Hospital and the Principal Investigator agree to allow to representatives of the Sponsor/CRO and of the competent authorities and agencies (including, where applicable, the United States Food and Drug Administration - FDA) to inspect at any time during normal business hours (i) the facilities where the trial is conducted; (ii) unprocessed Trial Data, including the original records of trial subjects, if so permitted by the terms of the Patient’s Informed Consent Form and by applicable legislation; and (iii) any other relevant information as necessary to verify that the Trial is conducted in accordance with the Protocol and in compliance with the applicable legislative provisions and regulatory requirements, including the laws and regulations on data protection and safety and confidentiality of processing. The Principal Investigator shall promptly notify the Sponsor of any planned or surprise inspection by any authority and shall promptly provide the Sponsor, together with the notification of the inspection, with copies of any follow-up correspondence from the competent authority.

5.2 The Hospital and the Principal Investigator agree to take all action as necessary and required by the Sponsor to remedy any shortcomings identified during an inspection. Furthermore, the Sponsor shall have the right to review and approve any correspondence addressed to the competent authorities as a follow-up to their inspection, prior to its submission by the Hospital or the Principal Investigator.

6. Compliance with applicable legislation

6.1 The parties agree to conduct the trial in accordance with the provisions of EU and national legislation on clinical trials and good clinical practice in the conduct of clinical trials on medicinal products for human use, in conformity with the ICH-GCP guidelines, the legislation on bribery and corruption including the U.S. Foreign Corrupt Practices Act and generally accepted international conventions such as the 1996 Declaration of Helsinki, national laws transposing the EU Directive on the implementation of good clinical practice in the conduct of clinical Trials on medicinal products for human use (2001), written instructions and practices provided by the Sponsor, as well as applicable laws for combatting bribery in interactions with government agents, employees and representatives (hereinafter the “Applicable Legislation”).

6.2 In particular, neither of the parties shall take any action that is prohibited by any local or other anti-corruption legislation (including the U.S. Foreign Corrupt Practices Act, and collectively referred to as “Anti-corruption Legislation”) as may apply to either or both of the parties to this Agreement. Moreover, neither party shall make any payment or offer or transfer of value to any government official or employee, member of a political party or candidate politician or any third party associated with this transaction, in a manner that could violate Anti-Corruption Legislation.

6.3 The parties agree to conduct the Trial and maintain records and data which need to be kept for legal purposes or for purposes of compliance with relevant medical and pharmaceutical regulations, insurance clauses or record retention requirements, during and after the end of this Agreement, in full compliance with the Applicable Legislation and regulations, as well as in accordance with the Sponsor’s retention policy with regard to third-party records and data and/or otherwise and in accordance with the terms and conditions set forth hereinabove.

6.4 Furthermore, the Principal Investigator agrees that the amounts to be paid by the Sponsor under this Agreement are not intended to influence any decision making by the Principal Investigator or any of the directors, co-investigators, employees or associates who happen to be government employees, nor is it intended to influence the Principal Investigators’ prescribing behaviour in favour of the Sponsor’s products or procurement, insurance coverage or any type of business gain of the Sponsor. In addition, the Principal Investigator shall ensure that all of his/her associates and agents and any satellite sites, including co-investigators involved in the conduct of the Trial, understand that, under the applicable rules and regulations, they may be required to report certain financial data to the relevant regulatory authorities within and outside Greece. Finally, the parties mutually agree that in the event of a material change of circumstances or a breach of the abovementioned legislative framework, the Sponsor shall have the right to immediately and unilaterally terminate this Agreement and claim reimbursement of any amounts paid, without precluding further claims for any damages suffered by the Sponsor.

6.5 The parties hereto expressly state that they are aware of the provisions of the General Data Protection Regulation [Regulation (EU) 2016/679 of the European Parliament of the Council of 27 April 2016, OJ L 119] and of the national legislation governing the lawful conduct of the Trial and the provision or the agreed services, and fully undertake their obligations under the applicable national legislation on the protection of personal data as regards the collection and any further processing of all the personal data collected and any other data which will come into their knowledge in the course of the provision of the agreed services as well as trial-related records containing personal data. In this regard, the parties acknowledge that the collection, maintenance and processing of personal data, such as information concerning the health and pharmaceutical treatment of trial subjects, as well as personal data concerning the Principal Investigator and any research staff (e.g. name, address and phone number of the Hospital, curriculum vitae), are subject to full compliance with the applicable laws, provisions and requirements under the EU or national data protection legislation, and in collecting and processing such data they agree to take appropriate security measures to prevent any breach of privacy (theft, embezzlement, falsification, unauthorised access, etc.) in the archiving systems, to preserve the confidential nature of the information on the health and pharmaceutical treatment of trial subjects, to properly inform the data subjects of the purpose, collection and any other processing of their personal data, to provide the data subjects with the right to access their personal data and to restrict access thereto by unauthorised persons.

6.6 The Sponsor shall have the right to transmit personal data to other subsidiaries of its Group established within the European Union or to representatives and/or contractors acting on behalf of or for the Sponsor, as well as to any regulatory authority. Similarly, personal data may be transmitted to regulatory authorities across the world or to other subsidiaries of the Group in countries outside the European Union, such as the United States of America, whose data protection framework is considered by the EU as inadequate to ensure a satisfactory level of personal data protection. Any such transmission of personal data, irrespective of whether the recipient is located within or outside the European Union, will strictly take place in accordance with the terms and conditions stipulated by national or EU legislation and in full compliance with the currently applicable guidelines, decisions, circulars and regulations of the Hellenic Data Protection Authority that are relevant to the subject-matter of this Agreement. In any event, the Sponsor, the subsidiaries of its Group and their respective representatives undertake to have adequate safeguards in place in order to protect such personal data. Personal data may also be disclosed where required by individual supervisory or judicial authorities or by applicable legislation. Finally, the parties agree that the Sponsor may use personal data that concern the Investigator and his/her associates for purposes of internal management and communication.

6.7. The Hospital and the Principal Investigator shall inform the research staff and any other staff involved in the conduct of the Trial that their personal data may be collected as provided for in Article 6 and, where required, they shall obtain the written consent thereof.

6.8 If any of the parties hereto considers that any term of this Agreement is in breach of applicable laws and provisions, the parties agree to negotiate in good faith a revision of the term(s) in question. If the parties fail to reach an agreement on the new or amended terms in order to ensure that the Agreement in its entirety is in compliance with the Applicable Legislation, then either party may terminate this Agreement subject to on a sixty (60) days’ prior notice duly communicated to the other parties.

7. Intellectual Property Rights – Confidentiality – Publication

## 7.1 All the Data, including without limitation, documents, whether handwritten or printed, graphs, video and audio material, as well as information contained in any record, electronic database or electronic information, generated and/or produced in connection with the Trial, shall be property of the Sponsor, and the Sponsor may use the Data in any manner it deems appropriate, in accordance with the applicable laws and regulations on personal data protection, safety of processing and secrecy, as well as in accordance with the terms and conditions of this Agreement. Any work or intellectual asset which can be protected under intellectual property legislation which will be created in connection with the conduct of the Trial and be included in the Data (with the exception of any publication by the Principal Investigator, as provided for in paragraph 7.3 below) shall be the property of the Sponsor as the owner of the unlimited intellectual property right thereon. All the royalties of the Principal Investigator and of other creators, contributors, associates, co-investigators and other participants who may contribute in any manner to the work, which relate to this Agreement, including those referred to in Article 8, shall accrue to the Sponsor. To this end, it is expressly agreed between the parties that the unlimited property right on the overall research to be conducted (indicatively, results, reports, final report, etc.) shall be hereby transferred by the Hospital, ELKE/ELKA and the Principal Investigator, all of which state that they have authority to act on behalf of any other creator, contributor, co-investigator, associate and other participant, exclusively and for an indefinite period of time to the Sponsor, and the latter shall be entitled to exercise any powers deriving from such right, without being required to pay any consideration or compensation other than as agreed herein. The Sponsor’s counterparties hereby waive any intellectual property claim in relation to work executed, expressly stating that the consideration they have received is in full settlement of any value thereof. The Hospital and the Principal Investigator hereby undertake to promptly disclose to the Sponsor any know-how gained in the course of and/or in connection with this Trial and undertake not to use such know-how other than for the purposes of this Agreement without the prior written consent of the Sponsor. The Hospitals and the Principal Investigator hereby grant to the Sponsor an exclusive, universal, irrevocable, royalty-free licence to use any know-how not specifically granted under the preceding sentence.

7.2 All information, including information regarding the Investigational medicinal Product (The Study Product) or any activities of the Sponsor, such as patent applications, formulas, production processes, key scientific data, previous clinical data and formulation data provided to the Hospital, to ELKE/ELKEA or to the Principal Investigator and thitherto unpublished, as well as any data considered to be a result or outcome of this Trial, shall be treated as confidential (hereinafter the “Confidential Information”) and shall remain in the exclusive ownership of the Sponsor. Both during the term and after the expiration/termination of this Agreement, the Hospital, ELKE/ELKEA or the Principal Investigator shall keep confidential and use only for the purposes envisaged in this Agreement: (i) information which is considered confidential or which any reasonable person would consider confidential and property of the Sponsor, which are disclosed on behalf of or by the Sponsor to the Hospital, ELKE/ELKEA or to the Principal Investigator; and (ii) Data generated or produced as a result of this Trial. The preceding requirements shall not apply to data or information which (i) have been made public through no fault of the Hospital, ELKE/ELKEA or the Principal Investigator; (ii) the Sponsor has agreed in writing to their use or disclosure; or (iii) are published in accordance with paragraph 7.3 hereinbelow.

7.3 In the case of Data or other information arising from the provision of services in accordance with and in fulfilment of the terms and conditions of this Agreement by the Hospital, ELKE/ELKEA or the Principal Investigator, the Sponsor or the duly appointed representatives thereof shall have the right to publish such data and information without any approval from the Principal Investigator. The Principal Investigator shall have the right to publish the results of the Trial and any supporting evidence required to be included in any publication of the Trial results or necessary for other scientists to verify the results of the Trial. If the Principal Investigator wishes to publish any information from the Trial, a copy of the draft paper to be published must be submitted to the Sponsor for review, at least sixty (60) days before its submission for publication or presentation. The Sponsor and the Principal Investigator shall undertake a fast-track review of any abstracts, poster presentations or other relevant material. In view of the above, no document containing Confidential Information shall be submitted for publication without the prior written consent of the Sponsor. If requested in writing, the Principal Investigator shall delay publication for up to sixty (60) more days, to allow time for a patent application to be submitted. If an individual Trial is part of multi-site Trial, the Principal Investigator shall not publish any data derived from the specific investigator site until the consolidated results from the completed multi-site Trial are reported in a joint publication. However, if such a multi-site publication is not submitted within twelve (12) months following the conclusion, cancellation or expiration of the trial in all sites or after the Sponsor confirms that there shall be no multi-site publication for the Trial, the Principal Investigator may issue/publish the results derived from the site of the Hospital independently, in accordance with the terms of this paragraph.

7.4 The Principal Investigator warrants compliance with the provisions of this Article 7 by all co-investigators and any other personnel involved in the Trial in any manner whatsoever or otherwise connected thereto.

7.5 The Sponsor shall have the right to use the name of the Hospital and of the Principal Investigator (and co-investigators) in its newsletters to other Investigation Sites updating on any developments in area of clinical trials, the patient recruiting procedure and other relevant issues of a more general interest. The Hospital and the Investigator shall not use the name of the Sponsor or of any employee and associate thereof, or of a company that is a subsidiary of or affiliated to the Sponsor, as well as any sign, logo or trade mark or proprietary feature in any advertising or informational communication without the prior written consent of the Sponsor.

7.6 Without prejudice to any other provision of this Agreement to the contrary, the Sponsor shall have the right to disclose the results of the Clinical Trial in order to comply with any legislative or regulatory provision prior to the conclusion of the Clinical Trial or before any proposed publication, under the terms on Publication as set forth in this Agreement. In any event, it is hereby agreed that the Investigator shall comply with any legislative or regulatory provision concerning the procedure, the subject-matter or the disclosure of the results of the Clinical Trial.

7.7 In providing the services described above, the Principal Investigator shall commit to comply with all provisions of the relevant laws and any good practice/professional conduct principles as may be communicated by the Sponsor, and to duly provide a statement of interest if the law imposes any type of obligation to disclose information as to the nature and remuneration of his/her services.

7.8 The Principal Investigator is aware and accepts that the Sponsor and its Group of Companies, as part of its lawful business activity, collects, keeps and processes, either by itself, or via third-party contractors within or outside the European Union, the personal data of the Investigator, always in compliance with the stipulations of any laws that may apply, including Laws 2472/1997, 3471/2006, 3472/2006 and 3115/2003.

7.9 The Principal Investigator is aware and accepts that the Sponsor may disclose to any third parties information that concerns the provision of the above services, including the name, the place of provision and the value of any payment or compensation in kind he/she receives from the Company for the above services, such as the fee, payment details, travel and accommodation costs or any other expenses. In particular, the Investigator is aware and accepts that the Company may disclose the above data on a website of the Sponsor or its Group of Companies. The parties are aware of the requirement to post the key data of the Agreement on the “Diavgeia” website under Law 3861/2010.

8. Patents

8.1 All the rights on any discovery or invention, which has been conceived or has been conceived and has been put into practice as a result of the work performed in accordance with and in fulfilment of the terms of this Agreement and/or after the expiration thereof shall belong to the Sponsor or the duly authorised representative thereof. The Hospital, ELKE/ELKEA and the Principal Investigator shall promptly disclose any invention or discovery resulting from the implementation of this Agreement. The Hospital, ELKE/ELKEA and the Principal Investigator agree to transfer to the Sponsor or the duly authorised representative thereof the exclusive ownership of the invention/discovery, upon the repayment by the Sponsor of any expenditure incurred by the Principal Investigator, ELKE/ELKEA and/or the Hospital in the context of application and follow-up procedures for obtaining a patent or maintaining in effect an existing patent for such inventions/discoveries. These applications, if any, shall be submitted and defended both in and out of court by the Sponsor or a duly authorised representative thereof.

8.2 The Hospital, ELKE/ELKEA and the Principal Investigator agree to sign, and ensure that all their associates and employees will sing, all documents required for the transfer of all rights, titles and interests on any such invention or discovery to the Sponsor or a duly authorised representative thereof.

9. Budget – Fees

NOTE: This paragraph is to be completed by the Sponsor according to the principles and procedures thereof.

A. Fees and Payment Schedule

9.1 For the implementation of the Project, it is hereby agreed that the Sponsor shall pay to each patient completing the trial the amount of ……………..……euro (€…………..) per patient, which is acknowledged to be fair and reasonable compensation in view of the engagement required under the Protocol. This amount, which shall cover all expenses arising from the conduct of the Trial in accordance with the Protocol, shall include all the fees, the costs incurred in the context of the project, as well as any third-party charges and taxes that are included in this amount and shall be withheld therefrom. The fees shall include, inter alia and without limitation, the fees of the Principal Investigator (PI), the fees of the scientific and other personnel engaged in the project, the fee for the archiving of important documents, and Hospital fees, withholding charges and any other cost or expense required for or incurred in the conduct of the project. This amount does not include VAT.

The charges in favour of ELKE/ELKEA and in favour of the hospital shall be included together with any other contributions and taxes in the above amount and shall be withheld therefrom.

The total budgeted expenditure for the conduct of the Trial, as broken down in the TABLE OF PAYMENTS below, shall be paid by the Sponsor in …. instalments, with the first instalment being payable ….. (…) months after the admission of the first patient to the Investigator Site, as evidenced by the data entered in the relevant Case Report File, or as a lump sum at the end of the trial. The amount of each instalment shall depend on the number of visits that each patient has made during the reference period and shall be determined accordingly. The aforementioned payments shall be subject to the completion of each phase of the trial, as confirmed in writing by the Principal Investigator and the Sponsor’s project manager.

The payments shall be made into the following bank account:

Name of recipient bank:

Bank account No:

IBAN:

All the payments provided for by this Agreement and corresponding, as specified hereinbelow, to services rendered and works executed shall be made, in accordance with the law, into the above bank account held by the ELKEA of the ….Healthcare Region of…………….., the ELKE of the University of …………, after the ELKE of the ….Healthcare Region of ……………….or the ELKE of the University of ………… have issued and delivered to the Sponsor the respective official certified Invoice for the Provision of Services, as required by the Greek Code of Books and Records, which the Sponsor shall settle within ………… (…) days of the issue and delivery thereof.

The Sponsor shall communicate to the Hospital a copy of the invoices for the provision of services received from the ELKE, whenever the Sponsor makes a deposit.

Any deposit made by the Sponsor in favour of the ELKEA of the …. Healthcare Region of ………………./ELKE of the University of ……………. shall count against the total amount payable by the Sponsor and shall be evidenced by the deposit voucher issued by the bank. Such payments shall be deemed a discharge on the part of the Sponsor of its obligations in respect of the Principal Investigator fees, the fees of scientific experts other associates, secretarial and administration staff and any other human resources in general to be involved in the conduct of the Clinical trial and to be used for the provision of services as specified in the Clinical Trial Agreement, it being understood that the Sponsor does not hereby conclude any dependent employment contract or independent service provision contract or works contract or any other type of employment relationship with the various categories of personnel to be engaged in the conduct of the Clinical Trial in accordance with the above. Accordingly, such persons shall have no claim on the Sponsor for the provision of their services during the conduct of the Clinical Trial, in particular claims with respect to any salaries, wages, fees, compensation, social security contributions, etc. typically payable by an employer.

TABLE OF PAYMENTS

Breakdown of fees by participating patient

|  |  |  |
| --- | --- | --- |
| Visits | Investigator’s fee  (euro) | Handling fee  (…%) |
| Initial estimate of number of visits |  |  |
| Startup visit |  |  |
| Visit 1 |  |  |
| Visit 2 |  |  |
| Visit 3 |  |  |
| Visit 4 |  |  |
| Visit 5 |  |  |
| Visit 6 |  |  |
| Visit 7 |  |  |
| Visit 8 |  |  |
| Visit 9 |  |  |
| Visit 10 |  |  |
| Visit 11 |  |  |
| Visit 12 |  |  |
| Visit 13 |  |  |
| Visit 14 |  |  |
| Visit 15 |  |  |
| Visit 16 |  |  |
| Visit 17 |  |  |
|  |  |  |
| Completion of treatment/Early withdrawal |  |  |
|  |  |  |
| Total |  |  |
|  |  |  |
| Total + VAT |  |  |

Total: EUR …./patient (+….management cost).

Screening failure: EUR…/patient.

9.2 The above eCRF/CRF handling fee is aimed to cover the cost of the operations required for entering all the data in the file within ……… (….) business days after the patient’s visit, with the exception of the startup visit and the Serious Adverse Reactions which must be added within 24 hours.

9.3 The Principal Investigator is expected to admit to the investigator site …………..(….) eligible patients to participate in this trial. The Sponsor shall reserve the right to terminate the Clinical Trial Agreement with immediate effect and at no loss to itself, if no patient has been admitted to the Investigator Site by ………………. [date].

9.4 While the trial is underway and provided that the patient uptake envisaged herein has been met, the Sponsor may request the Hospital and the Principal Investigator to recruit more patients. If acceptable to the Hospital and the Principal Investigator, the written notification by the Sponsor to the Hospital and to the Principal Investigator to approve the inclusion of more patients in the Trial shall suffice to document and prove the consent of the Parties. For such new recruits, the same amount as provided for in paragraph 9.1 hereof shall be paid per completed CRF to be evaluated, without any further amendment to this Agreement being required.

9.5 All payments shall be made according to the Payment Schedule above. Patients joining but not completing the trial shall receive payment on a pro rata basis according to the Payment Schedule. No payment shall be made to any subjects who withdraw from the Trial or complete the Trial but do not fulfil the inclusion criteria and the requirements of the approved Protocol, with the exception of cases specifically approved by the Sponsor and entailing follow-up visits or collection of data. The amount of ………….. euro (€…………) shall be paid to each participating failing the screening process due to unexpected out-of-range values in laboratory tests. This amount shall be paid for a maximum of ……………….(…..) participating patients. If more than ………………….(…..) patients are excluded due to screening failure, the Sponsor shall not cover such expenditure, and the aforementioned compensation for the additional patients shall not be paid, except with the prior written consent of the Sponsor.

9.6 The final payment shall be effected after the Case Report File (CRF) has been completed (including follow-up visits) and delivered to the Sponsor and after all questions regarding the data have been answered at the Investigation Site. The final amount payable shall be calculated according to the total number of patients included and the criteria, terms and conditions of payment set forth above.

9.7 The parties acknowledge and agree that the fee and any financial or other support provided by the Sponsor in accordance with and in performance of this Agreement represents the normal transaction value of the services rendered and the work executed by the Principal Investigator and the Hospital for the conduct of the Trial, has been negotiated and agreed upon on an arm’s length basis and has not been determined in such a way to include the volume or value of any services or other work which have occurred in any manner between the Sponsor, the Hospital and the Principal Investigator.

9.8 Neither the Hospital and the Principal Investigator shall invoice any third party for the Investigational Medicinal Product (The Study Product) or for any other items, materials or services supplied by the Sponsor in connection with the Trial or for any services provided to trial subjects in connection with the Trial, for payments are envisaged and effected as part of the trial, unless specifically permitted by the provisions on and the terms and conditions for the payment of fees.

B. Special terms

This Trial shall be conducted in line with a policy of guided enrollment (inclusion/exclusion criteria). The Sponsor expects the completion of the enrollment process once a total number of ……………(….) validly enrolled subjects is reached across all the Investigator Sites involved. If a total of …………….. (…..) subjects are validly enrolled before the Investigation Site achieves its target of ……………… (…..) validly enrolled subjects, the Sponsor shall reserve the right to restrict or suspend any further admission to the Investigator Site. In this case, the Sponsor shall notify the Principal Investigator thereof, and the Principal Investigator shall promptly restrict or stop any further admission immediately upon the notification.

10. Liability/Indemnification

10.1 The Sponsor shall be obliged to restitute any loss or damage which the Principal Investigator and/or the Hospital may sustain as a result of personal injury to any of the clinical trial subjects directly caused by the use of the Investigational Medicinal Product (the Study Product) during the Trial or by any intervention or procedure provided for or required by the Protocol which the subject would not have undergone had he/she not participated in the trial, provided that the following conditions are met:

(a) the event was the result of a substance of the Sponsor being tested, provided that such substance was administered in line with the Sponsor’s Clinical Trial Protocol approved by the relevant ethics and regulatory authorities, as in force from time to time and in accordance with any future subsequently amendments thereof.

(b) the event was associated with the use of comparative substances legitimately administered in line with the Clinical Trial Protocol;

(c) the event occurred as a result of diagnostic procedures performed in line with the Protocol, as applicable from time to time following any subsequent approved amendments thereto.

(d) the event was the result of therapeutic or diagnostic actions legitimately required due to the occurrence of unexpected adverse reactions to the Sponsor’s investigational substance, to a comparative treatment or to diagnostic procedures required under the Protocol, as applicable from time to time following any subsequent approved amendments thereto.

The Sponsor shall have the absolute right to proceed with any settlement, excluding an admission of fault on the part of the beneficiaries of the indemnification without their written consent. Furthermore, the obligation for indemnification shall exclude cases of loss, damage or expenditure resulting from negligence, wilful misconduct or misuse by the beneficiaries of the indemnification, it being understood that the administration of any substance in accordance with the instructions of the Clinical Trial Protocol shall not constitute negligence or misuse in the context of this Agreement.

10.2 The above obligation of the Sponsor, as laid down in paragraph 10.1, shall not apply and the Sponsor shall not be liable to pay any indemnification or expenditure, but instead the Principal Investigator, the Hospital, any associates and agents thereof as well as any personnel to be engaged in the conduct of the Trial shall be obliged to compensate the patient and restitute any loss or damage to the Sponsor, including actual and consequential damage, loss of income and material and moral harm, arising from civil or criminal provisions, sustained by the Sponsor due to any actions or omissions of any of the aforementioned persons to the effect that the Trial is not duly conducted in accordance with (a) the Protocol; (b) the Sponsor’s written recommendations and instructions regarding the use of the Investigational Medicinal Product (the Study Product); (c) the provisions of the Applicable Legislation governing the subject-matter of this Agreement; and (d) the terms of this Agreement,. The Sponsor shall have no liability for events occurring exclusively as a result of the underlying disease of any trial subject or for events resulting from diagnostic or therapeutic actions not specifically stated in the Protocol, as applicable from time to time following any subsequent approved amendments thereto.

10.3 The obligation of the indemnifying party hereunder shall apply only if the other party provides prompt notification upon receipt of notice of any claim or lawsuit, permits the indemnifying Party and its attorneys and personnel to handle and control the defence of such claims or lawsuits, including pre-trial, trial or settlement, and the indemnified Party fully cooperates and assists in such defence. The indemnified party further agrees that it will not settle or compromise any such claim or lawsuit without the prior written consent of the indemnifying Party.

10.4 The liability, contractual or arising from the law, of the ELKEA of the …. Healthcare Region of …..……………/ELKE of the University of ……………… as co-signatory to this Agreement shall be limited to and exclusively concern the financial management of the Trial, which will be conducted in accordance with the terms of this Agreement.

11. Insurance

The Sponsor will ensure and maintain in full force throughout the conduct of the Trial (and also after the end of the Clinical Trial, in respect of any claims that might arise in connection with the Trial) insurance coverage for: (i) product liability; and (ii) general liability. Any insurance coverage will be in the amounts expressly stated in the Applicable Legislation.

12. Financial data disclosure/erasure

12.1 The Hospital and the Principal Investigator agree to provide to the Sponsor any information required for its compliance with any disclosure requirements of competent authority (including, if applicable, the U.S. FDA – United States Food and Drug Administration), including any information that is required to be disclosed in respect of any financial relationship between, on the one hand, the Sponsor and other subsidiaries of the Group […] and the respective representatives thereof and, on the other hand, the Principal Investigator and any co-investigator involved in the Trial and between any other representative or employee of the Hospital and of the Sponsor. This disclosure requirement may extend to the disclosure of information concerning members of the family of the persons involved in the trial.

12.2 The Hospital and the Principal Investigator confirm that there is no conflict of interest that will inhibit or affect the performance of the Hospital and/or the Principal Investigator under this Agreement and confirm that their performance under this Agreement does not violate any other agreement with third parties. The Hospital and the Principal Investigator shall promptly inform the Sponsor if any conflict of interest arises during the conduct of the Trial and the performance of this Agreement.

12.3 The Principal Investigator and the Hospital shall not hire, contract or maintain as an associate or employee any person, directly or indirectly, to render the services and works foreseen in this Agreement, if this person (i) has been disqualified by any competent supervising Authority (including, if applicable, the U.S. FDA – United States Food and Drug Administration); or (ii) has been convicted for professional malpractice or tort relating to the conduct of clinical trials. Upon the Sponsor’s written request, the Principal Investigator and the Hospital shall, within a period of ten (10) days, confirm in writing that they have complied with the aforementioned requirement. This ongoing assurance and warranty is provided on an ongoing basis throughout the duration of this Agreement, and the Principal Investigator and the Hospital shall promptly notify the Sponsor of any change in the assurance and warranty situation stated in this article.

13. Independent parties

The Hospital and the Principal Investigator shall be independent contractors to the Sponsor, and no dependent employment or service relationship is established between them and the Sponsor. The Principal Investigator and any personnel that he/she may use in the trial shall not be entitled to participate in or benefit from any benefits and allowance plan, worker policies or staff insurance coverage for the employees of the Sponsor.

14. Publicity

None of the parties shall use the name of any other party for marketing or promotional purposes without the prior written consent of the party whose name is proposed to be used, nor shall any of the parties disclose the existence or substance of this Agreement except as required by law. Notwithstanding the above, the Sponsor may publish website contact details and reference to the trial conducted on the www.clinicaltrials.gov portal, or equivalent official websites and on the websites of the Sponsor and its affiliated companies. Furthermore, the Sponsor shall have the right to publicly disclose in public the terms and conditions of the Agreement, including, but not limited to, the name of the Hospital, the description of services and the payment amount.

15. Notifications/Project Manager of the Sponsor

Mr/Mrs……………….(please indicate capacity)………..is hereby appointed as the Project Manager of the Sponsor, entrusted with ensuring the Conduct of the Trial and dealing with any issues relating to the Trial. The same person shall be responsible for verifying the fulfilment of the obligations under this Agreement. Any notifications required by this Agreement shall be communicated via registered mail or fax or by prepaid personal delivery addressed as follows:

To: COMPANY…………..

To the attention of Mr/Ms………………, Clinical Trial Project Manager

To: ELKEA of the ….Healthcare Region of ………………/ELKE of the University of …………….

To the attention of ………………., Chair of the ELKEA Committee of the …Healthcare Region/ELKE Committee of the University of……..

To: …………..Hospital of …………..

To the attention of: ……………Governor of the Hospital

To: Dr ………….. (please insert name, title and address of the Principal Investigator)

16. Assignment

16.1 The Sponsor shall have the right to assign this Agreement to an affiliate of the Sponsor or to a third-party outsourcee upon prior written notice to the Principal Investigator and the Hospital. In all other instances, neither Party shall assign its rights or duties under this Agreement to another or substitute itself with another in the project, in whole or in part, without prior written consent of the other Party. Subject to the foregoing, this Agreement shall bind and inure to the benefit of the respective Parties and their successors and assignees.

16.2 If the Principal Investigator or the Hospital employ for the performance of the project or part thereof, upon prior written consent of the Sponsor, any third party (natural or legal person) as an associate, they shall enter into an specific agreement with such person binding itto respect all the terms of this Agreement and to be liable jointly and severally with the Principal Investigator of the Hospital to the Sponsor for any loss or damage the Sponsor may sustain from the acts and omissions of such person.

17. Miscellaneous

17.1 This Agreement may not be supplemented, altered or otherwise amended except by a written document signed by all the parties. This Agreement constitutes the entire agreement of the parties with respect of the subject-matter hereof. It expressly supersedes any prior or contemporaneous oral or written representations, warranties or agreements. Any Annexes attached to this Agreement form an integral part hereof.

17.2 Any failure of the parties to exercise their rights hereunder or failure to exercise such rights promptly, in particular the right to enforce the counterparty’s obligations hereunder, shall not in any way be construed as waiver of any such right.

17.3 If any of the provisions of this Agreement conflicts with any provision of the Protocol or any other relevant document, this Agreement shall take precedence.

18. Applicable law

This Agreement shall be governed by Greek law. The parties agree that the Courts of [………..] shall have exclusive jurisdiction to resolve any dispute arising in connection with this Agreement and concerning the execution, performance and interpretation hereof and, in general, the relationships established hereunder.

It is understood that, before any recourse to the Courts in accordance with the above, the parties shall use their best efforts to settle amicably any dispute that may arise between them.

IN WITNESS WHEREOF, the parties executed this Agreement via their legal representatives on the date stated above, in three (3) identical and equally authentic counterparts, and each party received one.

THE PARTIES

For the HOSPITAL

Governor of ……………………………………………………………

Signature/Stamp:

Date:

For the SPONSOR

Signature/Stamp:

Date:

THE PRINCIPAL INVESTIGATOR

Signature/Stamp:

Date:

For ELKE/ELKEA

Signature/Stamp:

Date:

**ACCEPTANCE OF PROJECT MANAGEMENT**

Details of Scientific Supervisor

|  |  |
| --- | --- |
| Name |  |
| Capacity |  |
| Department |  |
| Laboratory |  |
| Division/Hospital |  |
| Telephone and fax no. |  |
| e-mail |  |

**To the ELKEA Committee of the …Healthcare Region**

Please accept the management of the project

|  |  |
| --- | --- |
| Project title (in Greek) | |
| Project title (in English) | |
| Sponsor(s) | |
| Total budget (targeted patient number INSURANCE CONTRACTS x Compensation per patient) | Duration (in months): |
| Commencement date: | End date: |

The Director of the Department The Scientific Supervisor

(name, signature and stamp) (signature)

**PROJECT TEAM MEMBERS**

**To the ELKEA Committee of the…Healthcare Region**

We hereby provide a comprehensive list of project team members as follows:

|  |  |
| --- | --- |
| Scientific supervisor: | Code: |
| Project title: | |
| Sponsor: | Funding percentage: 100% |
| Commencement date: | End date: |

**COMPREHENSIVE LIST OF PROJECT TEAM MEMBERS**

|  |  |  |  |
| --- | --- | --- | --- |
| **FULL NAME** | **CAPACITY** | **TAX REGISTRATION No/ID No.** | **TOTAL FEES (EURO)** |
| **SCIENTIFIC SUPERVISOR(S)** | | | |
|  |  |  | **.10%** |
|  |  |  |  |
| **GOVERNMENT EMPLOYEES** | | | |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |
| **THIRD-PARTY CONTRACTORS (AGAINST RECEIPT)** | | | |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |
| **THIRD-PARTY CONTRACTORS (NO A RECEIPT)** | | | |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |

Note: Please use an additional page, if necessary. ………., …./…/…

**The Scientific Supervisor**

(signature)

**PROJECT BUDGET**

**To the ELKEA Committee of the…Healthcare Region**

We hereby provide the project budget as follows:

|  |  |
| --- | --- |
| Scientific supervisor: | Code: |
| Project title: | |
| Sponsor: | Funding percentage: 100% |
| Commencement date: | End date: |

|  |  |
| --- | --- |
| **EXPENDITURE BREAKDOWN** | **BUDGET (€)**  (targeted patient number INSURANCE CONTRACTS x Compensation per patient) |
| 1. Fees of government employees |  |
| 2. Third-party contractors’ fees (against receipt) |  |
| 3. Third-party contractors’ fees (no receipt) |  |
| 4. Equipment (instruments, materials) |  |
| 5. Consumables |  |
| 6. Domestic travel |  |
| 7. Travel abroad |  |
| 8. Purchase of knowhow/technology |  |
| 7. Studies |  |
| 10. Project assessment |  |
| 11. Laboratory tests |  |
| 12. Other costs |  |
| 13. |  |
| 14. |  |
| 15. General costs (charge in favour of ELKEA) |  |
| **TOTAL (€)** |  |

**If the project is subject to VAT (e.g. studies), please add: Amount of VAT (€)**

**The representative of the Sponsor …………, ……../…../…….**

(signature)  **The Scientific Supervisor**

(signature)

This Decision shall take effect as from its publication.

We order that this Decision be published on the Government Gazette.

The Ministers

of Economy and Development of Health

**IOANNIS DRAGASAKIS ANDREAS XANTHOS**