GOVERNMENT GAZETTE
OF THE HELLENIC REPUBLIC

SECOND ISSUE **No 390**

February 21, 2013

DECISIONS

No ΔΥΓ3(α)/οικ. 18910
Supplementation of the Joint Ministerial Decision No ΔΥΓ3α/89282/2003 (Gov. Gazette B' 1973) "Approximation of the laws of the Hellenic Republic to the respective European" in accordance with the Directive 2001/20/EC |on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use" as amended and today in force, for the purposes of approximating, simplifying and rationalising the procedures for the conduct of Clinical Trials".

THE MINISTERS OF:
FINANCE – NATIONAL DEFENSE – DEVELOPMENT, COMPETITIVENESS, INFRASTRUCTURE, TRANSPORTATIONS AND NETWORKS – EDUCATION AND RELIGION, CULTURE AND SPORTS – HEALTH – JUSTICE, TRANSPARENCY AND HUMAN RIGHTS

Having considered:
1. The provisions of article 1, par. 1, 2 and 3 and of article 3 of Law 1338/1983 "Application of EC Law", as amended by article 6 of Law 1440/1984 "Participation of Greece in the fund, reserves and provisions of the European Community for Carbon and Steel and of the European Atomic Energy Community (EAEC or Euratom) (Gov. Gazette A' 70) and of article 65 of Law 1982/1990 (Gov. Gazette A' 101).
2. The provisions of Law 1316 /1983 "Incorporation, Organising and competencies of E.O.F." (Gov. Gazette A' 3) and in particular the provisions of article 14, par. 4 and article 2 par. 1 and 2, as the latter was substituted by the provisions of article 1 of Law 1965/1991 (Gov. Gazette A' 146) and is today in force.
3. The provisions of articles 47 and 48 of Law 3370/2005 (Gov. Gazette A' 176) and of Law 3329/2005 (Gov. Gazette A' 81) as amended and today in force and of Law 4052/2012 (Gov. Gazette A' 41).
4. The provisions of article 90 of the Legislative Code on the Government and Governmental bodies which was ratified by article 1 of the P.D. 63/2005 (Gov. Gazette A' 98).
5. The P.D. 95/2000 "Organisation of the Ministry of Health and Welfare" as amended and today in force (Gov. Gazette A' 75).

6. The provisions of the P.D. 85/2012 “Establishment and renaming of Ministries, transfer and abolishment of services” (Gov. Gazette A’ 141).
7. The P.D. 86/2012 “Appointment of Ministers, Alternate Ministers and Deputy Ministers (Gov. Gazette A’ 141).
8. The Joint Ministerial Decision No ΔΥΓ3(α)/89292/31.12.2003 (Gov. Gazette B’ 1973) “Approximation of the laws of the Hellenic Republic to the respective European” in accordance with the Directive 2001/20/EC “on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use” as amended and today in force, for the purposes of approximating, simplifying and rationalising the procedures for the conduct of Clinical Trials” as amended and in force.
9. The Joint Ministerial Decision No ΔΥΓ3α/79602/2007 (Gov. Gazette B’ 64) “Approximation of the laws of the Hellenic Republic to the respective European, in accordance with the Directove 2005/28/EC “laying down principles and detailed guidelines for good clinical practice as regards investigational medicinal products for human use, as well as the requirements for authorisation of the manufacturing or importation of such products”. Amendment of the Joint Ministerial Decision ΔΥΓ3(α)/89292/31.12.2003 (Gov. Gazette B’ 1973) “Approximation of the laws of the Hellenic Republic to the respective European” in accordance with the Directive 2001/20/EC dated April 4, 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 conduct of clinical trials on medicinal products for human use” as amended and today in force, for the purposes of approximating, simplifying and rationalising the procedures for the conduct of Clinical Trials”.
10. The Joint Ministerial Decision No ΔΥΓ5α/οικ/1197/2001 (Gov. Gazette B’ 1206) “Creation of Special Accounts for Research and Development Sums (ELKEA) in the Regional Systems of Health (Pe.SY)”.
11. The Ministerial Decision No B1 819 “Creation of Special Accounts for the financing of research projects and relevant services or activities performed in Universities or in Technological Universities of the Country” as amended and substituted by the Ministerial Decision No ΚΑ/69/1996 (Gov. Gazette B’ 826).
12. The Joint Ministerial Decision No ΔΥΓ3α/69150/24.09.2004 (Gov. Gazette B’ 1503) “Establishment and bylaws of the (Hellenic) National Ethics Committee (NEC) for Clinical Trials”.
13. The Joint Ministerial Decision No ΔΥΓ3α/Γ.Π. 125341/2006 (Gov. Gazette B’ 72/29.01.2007) “Expansion of competencies of the National Ethics Committee for the granting of opinion on clinical trials with medical devices”.
14. The Joint Ministerial Decision No ΔΥ8δ/Γ.Π.οικ.130644/2009 (Gov. Gazette B’ 2197) for the approximation of the law of the Hellenic Republic to the provisions of the Directive 90/385/EEC “on active implantable medical devices”.
15. The Joint Ministerial Decision No ΔΥβδ/Γ.Π.οικ.130648/2009 (Gov. Gazette B’ 2198) regarding the approximation of the laws of the Hellenic Republic to the provisions of the Directive 93/42/EEC on medical devices”.

16. The Decision No Υ47/3.7.2012 of the Prime Minister (Gov. Gazette B 2105) "Assignment of competencies to the Alternate Minister of Health Marios Salmas" as amended by the similar decision No ΔΥ1α/οικ.78084/25.7.2012 (Gov. Gazette B 2339/2012).
17. The Decision No Υ48/9.7.2012 of the Prime Minister (Gov. Gazette B 2105/B/2012) "Assignment of competencies to the Alternate Minister of Finance Christos Staikouras".
18. The Recommendation of the National Ethics Committee of EOF No 90919/20.12.2012 and the letter dated 20.12.2012 that included the draft decision for Clinical Trials of the President of EOF.
19. The fact that no expenditure is generated against the State Budget from this Decision.
20. The fact that problems concerning the overlapping of competencies between the NEC, the Regional Departments of Health (YPE), Universities and Hospitals must be resolved, delays in the approval and completion of Clinical Trials must be eliminated and that their effective and unobstructed conduct must be ensured.
21. The fact that a unified operation framework must be created, which will support the conduct of clinical trials in Greece. The realisation of reliable clinical trials is, for our country, an opportunity for foreign exchange inflow, and a substantial alternative source of financing Hospital Institutions and producing research work,

WE DECIDE:
The supplementation by means of the addition of articles 18 to 22 of the Joint Ministerial Decision ΔΥΓ3(α)/89292/31.12.2003 (Gov. Gazette B' 1973) "Approximation of the laws of the Hellenic Republic to the respective European" in accordance with the Directive 2001/20/EC dated April 4, 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 conduct of clinical trials on medicinal products for human use" as amended and today in force, for the purposes of approximating, simplifying and rationalising the procedures for the conduct of Clinical Trials and the supplementation and renumbering of article 18 there to article 23, as follows:

"Article 18
Organising and procedures for the conduct of a clinical trial in health structures

1. The National Health System (NHS) in parallel with the provision of healthcare, is obliged to have a research background (proper infrastructure and orientation) for the complete conduct of clinical research trials in the respective health structures, whose results will be utilised for improving healthcare provided to patients.
2. In the context of the applicable legislation on the approval and conduct of clinical trials, this decision sets out special provisions, regarding the conduct of clinical trials, which are effected on human and concern medicinal products and medical devices, in health structures supervised by the Ministry of Health, NHS hospitals, the Public Law

Legal Entities described in par. 1 of article 37 of Law 3918/2011 (Gov. Gazette A' 31), including the "Onassio Heart Surgery Centre" the Papageorgiou University Hospital, the Athens Eginitio Hospital, the Athens Areteio Hospital, the Psychiatric Hospital of Attica "Dromokaitio", Psychiatric and University Clinics, Hospitals and Healthcare Units of the IKA, Hellenic Army Hospitals and of the 417 NIMITS, Private Clinics and Hospitals.

3. A prerequisite for the approval for the conduct of a clinical trial is the acceptance, as defined below, by health structures, of the conduct of the clinical trial inside the Hospital by its scientific personnel.

4. In each hospital there is a Scientific Board, in accordance with the provision of article 9 of Law 3329/2005. The Scientific Board of each Hospital plays the role of the Ethics Committee of the respective YPE, as this role is described in ΔΥΓ3/98292/2003 (Β' 1973). Any objections on the conduct of an invasive clinical trial and of the content of the file, must be notified to the NEC within thirty (30) days from the date the file is filed to the Scientific Board. If, within a maximum deadline of thirty (30) days from the delivery date of the file, the Scientific Board raises no objections to the Administration of the Hospital, then a tacit positive opinion is deemed to have been granted.

5. In parallel with the above procedure, the Administration of the Hospital is obliged to have completed the review procedures of the quadripartite agreement for the conduct of the Clinical Trial (see paragraph 8.1).

The Administration of the Hospital proceeds with the execution of the Agreement or the justified rejection thereof within five (5) days from the positive opinion or the tacit positive opinion granted by the Scientific Board.

6. In order to simplify and accelerate the procedure for the audit and execution of the agreements both from the Administration of the Hospital, as well as by the Administration of ELKE/ELKEA, a model quadripartite agreement is enacted, as well as model forms for the project's budget, the research team and the acceptance of the project's management, which are attached to this Decision (see ANNEX), which have been prepared and adopted by the NEC. The quadripartite agreement will be also signed by the Sponsor, the Scientific Supervisor, the Governor of the Hospital and the Management Supervisor of ELKE/ELKEA.

In particular, the following is provided for:

6.1. The agreement with the Administration of the Hospital is signed by Sponsor, the Scientific Supervisor and the Governor (or the legal alternate thereof in case he/she is impeded). The review and signing procedure is completed within 35 days, as provided for by par. 4 and 5 of this article.

6.2 Following the signing of the agreement at Hospital level, the signed agreement is forwarded within 5 days to the manager of ELKE/LKEA for the relevant review and signing within (10) days from the date it was signed at Hospital level.

7. When required by the Sponsor, any additional terms or clarifications on the Model Agreement are attached to a relevant Annex thereof. In case of major deviation from the attached Model Agreement, the Sponsor addresses the National Ethics Committee, which grants its opinion in relation to the suitability of the Annex of the Agreement.

The National Ethics Committee grants its opinion within thirty (3) days from the date the relevant request was submitted and its decision must be automatically accepted by all parties involved. The Administration of the Hospital proceeds with the signing of the agreement within five (5) days. The NEC undertakes and resolves any issues that concern the contents of the agreements.

8. In case of any amendment of the agreements with the Hospital and the Financial Management Agencies, the same procedures apply, the same supporting documents and the same time-schedules described in this decision.

9. The creation of an email address is provided for, within one year from the date this decision is published, to all agencies and services in charge for the approval and management of the trials, for the filing by the Sponsors, of documents and supporting documents in electronic form.

Article 19
Approval Procedure at Hospital Level

1. The head researcher/ scientific supervisor submits the trial file, to the secretariat of the Scientific Board, a registration is entered in the protocol (copy of the registration is delivered to the head researcher/ scientific supervisor and next the file is forwarded to the Scientific Board of the Hospital.

2. The content of the trial files submitted to the Scientific Board of Hospitals is the same and unified for all hospitals and health structures and includes, but not limited to, the following:

3. In the case of invasive clinical trials, the Researcher files the protocol (it suffices upon the submission, the protocol in English and an abstract thereof in Greek), the consent form, a copy of the materials administered to the participating patients, the insurance policy and a certificate for the cost-free administration of the medicinal product under investigation.

4. In case of non-invasive trials, the Researcher files for approval the protocol (the protocol in English and an abstract thereof in Greek suffices upon the filing), the consent form and a copy of the materials administered to the participating patients. For the issues concerning the financial management of these trials, the same procedure is followed, as in the case of invasive trials, and more specifically, immediately after the approval by the Scientific Board of the Hospital, within not later than thirty (3) days, the procedures for the signing of the quadripartite agreement can be promptly concluded, as provided for by this Ministerial Decision.

5. In parallel, a file is submitted to the Administration of the Hospital which includes the protocolled letter that was filed to the Scientific Board and the agreement with all completed model forms set out in par. 8 of article 18, in order to be evaluated.

6. Pricing of laboratory and diagnostic tests and other procedures that may be performed in the hospital, in the context of the conduct of the clinical trial, will be effected by the financial department of the hospital, based on the official pricelists as these are defined by the relevant ministerial decisions. The said pricing will be performed with the issue of an invoice for the provision of services, on which

personal data of the patients who participated in the clinical trial must not be recorded.
7. The Governor of the hospital, after reviewing the recommendation of the Scientific Board of the Hospital for the conduct of a clinical trial, any pricing of the relevant expenses that relate to the conduct of the trial and after certifying the coverage of the said expenses by the Sponsor, proceeds with the execution of the agreement for the conduct of the trial in the specific hospital within the time schedules set out in par. 5 of article 18 hereof, and following the consent of the Board of Directors of the Hospital. The Board of Directors of the hospital may decide, with justified cause and within the deadlines provided for in this Decision, to reject the conclusion of the agreement for the conduct of the clinical trial.

Article 20
Agreement of the Clinical Trial with a Financial Management Agency (ELKE/ELKA)

1. The quadripartite agreement of the clinical trial is forwarded to the financial management agency, so that it will be signed within a maximum period of ten (10) days from the execution thereof at Hospital level. For any delay in the execution of the agreement by the Administration of the Financial Management Agency that exceeds the period of fifteen (15) days, penalties and administrative sanctions will be imposed to the persons liable for such delays and the loss of income, as described in article 22 hereof.
2. The agreement is signed by the Financial Management Agency, given that the clinical trial will commence after its approval by the NEC and EOF, the Scientific Board and the Administration of the Hospital, with regard to the design of the trial and requirements of applicable law. In case the clinical trial is not approved by the above competent agencies, the signed agreement remains inactive and without effect. The Sponsor informs the Financial Management Agency for the approval or non-approval of the clinical trial, immediately after obtaining the relevant decisions.
3. Regardless of the outcome of the implementation of the clinical trial in any Hospital, the Sponsor pays the amount of Euro (500) to the Hospital and the amount of Euro two hundred and fifty (€250) to the Financial Management Agencies for the evaluation of the file submitted and of the agreements respectively, in accordance with this Decision.

Article 21
Financial Management of clinical trials and non-invasive trials

1. A unified withholding percentage amounting to five per cent (5%) is enacted in favour of the DYPE and fifteen per cent (15%) in favour of the Hospital, on the total executed budget for the conduct of the trial. By virtue of a specially justified application to the competent financial management agency, the Hospital may claim, further to the above amount, an additional payment of five per cent (5%), if it invokes and proves its special contribution to the development and performance of clinical

trials. Apart from the above, there will be no further financial claim by the financial management agencies and the Hospitals.
2. The financial management of clinical trials realised in health structures of the NHS, is effected via the Special Account for Research and Development Sums (ELKEA) or via the Special Account for University Research Sums (ELKE).
3. If the financial management agency is the Special Account for Research and Development Sums (ELKEA), it is also liable for reimbursing the Hospital with the amount corresponding to it.
4. The financial management of the clinical trials performed in health structures of the NHS with the participation of university researchers (members of DEP) may be effected either via the ELKE or the University's ELKE. In the second case, the amount in favour of the Hospital (a percentage of 15% on the respective executed budget) is paid to the Financial Department of the Hospital by the Sponsor of the trial.
5. The payment of the above amounts withheld for the conduct of the clinical trial is effected via the respective financial management agency as well as the fees paid to the researchers which are paid within thirty (30) days from the submission.
6. Payments are gradually effected, in accordance with the payment schedule included in the Agreement.
7. Laboratory and diagnostic tests must be performed within the time schedules set out in the protocol of the clinical trial and in accordance with the required technical specifications. In any different case, patients will be referred to other health structures or diagnostic centres, at the cost of the Sponsor of the Trial.
8. Pricing of laboratory and diagnostic tests except of those applied in the usual clinical practice, which are required by the protocol, will be performed by the financial department of the Hospital, based on the official pricelists, as those are defined by the relevant ministerial decisions.
9. Payment of the amount that concerns laboratory tests and other hospital expenses, is effected by the Sponsor, who pays the said amount to the Financial Department of the Hospital, along with a justification connected to the conduct of the trial.

Article 22
Penalties

1. Subject to the provision of par. 3 of this article, in case of unjustified delay in the above procedure for the acceptance of the conduct of a clinical trial in health structures or in case of transgression of competencies or delinquent exercise of duties, the Governor of the Hospital, as the Disciplinary Supervisor, imposes to the members of the Scientific Committee the penalty of Reproach and a fine, up to the half of their monthly wages.
2. Subject to the provision of the following paragraph on unjustified delays in the above procedure or delinquent exercise of duties, the Minister of Health, as the Disciplinary Supervisor, imposes to the Governors of Hospitals and of YPE the penalty of Reproach and fine of up to the amount of their monthly wages, and in case of repeated delinquencies, the removal from the Governor's post.

3. As regards the disciplinary inspection of the Directors of Army Hospitals and of the 417 NIMITS, the provisions in force from time to time for the category of the said personnel apply.

Article 23

Effective date and final provisions

Articles 1 to 17 of this decision apply from 1.05.2004, while articles 18 to 22 apply from the date of publication of the Decision No ΔΥΓ3(9)/οικ.18910/19-2-2013. Any regulation or provision to the opposite, is abolished once this Decision enters into force.

ANNEX

Contents of Annex:

AGREEMENT FOR THE CONDUCT OF CLINICAL TRIAL

Trial titled:……
(hereinafter the "Trial" and/or the "Clinical Trial"

Sponsor:

The Company representing the Sponsor in Greece

Investigational Medicinal Product (Medicine/Medical Device of Trial):

Protocol
No: EUdraCT

Research Centre for the Conduct of the Trial

Today in Athens, this …… (hereinafter the "Execution Date") the following contracting parties, i.e.:

On one hand, the company under the name …….. with registered office in …….., VAT Registration No……. legally represented by …….. (hereinafter called the "**Sponsor/CRO**"), acting in Greece as the Sponsor of the Trial, under a special to that end agreement/authorisation, in the name and on behalf of the foreign company under the name ……..

On the other, Mr/Mrs……. Physician [insert title]……. of the …….. Clinic of the …… Hospital of…….., resident in ……, at ……St., called in the Agreement as well as in the Annexes thereof the "**Principal Investigator**" and/or the "**Scientific Supervisor**" of the Trial.

In addition, the ……. Hospital of……..with registered officer in …….. at……..St., legally represented by the governor thereof Mr ……., hereinafter called the "**Hospital**".

And the Management Agency ELKE/ELKEA…… with registered office in …….. at…….St., legally represented by Mr …….[insert title] hereinafter called "**ELKE/ELKEA**".

GIVEN THAT:

I. The company under the name "……..", which is the Sponsor of the Trial, having for its account, as well as for account of the above foreign company, all rights and obligations entailed in the Sponsor's capacity both legally and practically by the applicable European and National Legislation, before all competent authorities and agencies, and is able and entitled to proceed with all acts required by the law for the adoption of approvals and permits for the legal conduct of the Clinical Trial, in accordance with the provisions of applicable law related to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use as well as in accordance with the ICH Guidelines (Good Clinical Practices).

II. The Sponsor/CRO has requested from the Principal Investigator to conduct the Trial and from the Hospital and the personnel thereof to accept the conduct of the Trial in the Hospital's facilities, which (Trial) is sponsored by the Sponsor and concerns the investigational medicinal product (Trial Medicine or Medical Device) in accordance with the approved Protocol of the Trial.

III. The Hospital has the authority to approve/accept the conduct of the Trial and has the suitable equipment so as to accept the conduct thereof in its premises and the Principal Investigator states that he/she has agreed to undertake the responsibility for the conduct of the Trial, which will be conducted in the …….. Clinic of the …….Hospital of …….., which is subjected to the Regional Department of Health …….

IV. The parties declare that the Trial will be conducted in accordance with (a) the applicable legislation on clinical trials for medicinal products intended for human use, b) the relevant approval for the conduct of the Trial by the National Ethics Committee (NEC) (ΔΥΓ3/89292/2003) and of the National Organisation for Medicines (EOF), c) the terms specified in the Protocol, the amendments and/or Addenda thereof, d) the ICH (Good Clinical Practices) Guidelines e) the Code of Medical Conduct and f) the terms and conditions set out herein below.

V) The financial management of the project will be conducted via the **ELKEA** of the ….. YPE of ……, which has been established in the …… Regional Department of Health (…. YPE) of ……..……., for the purposes of managing the sums deriving from the implementation of investigating, developmental, training and educational programmes, projects for training and provision of scientific and technological services, preparation of special designs, special measurements of laboratory tests and analyses, an experiences exchange programme as well as other relevant services or activities that derive from the financing of respective scientific suggestions of persons employed in the NHS and in the Social Care Units, which are included in the investigational programmes and projects set out in article 6 of Law 1514/85 and/or through the Special Account of the University of ……. ("Special University Account"), which has been created for the purposes of rendering

and managing sums deriving from any source and intended for the coverage of any expenses which are required for the needs of investigational, training, educational, developmental projects as well as vocational training projects and projects for the provision of scientific, technological and artistic services, the preparation of special designs, the conduct of tests, measurements, laboratory measurements and analyses, the granting of opinions, the preparation of specifications on behalf of third parties as well as any other relevant service of activity, that contribute to the linking of training and research to the production and are performed or provided by the scientific personnel of Universities or Technical Universities, and with the co-operation of other special scientists, in accordance with article 1, par. 2 KYA KA 679/96/22.08.96 (Gov. Gazette 826 vol. B).

VI. The Scientific Board of the Hospital, according to the relevant resolution of the BoD of the Hospital, has already approved with the Approval of Clinical trials dated ……., on one hand the conduct of the Clinical Trial at its premises, and more specifically the premises of the ……Clinic and on the other the Patients Informed Consent Form, issued on ……

Taking into account the introductory statements, the mutual covenants and agreements hereby stipulated, the contracting parties agree specifically the following:

1. Conduct of the Trial

1.1 The parties agree that the Protocol, as well as any lawfully approved amendment thereof, constitute an integral part of this Agreement.

1.2 The Principal Investigator agrees to grant his professional expertise and knowledge for the conduct of the Trial according to the Protocol under Code No ……. with issue date ……., as well as in accordance with any lawfully approved amendment thereof and in accordance with the applicable European and National Laws on the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use and in accordance with the ICH-Good Clinical Practices (hereinafter "ICH-GCP Guidelines"), the deadlines set out and the terms and conditions of this Agreement.

1.3 In case the Principal Investigator ceases to co-operate with the Hospital, he/she will file a written notice to the Sponsor within a period of five (5) days before the date he/she departs. For the purposes of continuing the normal conduct of the Clinical Trial, the Principal Investigator guarantees to the Sponsor that he/she will remain the Scientific Supervisor of the Clinical Trial until a new Principal Investigator is appointed. The Sponsor will be entitled to appoint any new Principal Investigator, appointed in the Hospital. The new

Principal Investigator is obliged to agree upon the terms and provisions of this Agreement. In case the Sponsor does not appoint the new Principal Investigator, it is entitled to terminate this Agreement in accordance with Article 2.2 below and the Hospital will proceed with all actions necessary in order to implement the decision of the Sponsor.

1.4 The Principal Investigator can appoint third parties as he/she may deem necessary, to act as co-operating investigators and contribute to the conduct of the Trial. All co-operating investigators will be adequately trained, timely appointed in a co-operation regime known to the Sponsor and a relevantly fully informed status of the persons participating in this capacity will be maintained. Prior to the assumption of any obligation and conduct of any process in the context of the Trial, the co-operating investigator(s) will have obtained all necessary approvals by the Authorities (EOF and NEC) according to the relevant provisions. The Principal Investigator will be solely responsible for the management and supervision of these teams of investigators, who in any case will be bound by the same terms and conditions binding the Principal Investigator, in accordance with this Agreement. The Hospital and the Principal Investigator are solely liable for the services rendered by their personnel and guarantee that these will be rendered by the relevant competent persons.

1.5 The Principal Investigator states that both he/she and the co-operating physicians (or the residents), have obtained the professional license to practice medicine in Greece provided for by the law and they have not committed any disciplinary or penal offense that relates with medicine practicing. Furthermore, he states for his account and for account of the co-operating investigators, that they have read and understood any information of the Investigator's Brochure provided by the Sponsor/CRO, including the potential risks and side effects of the Trial medicine.

1.6 For the conduct of the Trial, the Sponsor will provide the Investigational Medicinal Product (Trial Medicine or medical device) all documents that relate to the Trial (such as the Case Report Forms) and as the case maybe, will concede the use of the equipment analytically described in Annex A or the equipment that may be required during the conduct of the Trial. The equipment shall be exclusively owned by the Sponsor if so permitted by the nature thereof (gratuitous loan) and will remain in the condition it was delivered, throughout the term of the Trial, taking into account the normal wear due to normal use. The Hospital hereby accepts the said gratuitous loan and concedes the premises suggested for the installation thereof. The Principal Investigator will be responsible and liable for the equipment, including the maintenance (excluding the consumables) or any risk of loss that relates to the equipment during the term of the Trial. The Sponsor will not be responsible

for the replacement of the equipment due to improper use. Upon the completion of conclusion of the Trial, the instructions of the Sponsor will be applied for the offer/return of the equipment due to termination of the gratuitous loan A.

1.7 The Hospital and the Principal Investigator will not use the Investigational Medicinal Product (Trial Medicine or medical device) and the documents, materials and equipment provided by the Sponsor for the Trial, whose use is hereby concede, for a purpose other than the conduct of the Trial and in accordance with the terms and conditions of use ,which are analytically set out in Annex A thereof. The responsibility for the due delivery, storage, distribution, use, safekeeping, return and count of the reserves of the Trial Medicine shall be borne by the Hospital and the Principal Investigator. Especially as regards the medicines granted for the Trial, these will be exclusively used in accordance with the instructions set out in the Protocol and only for the Trial. The instructions granted by the Sponsor regarding their disposal will be observed. Upon the conclusion or termination of the Trial and reserves of medicines, will be disposed of or returned in accordance with the instructions of the Sponsor on the given date and in the manner provided for below (Article 2.4).

2. <u>Term and Termination</u>

2.1 The term of this Agreement commences directly on the Execution date set out in the beginning hereof, provided that the relevant permits will be issued by EOF and NEC and ends on …….[month] of the year …….. unless earlier terminated in accordance with the terms hereof. The contracting parties agree that the expiration of the term of effect of this Agreement may occur earlier from the above date in case the contracting parties mutually accept that the above contractual obligations have been fulfilled earlier or after the above concluding date of this Agreement, exclusively and only in case the deadline for the fulfilment thereof has been extended by mutual written agreement of the contracting parties, in the context of the terms of this Agreement.

2.2 This Agreement is terminated upon the expiration of the above set out term thereof. However, it can also be terminated before the lapse of its term, in case the necessary permits are not issued by EOF and/or NEC and at any time (a) upon the mutual written agreement between the contracting parties which shall regulate the consequences of the termination in that manner or (b) upon the written termination thereof by any of the contracting parties, at any time, after the relevant prior written notice, which is lawfully communicated to the counterparties fifteen (15) days before hand and (c) upon the unilateral notice of the Sponsor, fifteen days beforehand without material cause. The effects of the said termination occur before the lapse of the above period. This Agreement is terminated without prejudice for any of the contracting parties,

while the contractual obligation of the Sponsor to the Principal Investigator and the Hospital is limited only to the part of the fee that corresponds to the services rendered and works executed until the date the effects of the termination enter into force, releasing the Sponsor from the obligation to pay the rest of the fee, which is not yet due and payable. As the case may be, any additional amount paid as fee will be returned to the Sponsor within thirty (30) days.

2.3 Each contracting party is entitled to proceed in writing with the prompt, early and harmless termination of this Agreement, for material cause. Material causes are, among other things, the breach of any of the terms of this Agreement, all being deemed essential, the non-compliance with the applicable European and national legislation that governs the conduct of clinical trials and the provision of the services hereby agreed, the receipt of information related to the safety of the patients participating in the Trial, which render necessary the termination of the Agreement and the receipt of information that show the lack of adequate efficiency. The above termination is effected in writing and the effects thereof are occur directly upon the service thereof. If the material cause is the result of any of the parties' default, the non-default party reserves all right granted thereto by the law against the default party, and mainly the right to restitute any damage it will sustain due to the said cause. Upon the communication of this termination, the Principal Investigator agrees to promptly end the conduct of the Trial, to the degree medically permitted for the patients participating in the Trial.

2.4 The Hospital and the Principal Investigator will return to the Sponsor or will destroy in accordance with the express instructions of the Sponsor, any non-used quantity of the Investigational Medicinal Product, all documents, materials and equipment granted by the Sponsor/CRO and all Confidential Information, as set out in Article 7.2 below, with the completion of the trial or the termination/expiration of this Agreement in any manner. This provision does not apply to documents and files, which must be kept by the Principal Investigator and remain to the Research Centre under his responsibility, as set out in the Protocol and as required by the applicable National and European Legislation.

3. Competent Authorities – Written Informed Consent – Approvals

3.1 Pursuant to the provisions of applicable National and European Legislation, the Principal Investigator will be responsible to obtain the approval of the Protocol and of the amendments thereof, the Patients' Informed Consent Form, the budget (fees) and any other documents related to the Trial by the Scientific Board and/or the Management Board of the Hospital, before the commencement of the trial. In case the Board of Directors and/or the

Scientific Personnel of the Hospital requires any changes in the Protocol or the Patient's Informed Consent Form, such changes shall not be implemented until the Sponsor is informed and grants its consent. The Principal Investigator will be responsible for filing all documents required for obtaining the necessary approvals and permits that relate to the lawful conduct of the Trial, in accordance with applicable legislation.

3.2 The Principal Investigator will also be responsible for obtaining the Patients Informed Consent Form signed by or on behalf of each patient participating in the Trial, which (Patients Informed Consent Form) will be approved by the Sponsor, the Scientific Board and/or the Board of Directors of the Hospital and by the competent authorities and agencies (EOF and NEC). These signed Forms, are kept in an archive by the Principal Investigator and are not transferred to the Sponsor, in accordance with applicable laws of personal data. This archive must, if so requested, be made available to the competent bodies of EOF or of other authorities. In case the Principal Investigator is requested, he/she is able to certify by means of a solemn declaration, the observance of the procedure and the keeping of the archive, for all patients participating in the Trial, bearing any liability, in case of any misrepresentation.

3.3 The Sponsor/CRO will, with the co-operation of the Principal Investigator, be responsible for the completion of all typical approving procedures that relate to the conduct of the Trial (such as the filing of the application for the conduct of a clinical trial) and the procurement or import of the Investigational Medicinal Product (Trial Medicine) and if required, for obtaining the written consent of the competent authorities and of the National Ethics Committee (NEC) before the commencement of the Trial.

3.4 The Principal Investigator is obliged to duly and fully observe the applicable laws governing the object of this Agreement and in particular the relevant Joint Ministerial Decision (KYA) ΔΥΓ3/89292/2003 and the Ministerial Decision (YA) A6/10983/1/1984 as in force from time to time.

3.5 In any case, the written approval of the Protocol and of the Patients Informed Consent Form must be obtained by the Principal Investigator before the commencement of the Trial. The Sponsor will allow the delivery of the reserves of the Investigational Medicinal Product only upon obtaining a copy of the written approval. The Principal Investigator agrees not to include any subject to the trial, both before obtaining the written positive opinion by the competent ethics authority and before the express approval of the conduct of the Trial by EOF. The Hospital and the Principal Investigator are obliged to promptly inform the Sponsor for any audit or inspection by any regulatory authority which is related to the Trial conducted by virtue of this Agreement.

4. Notification of Data and Adverse Events

4.1 The Principal Investigator agrees to periodically and regularly provide the Sponsor/CRO all results of the Trial and other data dictated by the Protocol (the "Data") in properly filled in (in writing and/or electronically) Case Report Forms (CRFs) within …. (…) days from each visit of a patient participating in the Trial to the centre, with the exception of the initial visit and the Serious Side Effects that must be added within 24 hours. For the avoidance of any doubt, Data includes, without limited to, documents, either manuscripts or printed material, graphs, video and audio material, as well as information included in any file, electronic database or information in electronic form, which is created and/or produced in relation to the conduct of the Trial. The reference documents must be separately kept in order to support the data entered in the e-CRF/CRF for fifteen (15) years and/or more, if the applicable local or international specifications set a longer period. All identification codes of the subjects of the Trial must be kept in a safe place for fifteen (15) and/or more if the applicable local or international specifications set a longer period.

4.2 The Principal Investigator also agrees to record and immediately report to the Sponsor, and in any case not later than twenty four (24) hours after obtaining knowledge, any serious adverse reactions, pregnancy and other serious medical cases as these are defined in the Protocol, which may be observed during the conduct of the Trial and affect any patient participating therein. The Principal Investigator further agrees to follow-up the course of such cases with thorough, written follow-up reports which he/she will sent to the Sponsor in accordance with the time schedules set out 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 toy EOF, only in the case EOF requests so, in accordance with the applicable laws.

4.3 The Principal Investigator is also obliged to report to the Local Pharmacovigilance Supervisor of the Sponsor, within 24 hours from the moment he/she shall obtain knowledge, all possible Adverse Effects that concern the medicinal products of the Sponsor, in accordance with the provisions of the internal procedures of the Sponsor regarding reporting and management of Adverse Events and applicable legislation. He is also obliged to report any Complaint regarding Quality of Product notified to it, within 24 hours from the moment he/she obtains knowledge thereof, to the Head of Production –Planning, as the specialised person or alternatively, to the Local Supervisor Pharmacovigilance Supervisor of the Sponsor.

4.4 The Principal Investigator is also obliged to report to the Pharmacovigilance Supervisor of the Sponsor within 24 hours from the moment he/she obtains knowledge thereof any complaint that concerns the quality of a product. A complaint in any apparent concern that could be related to the possible failure of the product to meet any of the specifications thereof after being administered. More specifically, a Complaint that concerns the Quality of a Product is any concern related to the identity, credibility, efficiency or performance of the product. The Complaints concerning the Quality of a Product include, without limitation, the following:

- Complaints concerning the package, such as deficient or defective content or illegible number of batch or expiry date.
- Complaints concerning the natural characteristics, such us change of colour, volume or cleanness of the product.
- Complaints concerning the presence of particles or sediment, for instance the report of existence of small particles or dapples in a fluid which should be lucid.

4.5 Both the Principal Investigator and the Sponsor/CRo are obliged to notify the Hospital, EOF and the NEC for the course of the Trial and after the end thereof, to file a detailed report with the results of the Trial.

4.6 The Principal Investigator is expressly obliged to preserve, after the end of the conduct of the Trial, all archives that concern and relate to the Trial, for the period set out in the Protocol and required by the applicable European and Greek legislation, as well as for as long as he/she requested in writing by the Sponsor to preserve them.

4.7 The Principal Investigator is obliged, throughout but also after the end of the conduct of the Trial, to respond to any query that relates to this Agreement, the patients participating in the Trial and the procedure for the conduct thereof, which will be posed to him/her by the Sponsor, EOF, and the competent authorities upon prior notification of the Sponsor in these cases. In case that during the term or after the end of the Trial reporters or financial analysts pose any questions, the Principal Investigator agrees to consult and previously inform the Scientific Supervisor of the Sponsor (Medical Director) and could potentially refrain from answering in the context of the principle of confidentiality and secrecy governing this Agreement, but also of the medical privacy, EOF and the competent authorities with prior or parallel notification to the Sponsor.

5. <u>Supervision – Monitoring of the Trial</u>

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, if possible, of the U.S. F.D.A. – United States Food and Drug Administration) to inspect at any time during the normal business hours (i) the facilities where the trial is conducted, (ii) non-processed Data from the Trial, including the original archives of the patients participating in the Trial, if so permitted by the terms of the Patient's Informed Consent Form and applicable law and (iii) any other relevant information which is necessary in order 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 the Protection of Personal Data and on secrecy and safety of processing. The Principal Investigator will immediately notify the Sponsor in case any authority schedules or conducts a 'surprise' inspection and will promptly provide the Sponsor, upon notification of the inspection, copies of any correspondence sent by the competent authority, which results from such an inspection.

5.2 The Hospital and the Principal Investigator agree to adopt all measures necessary that are required by the Sponsor in order to remedy any deficiencies noticed during an inspection. In addition, the Sponsor shall be entitled to inspect and approve any correspondence addressed to the competent authorities which derives from such an inspection by the said authorities, prior to its submission by the Hospital or the Principal Investigator.

6. <u>Compliance with Applicable Laws</u>

6.1 The contracting parties agree to conduct the trial in accordance with the provisions of European and National laws relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use, in conformity with the ICH-GCP), the legislation on bribery and corruption including the U.S. Foreign Corrupt Practices Act and the generally accepted Treaties such as the Declaration of Helsinki (1996), local laws applying the European Directive for Good Clinical Practice in Conduct of Clinical Trials on Medicinal Products for Human Use (2001), written instructions and practices granted by the Sponsor as well as applicable laws for combating bribery that concern interactions with State agencies, employees and representatives (the "Applicable Legislation").

6.2 More specifically, none of the contracting parties will proceed with any action which is prohibited by local or other laws against corruption (including the US Foreign Corrupt Practices Act and collectively "Anti-corrupt Legislation") which probably applies for one or both parts of the Agreement. In addition, none of the contracting parties will make any payment nor offer or transfer any valuable object to any State officer or public servant, member of a political party or candidate politician or any third party associated with this transaction, in a manner that could violate Anti-Corrupt Legislation.

6.3 The contracting parties agree to conduct the Trial and maintain archives and data whose keeping is necessary for legal reasons or for reasons that relate to the implementation of the relevant medical and pharmaceutical regulations, insurance clauses or obligations on archives keeping, during and after the end of validity of this Agreement, in full compliance with Applicable Legislation and regulations, as well as in accordance with the relevant policy of the Sponsor for the keeping of archives by external associates and/or otherwise and in accordance with the terms and conditions set out above.

6.4 Moreover, the Principal Investigator agrees that the fees provided for by this Agreement by the Sponsor do not intend to affect the making of any decision that he may be called to make, or any of the directors, co-investigators, employees, associates who happen to be public servants, nor do they intend to affect the prescription process to the benefit of the products of the Sponsor or the procurement, insurance coverage or in any manner, the business benefit of the Sponsor. To that end, the Principal Investigator will ensure that all associates and persons drawing rights thereunder and any satellite centres, including the co-operating investigators who are involved in the conduct of the Trial, understand that in accordance with the applicable rules and regulations, they may be required to notify certain financial data to the competent regulatory authorities in and outside Greece. Finally, it is mutually accepted that in case the present conditions are altered or the above legislative framework is infringed, the Sponsor is entitled to immediately and unilaterally terminate this Agreement and redeem any amounts paid. Any further indemnity right of the Sponsor is not excluded.

6.2 The contracting parties expressly state that they are aware of the provisions set out in the Directive (EC) on Personal Data Protection (EC/95/46), as amended and updated in Law 2472/97 and all present directives, decisions, circulars and regulations of the Personal Data Protection Authority, that govern the lawful conduct of the Trial and the provision of the services agreed upon, and fully undertake their obligations under the applicable national legislation on the protection of a person against processing of Personal Data, as regards the keeping, management and processing of all personal data collected and those of which they may obtain knowledge in the context of providing the services agreed upon and of the archives that relate with the conduct of the Trial, which include such data. In this context, the contracting parties undertake that the collection, keeping and processing of personal data, such as information concerning health and pharmaceutical treatment of patients participating in the Trial, as well as personal data that concern the Principal Investigator and any Investigating personnel (e.g. name, address and phone number of the Hospital or the clinic, curriculum vitae), are subject to full compliance with the applicable laws, provisions and obligations imposed by the relevant National

Legislation on protection of a person against processing of Personal Data and that upon the collection and processing of the said data, they agree to adopt the appropriate safety measures for the avoidance of theft, embezzlement, falsification, unauthorised access etc. to the archives kept, to preserve the confidential nature of the information on health and pharmaceutical treatment of the patients participating in the trial, to properly inform the persons to whom the personal data relate, regarding the collection, the object and the processing of their personal data, to grant to the persons involved reasonable access to their personal data and to restrict access thereto, to unauthorised persons.

6.3 The Sponsor is entitled to forward personal data to other subsidiaries of the Group with a registered office in the European Union or to representatives and/or contracting parties employed on behalf or for account of the Sponsor, as well as to any regulatory authority. Respectively, personal data may be forwarded to regulatory authorities around the world or to other subsidiaries of the Group in countries outside the European Union, such as the United States of America, to whom the European Union has presently verified the lack of sufficient legislation on Personal Data Protection, which provides a satisfactory level of protection of personal data. Any such forwarding of personal data, regardless if the recipient thereof is in or outside the European Union, will be strictly effected in accordance with the terms and conditions stipulated by National or European Legislation and in full compliance with the directives, decisions, circulars and regulations of the Personal Data Protection Authority issued so far, that concern the object of this Agreement. In any case, the Sponsor, the subsidiaries of the Group as well as the respective representatives thereof undertake to implement satisfactory safety devices in order to protect the said personal data. Personal data may also be disclosed, if so required by individual supervising or court authorities or by applicable legislation. Finally, the parties agree that the Sponsor can use personal data that concern the Investigator and his/her associates for the purposes of internal management and communication.

6.4 The Hospital and the Principal Investigator will inform the investigating personnel and any other personnel participating in the conduct of the Trial that their personal data may be collected, as set out in Article 6 and when required, they will obtain the written consent thereof.

6.5 In case any of the contracting parties hereto is deemed to violate applicable laws and provisions, the contracting parties agree to negotiate in good faith the revision of the term or the terms constituting the violation. In case the parties cannot reach an agreement as to the new or amended terms, as required so that the Agreement in whole is in compliance with the Applicable Legislation, then each contracting party may terminate this Agreement upon written notice of

termination which will be lawfully communicated to the contracting parties sixty (60) days beforehand.

7. <u>Intellectual Property Rights – Confidentiality – Publication</u>

7.1 Any and all Data, including without limitation, documents, manuscripts or printed material, graphics, video and audio material, as well as information contained in any record, electronic database or electronic information, created and/or provided in relation to the conduct of the Trial, will be property of the Sponsor, who may use the Data in any manner it deems expedient, 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 of this Agreement. Any work, object of intellectual property right that may be protected by the provisions on intellectual property, which will be created in relation to the conduct of the Trial and is included in the Data (with the exception of any publication by the Principal Investigator, as provided for in Par. 7.3) will be the property of the Sponsor, as the holder of the unlimited intellectual property right of the said work. All intellectual property rights 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 set out in Article 8, will be held by the Sponsor. To that end, it is expressly agreed between the contracting parties that the unlimited property right on the conducted Trial in general (suggestively referred, the results, reports, the final report etc.) is hereby transferred by the Hospital, ELKE/ELKA and the Principal Investigator, all having the relevant authority by any other creator, contributor, co-investigator, associate and other participant upon the relevant notice thereof, exclusively and for an indefinite term to the Sponsor, who is entitled to exercise any powers deriving from such right, without being obliged to pay any fees or indemnification except of those agreed upon herein. The counterparties hereby waive any claim of any intellectual property right on the work conducted, expressly stating that the consideration paid to them, settled in full any value thereof. The Hospital and the Principal Investigator hereby undertake to promptly inform the Sponsor for any know-how that may result during the term and/or in relation to this Trial and undertake not to use this know-how for any purposes other than those of this Agreement, without the prior written consent of the Sponsor. The Hospitals and the Principal Investigator hereby grant the exclusive, universal, irrevocable, free of the obligation to pay any consideration, licence to use any know-how that may have not been specifically granted to the Sponsor under the provisions of the preceding clause.

7.2 Any information, including information regarding the Investigational medicinal Product (Trial Medicine) or the activities of the Sponsor, such as patent applications, formulas, production procedures, main scientific data,

previous clinical data and wording information provided to the Hospital, ELKE/ELKEA or to the Principal Investigator which has not been previously published, as well as any data deemed to derive from this Trial, are confidential (hereinafter the "Confidential Information") and will remain at the exclusive ownership of the Sponsor. Both during and after the expiration/termination of this Agreement, the Hospital, ELKE/ELKEA or to the Principal Investigator are obliged to keep confidential and us only for the purposes set out in this Agreement (i) information deemed confidential or which any reasonable person would deem confidential and property of the Sponsor, which are disclosed on behalf of the Sponsor or by the Sponsor itself to the Hospital, ELKE/ELKEA or to the Principal Investigator and (ii) Data created, produced as a result of this Trial. The former obligations do not apply to data or information (i) published without any default of the Hospital, ELKE/ELKEA or the Principal Investigator, (ii) which, upon the written consent of the Sponsor may be used or notified or (iii) published in accordance with paragraph 7.3 below.

7.3 As regards any Data or other information deriving from the provision of services in accordance with and in performance of the terms of this Agreement by the Hospital, ELKE/ELKEA or to the Principal Investigator, the Sponsor or the duly designated representatives thereof shall be entitled to publish the said data and information without any approval of the Principal Investigator. The Principal Investigator shall be entitled to publish the results of the Trial and any supporting information which is required to be included in any publication of the results of the Trial or which is necessary for other scientists, in order to validate the results of this Trial. If the Principal Investigator wishes to publish any information of the Trial, a copy of the original manuscript to be published must be filed to the Sponsor for certification, at least sixty (60) days before it is filed for publication or presentation. The Sponsor and the Principal Investigator will undertake the precipitated review of abstracts, presentations on posters or on other materials. Given the above, no document that includes Confidential Information shall be filed for publication without the prior written consent of the Sponsor. If requested in writing, the Principal Investigator is obliged to delay the said publication for up to sixty (60) more days, in order for an patent application to be filed. If a specific Trial is part of multicentre Trial, the Principal Investigator shall not publish for this Trial, any data that derive from the specific investigation/research centre, until the consolidated results from the completed multicentre Trial have been published in a joint publication of the results thereof. However, if such a multicentre publication is not filed within twelve (12) months following the conclusion, cancellation or expiration of the trial in all research centres or from the moment the Sponsor confirms that there shall be no multicentre publication for the Trial, the Principal Investigator may issue/publish the results deriving

from the research centre of the Hospital, in accordance with the terms of this paragraph.

7.4 The Principal Investigator guarantees the compliance of all co-operating investigators and of any other personnel which participates in any manner in the Trial or otherwise relates thereto, with the provisions of this Article 7.

7.5 The Sponsor is entitled to use the name of the Hospital and of the Principal Investigator (and co-investigators) in periodically circulated brochures it sends to other research centres in order to brief them for any developments in the clinical trials sector, the procedure for the inclusion of the subjects to the Trial and other relevant issues of a more general concern. The Hospital and the Investigator will not use the name of the Sponsor or of any employee and associate of, or any subsidiary or affiliated company of the Sponsor, as well as any mark, logo and sign or any other right vested to the Sponsor, in any advertising or informational announcement, without the prior written consent of the Sponsor.

7.6 Notwithstanding any other provision of this Agreement to the contrary, the Sponsor is entitled 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 suggested publication, under the conditions of Publication as these are described in this Agreement. In any case, it is agreed herein that the Investigator is obliged to comply with any legislative or regulatory provision concerning the process, the contents or the disclosure of the results of the Clinical Trial.

7.7 The Investigator undertakes that during the provision of the above-described services, he/she will observe all provisions of the relevant laws and the principles of practice/conduct that the Sponsor may communicate thereto, as well as that, in case any form of notification obligation provided for by the law as to the nature and the fees of his/her services, he/she will proceed with a declaration of interest, as the case may be.

7.8 The Investigator is aware and accepts that the Sponsor and the Group of Companies thereof, in the context of lawfully conducting its activities, collects, keeps and processes either by itself, or via third parties contracted therewith in or outside the European Union, the personal data of the Investigator, always in compliance with the terms of any laws that may apply, including laws 2472/1997, law 3471/2006, law 3472/2006 and law 3115/2003.

7.9 The 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 of

compensation in kind he/she receives for rendering the above services, by the Company, such as the fee, the payment details, the coverage of travelling and accommodation costs or any other expenses. In particular, the Investigator is aware and accepts that the Company may disclose the above data at a website of the Sponsor or of the Group of Companies thereof. The contracting parties are informed for the obligatory disclosure of the particulars of the Agreement in the Internet in accordance with Law 3861/2010 "Transparency Programme".

8. Patents

8.1 All rights of any on any discovery or invention, invented or to be invented which will be practically set in operation as a result of the works performed in accordance and in performance 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 will promptly notify any invention or discovery that results from the performance of this Agreement. The Hospital, ELKE/ELKEA and the Principal Investigator agree to transfer to the Sponsor or the authorised representative thereof the exclusive ownership thereon, with the Sponsor repaying any relevant expenses, which were born by the Principal Investigator, ELKE/ELKEA and/or the Hospital upon the filing, procedural pursue or preservation in effect of any patent applications or applications for the issue of patents for such inventions. These applications, if any, will be filed and supported both in and out of court by the Sponsor or the duly authorised representative thereof.

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

9. Budget – Fees

NOTE: This paragraph is filled in by the Sponsor in accordance with the principles and procedures thereof.

A. Fees and Payment Schedule

9.1 In order to conduct the Trial, it is agreed that the Sponsor will pay the amount of **Euro ……..……(€……..) per patient completing the Trial**, a fee deemed to be fair and reasonable, as concluded from the required engagement in the context of the Protocol. This amount, which will cover all expenses deriving from the conduct of the Trial in accordance with the Protocol, includes both the fees and the costs for the conduct of the project, as well as any other contributions in favour if third parties and tax encumbrances, which are included in the above amount and will be withheld

therefrom. These fees suggestively *inter alia* include, the fee of the Principal Investigator (PI), the fees of the scientific and other personnel who will be engaged in the project, the fee for the archiving of important documents and the Hospital fees, withholdings and any other cost or expenses required for or charged upon the conduct of the project. The said amount does not include VAT.

Withholdings in favour of ELKE/ELKEA and in favour of the hospital are included together with any other contribution and tax encumbrances in the above amount and are withheld therefrom.

The total calculated fee for the conduct of the Trial, as analysed in the following TABLE OF PAYMENTS will be paid by the Sponsor in **…. instalments, with the first being paid ….. (…) months after the admission of the first patient in the Research Centre of the Trial, based on the data entered in the Case Report File or as a lump sum at the end of the Trial. The amount of each isntalment will depend on the number of visits that each patient has effected within the specific period and will be shaped in accordance therewith.** A condition for the realisation of the above payments is the certification of the completion of each phase (stage) of the trial, which (certification) will be made in writing by the Principal Investigator and the officer of the Sponsor in charge of the Trial.

Payments will be made in the following bank account:
Name of the Beneficiary of payment:
Bank
Account No
IBAN

All payments provided for by this Agreement, which correspond, in accordance with the provisions hereof set below, to services rendered and works performed, will be made in accordance with the law, in the above bank account, whose beneficiary is the ELKE of the ….YPE of…….., the ELKE of the University of ……, after the issue and delivery by ELKE of the ….YPE of ……..ELKE of the University of …… to the Sponsor of the relevant official certified **Invoice for the Provision of Services**, as provided by the Greek Code of Books and Records, which the Sponsor will settle within …… (…) **days** from the issue and taking delivery thereof.
The Sponsor is obliged to notify to the Hospital a copy of the invoices for the provision of services that it obtains from the ELKE, each time it effects a deposit.

Any deposit effected by the Sponsor in favour of the ELKEA of the …. YPE of ……./ELKE of the University of ……. is a payment of the respective part of the fee and is proven by the deposit voucher issued by the Bank. By means of the above payments, the fees of the Principal Investigator are deemed settled against the Sponsor, together with the fees of the special scientists and other associates, of the secretaries and administration employees and any other personnel in general, who will participate in the conduct of the Clinical trial and will be employed during the work for the provisions of services, as these are specified in the Agreement for the Conduct of the Clinical Trial, since the Sponsor hereby concludes no dependent work relationship or relationship for the provision of independent works or any project agreement or any other form of employment relationship for the conduct of the Clinical Trial in accordance with the above. Subsequently, these persons have no claim against the Sponsor for the provision of their services during the conduct of the Clinical Trial and in particular, for the payment of salaries, daily wages, fees, indemnifications, insurance contributions and other amounts among those borne by the employer.

TABLE OF PAYMENTS

Analysis of Fee per participating patient

Visit	Fee of investigator in Euro	Management Cost ….%
Screening		
Start-up visit		
1st Visit		
2nd Visit		
3rd Visit		
4th Visit		
5th Visit		
6th Visit		
7th Visit		
8th Visit		
9th Visit		
10th Visit		
11th Visit		
12th Visit		
13th Visit		
14th Visit		
15th Visit		
16th Visit		
17th Visit		
18th Visit		
20th Visit		
21th Visit		
22th Visit		
23th Visit		
24th Visit		
25th Visit		
Conclusion of Treatment/ Early Termination		
Total		
Total + VAT		

TOTAL: EURO..…….

TOTAL + VAT: EURO.....

Total: EURO……./patient (+ EURO…….Management cost)
Screening Failure: Euro……./patient

9.2 The above eCRF/CRF fee concerns the financial cover of the actions required for the entry of all data within …… (….) business days after the visit of the patient, with the exception of the initial visit and the Serious Adverse Reactions which must be added within 24 hours.

9.3 The Principal Investigator is expected to include in the research centre ……..(….) assessable patients who participate in this Trial. The Sponsor reserves the right to terminate the Agreement for the Conduct of the Clinical Trial in any manner directly, at any time and without prejudice for itself, if no patient has been admitted in the Research Centre until…….

9.4 During the course of the Trial, and if the number of the patients participating in the Trial which is provided for herein to be admitted in the research centre is completed, the Sponsor may request by the Hospital and by the Principal Investigator to include more patients in the Trial. If this is accepted by the Hospital and the Principal Investigator, the written notification by the Sponsor to the Hospital and to the Principal Investigator, which will approve the inclusion of more patients participating in the Trial, will suffice to document and prove the consent of the Parties. The same amount provided in paragraph 9.1 hereof will be paid per filled in CRF to be evaluated and for such additional patients participating in the Trial, without any further amendment of this Agreement being required.

9.5 All payments will be effected in accordance with the above Payment schedule. A fee for the patients participating in, but not completing the Trial will be paid on an proportional basis, also in accordance with the above Payment Schedule. No payment will be effected for patients participating in the Trial, who either left or completed the Trial, but have breached the criteria for the inclusion in the trial and of the approved Protocol, with the exception of the cases specifically approved by the Sponsor, if screening or collection of data is required. The amount of Euro …….. (€……) will be paid per participating patient who is excluded in the initial screening (screening failure), due to unexpected laboratory values that fall outside the normal range. This amount will be paid for a maximum of …….(…..) participating patients. In case more than …….(…..) participating patients are excluded in the initial screening (screening failure) the Sponsor shall not cover such expenditure and the above compensation shall not be paid for those additional patients, save the prior written acceptance by the Sponsor.

9.6 The final payment will be effected after the Case Report File (CRF) will have been filled in (including the subsequent screening visits) and delivered to the Sponsor and after all queries in relation to the data will have been resolved in the research centre. The amount finally due will be calculated in accordance

with the total number of patients who will be included and the criteria, terms and conditions of payment set out above.

9.7 The contracting parties acknowledge and agree that the fee and any financial or other support granted by the Sponsor in relation to and in performance of this Agreement, represents the usual transacting value for the services rendered and the works for the conduct of the Trial which are performed by the Principal Investigator and the Hospital, it has been the object and the result of negotiations and agreement in the context of an independent transaction, and has not been determined in a manner that co-calculates the volume or the value of any services or other works which have occurred in any manner between the Sponsor, the Hospital and the Primary Investigator.

9.8 Both the Hospital and the Primary Investigator will not invoice any third party for the Investigational Medicinal Product (Trial Medicine) or for any other items, materials or services rendered by the Sponsor in relation to the Trial or for any services rendered to the participating patients in relation to the Trial, for which a payment is provided for and is effected as part of the trial, unless especially permitted by the provisions and terms for the payments of fees.

B. Special terms

This Trial is conducted in accordance with a policy of directed inclusion (admission/exclusion criteria). The Sponsor anticipates the completion of the inclusion process with the achievement of a total of ……(….) validly participating patients for all Research Centres participating in the Trial. In case that a total of …….. (…..) validly participating patients are admitted before the Research Centre achieves the target of …… (…..) validly participating patients, the Sponsor reserves the right to restrict or suspend any further admission in the Research Centre. In this case, the Sponsor will inform the Principal Investigator and the Principal Investigator will promptly restrict or limit any further admission of participating patients, upon the communication of the notice.

10 <u>Legal Liability/ Indemnification</u>

10.1 The Sponsor shall be obliged to restitute any damage the Principal Investigator and/or the Hospital may sustain, which derives from an injury of any patient participating in the Trial, directly incurred from the use of the Investigational Medicinal Product (Trial Medicine) during the Trial or from any operation or procedure, which is provided or required by the Protocol and which the patient would not have undergone if he/she did not participate 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 the said substance was administered in accordance with the Clinical Trial Protocol of the Sponsor approved by the competent

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 which were lawfully used in the context of the Protocol of the Trial.

(c) The event occurred as a result of the diagnostic procedures which were performed in accordance with the Protocol, as in force from time to time and in accordance with any subsequently approved amendments thereof.

(d) The event was the result of therapeutic or diagnostic measures lawfully required due to the occurrence of unexpected events caused by the substance of the Sponsor being tested, from a comparative medicinal treatment or from diagnostic procedures required in accordance with the Protocol, as in force from time to time and in accordance with any subsequently approved amendments thereof.

The Sponsor shall have the absolute right to proceed with any arrangements, provided that its shall not admit any error for account of the beneficiaries of the indemnification, without their written approval. In addition, the obligation for indemnification shall not include cases of loss, damage or expenditure deriving from negligence, willful misconduct or erroneous operation of the beneficiaries of the indemnification and it is naturally understood that the administration of any substance in accordance with the directors of the Protocol of the trial shall not constitute negligence or erroneous operation with regard to this Agreement.

10.2 The above obligation of the Sponsor, as set out in Paragraph 10.1 shall not apply and the Sponsor shall not be liable for the payment of any indemnification of expenses, but on the contrary the Principal Investigator, the Hospital, any associates and persons drawing rights thereunder as well as any personnel to be engaged in the conduct of the Trial, will be obliged to compensate the patient and restitute any damage of the Sponsor, direct or indirect, positive or negative, material or moral, deriving from the application of civil or penal provisions, which the Sponsor will sustain from the undue conduct of the Trial in accordance with (a) the Protocol, (b) the written recommendations and instructions of the Sponsor regarding the use of the Investigational Medicinal Product (Trial Medicine), (c) the provisions of Applicable Legislation governing the object of this Agreement and (d) the terms of this Agreement, due to actions, acts or omissions of the aforementioned. The Sponsor shall have no liability for events that will exclusively occur as a result of the underlying disease of any subject of the Trial or for events that resulted from diagnostic or therapeutic measures not specifically mentioned in the Protocol, as in force from time to time and in accordance with any subsequently approved amendments thereof.

10.3 The obligation of the contracting party liable for indemnification in accordance with this agreement, applies only if the other contracting party promptly serves the relevant notice, upon receipt of the notice of any such claim or action and allows the party liable for compensation, the attorneys-at-law and the personnel thereof, to operate and control the defence against such claims or actions, including the interlocutory procedure, the trial or any settlement, granting to the contracting party entitled to indemnification, the ability to fully co-operate in order to assist in the said defence. The party contracting entitled to indemnification further agrees that it shall not settle or compromise any such action or claim without the prior written consent of the party liable for indemnification.

10.4 The liability of the ELKEA of the …. YPE of …..……/ELKE of the University of …… entering into this Agreement, both contractual and legal, is limited to and exclusively concerns the financial management of the Trial, which will be conducted in accordance with the terms of this Agreement.

11. <u>Insurance</u>

The Sponsor will ensure and maintain in full force during the conduct of the Trial (and after the end of the Clinical Trial, with the coverage of any requirements deriving from the Trial) insurance coverage for: (i) product civil liability and (ii) general civil liability. Any insurance coverage will be of the amounts expressly set out by Applicable Legislation.

12. <u>Disclosure of Financial Data/ Erasure</u>

12.1 The Hospital and the Principal Investigator agree to grant to the Sponsor any information required for its compliance with any conditions on disclosure of data, imposed by any competent authority (including, if possible, of the U.S. F.D.A. – United States Food and Drug Administration), including any information that is required to be disclosed, in relation to any financial relationship between the Sponsor and other subsidiaries of the Group […] and the respective representatives thereof and 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 the 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 interests between the contracting parties, that will obstruct or affect the provision of services by the Hospital and/or the Principal Investigator in accordance with the Agreement and confirm that the provision of services on their part in accordance with and in performance of this Agreement, does not violate any other agreement with third parties. The Hospital and the Principal

Investigator will promptly inform the Sponsor if any conflict of interests emerges during the conduct of the Trial and the performance of this Agreement.

12.3 The Principal Investigator and the Hospital will not hire, contract with or maintain as an associate or employee any person, directly or indirectly, in order to render the services and works contemplated by this Agreement, if this person (i) has been erased by any competent supervising Authority (including, if possible, of the U.S. F.D.A. – United States Food and Drug Administration) or (ii) has been convicted for anti-professional conduct and tort that relates to the conduct of clinical trials. Upon the Sponsor's written request, the Principal Investigator and the Hospital will grant within a period of ten (10) days, written confirmation that they have complied with the above obligation. This will be an on-going reassurance and guarantee during the period this Agreement is in force and the Principal Investigator and the Hospital will promptly notify the Sponsor for any change in the conditions of the reassurance and guarantee stipulated by this Article.

13. <u>Independent Parties</u>

The Hospital and the Principal Investigator act in the capacity of the independent parties hereto and not as employees or representatives of the Sponsor and no relationship of dependent work is established between them or any employment relationship. The Principal Investigator and any personnel thereof that may participate in the trial are not entitled to participate in, nor any right to benefit from any benefits and allowance plan, employees policies or insurance indemnifications of the employees of the Sponsor.

14. <u>Publicity</u>

None of the parties will use the name of the other party for promotional purposes, without the prior written consent of the party whose name is to be used and none of the contracting parties will disclose the existence or the content of this Agreement, unless so required by the law. Despite the above, the Sponsor may publish website contact details and reference to the trial conducted at www.clinicaltrials.gov , at equally official websites and at the Sponsor's websites and of the subsidiaries of the Group. In addition, the Sponsor will be entitled to 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. Notices/ Person in Charge of the Sponsor for the conduct of the Trial

The person in charge of the Sponsor for the Conduct of the Trial and the management of any issues that relate thereto is Mr/Mrs…….(reference of the capacity thereof)…….. Any communication regarding the Trial is sent to the above Person in Charge. The

same person is also in charge of the certification for the fulfilment of the obligations set out in this Agreement.

Any notices communicated in accordance with this Agreement will be sent via registered mail, fax or will be delivered in hand, with prepaid delivery as follows:

To: COMPANY……..
To the attention of Mr……., Trial Supervisor

To: ELKEA of ….YPE of ……./ELKE of the University of …….
To the attention of …….

To: ……..Hospital of ……..

To the attention of …….

To: Physician ……Mr……
(Insert Name, title and Address of the Principal Investigator)

16. <u>Assignment</u>

16.1 The Sponsor will be entitled to assign this Agreement to a subsidiary of the Group of Companies or to contract research organisation (CRO) by means of assignment, upon the prior written notice to the Principal Investigator and the Hospital. In any other case none of the contracting parties will be entitled to assign the rights and obligations thereof hereunder or in any other manner substitute himself in the work, in whole or in part, without the prior written consent of the Sponsor. Subject to the above, this Agreement will bind and operate to the benefit of the respective contracting parties, the special and universal successors thereof.

16.2 In case the Principal Investigator or the Hospital employ for the performance of the work or part thereof, upon the prior written approval by the Sponsor, any third party (natural person or legal entity) as an associate, they will oblige it by means of a special agreement concluded between them, to respect all terms of this Agreement and will jointly rendered it liable jointly and in whole therewith against the Sponsor for any loss the Sponsor may sustain from the acts and omissions thereof.

17. <u>Miscellaneous</u>

17.1 This Agreement cannot be supplemented or otherwise amended, but only in writing, with a document signed by all contracting parties. This Agreement

constitutes the full agreement of the contracting parties in accordance with the subject matter thereof. It expressly supersedes any prior or simultaneous, oral or written confirmation, guarantees of agreements. Any Annexes attached constitute a unified and integral part of this Agreement.

17.2 The non-direct pursue or the non-purse of the rights of the parties hereunder and in particular, the performance of any obligation of the counterparty hereunder, shall in no way be deemed as waiver of their respective rights.

17.3 In case of conflict between the provisions of this Agreement and any other relevant documents, except of the Protocol, the provisions of this Agreement will supersede.

18. Applicable Law

This Agreement is governed by Greek Laws. It is agreed that the Courts of [……..] will have competent jurisdiction for the settlement of any dispute deriving from this Agreement which concerns the execution, performance and interpretation thereof and the relationships in general established hereunder.

It I self-understood that before any recourse to the Courts, in accordance with the above, the contracting parties will try their best to settle the disputes that may have emerged between them.

IN WITNESS WHEREOF, the contracting parties executed this Agreement by their legal representatives on the date recorded above in three (3) counterparts and each contracting party received one.

THE CONTRACTING PARTIES

FOR THE HOSPITAL……..
The Governor of ……

Signature/Seal

Date

For the SPONSOR
MANAGING DIRECTOR

Signature/Seal
Date:

…….
PRINCIPAL INVESTIGATOR

Signature/Seal
Date:

Annex Attached:
Annex A: Materials and Equipment

FOR ELKE/ELKEA_____

_____
[*insert the capacity of the signatory*]

_____
Signature/Seal

Date:

MINISTRY OF HEALTH AND SOCIAL SOLIDARITY
ELKEA of 1st YPE of ATTICA
Joint Ministerial Decision (KYA) No ΔΥΓ5γ/Γ.Π.οικ.75762/2005
of the Ministers of Finance, Health and Social Solidarity, and Development
Gov. Gazette 1037/21-07-05

ACCEPTANCE OF THE MANAGEMENT OF THE PROJECT

Details of Scientific Supervisor

Full Name:	
Capacity:	
Department:	
Laboratory:	
Field/Hospital:	
Tel. & Fax:	
e-mail:	

TO THE ELKEA COMMITTEE OF THE 1st YPE OF ATTICA
Please accept the management of the project

Title (in Greek):	
Title (in English):	
Financing Agency(-ies):	
Total Budget: (Target of patients number INSURANCE POLICIES x payment per patient)	Term: (in months):
Commencement Date:	**Ending Date**:

The Director of the Department

Name and Signature
Seal

…….___/___/___

The Scientific Supervisor

_____
Signature

ELKEA of 1st YPE of ATTICA
Joint Ministerial Decision (KYA) No ΔΥΓ5γ/Γ.Π.οικ.75762/2005
of the Ministers of Finance, Health and Social Solidarity, and Development
Gov. Gazette 1037/21-07-05

MEMBERS OF THE TEAM OF THE PROJECT

To the COMMITTEE OF ELKEA OF THE 1st YPE of Attica

We are sending you the consolidated statement of the members of the team of the project who will participate in the project under the following details:

Scientific Supervisor: Anna Efraimidou	Code:
Title of the Project:	
Sponsor: GlaxoSmithKline A.E.B.E.	Percentage of financing: 100%
Commencement Date:	Ending Date:

CONSOLIDATED STATEMENT OF MEMBERS OF THE PROJECT'S TEAM

FULL NAME	CAPACITY	TAX REG. No/ID Card No	TOTAL FEE (EURO)
SCIENTIFIC SUPERVISOR(S)			
			-10%
PUBLIC SERVANTS			
PERSONNEL WITH PROJECT CONTRACT UPON ISSUE OF RECEIPT			
External associates			
Residents			
PERSONNEL WITH PROJECT CONTRACT WITHOUT THE ISSUE OF RECEIPT			

Note: In case it is necessary, another page can be used.

……___/___/___

The Scientific Supervisor

_____
Signature

MINISTRY OF HEALTH AND SOCIAL SOLIDARITY
ELKEA of 1st YPE of ATTICA
Joint Ministerial Decision (KYA) No ΔΥΓ5γ/Γ.Π.οικ.75762/2005
of the Ministers of Finance, Health and Social Solidarity, and Development
Gov. Gazette 1037/21-07-05

TO THE ELKEA COMMITTEE OF THE 1st YPE OF ATTICA

We are sending you the budget of the project under the following details:

Scientific Supervisor:	Code:
Title of the Project:	
Sponsor:	Percentage of financing:
Commencement Date:	Ending Date:

CATEGORIES OF EXPENDITURES	**BUDGET (€)**
1. Fees of public servants	(**Target of patients number INSURANCE POLICIES x payment per patient) -10%**
2. Fees of third parties assigned works (with receipt)	
3. Fees of third parties assigned works (without receipt)	
4. Equipment (instruments, materials)	
5. Consumables	
6. Domestic transits	
7. Transits abroad	
8. Purchase of know-how/technology	
9. Designs	
10. Evaluation of Project	
11. Laboratory Tests	
12. Other Expenses	
13.	
14.	
15. General expenses (withholding in favour of ELKEA)	
GRAND TOTAL (€)	

In case the project is subject to VAT (e.g. Designs) please fill in: **VAT amount (€)**

The Representative of the Financing Agency

_____
Signature

……___/___/___

The Scientific Supervisor

_____
Signature

This decision must be published in the Government Gazette.

Athens, February 19, 2013

The Ministers of

ALTERNATE MINISTER OF FINANCE	DEPUTY MINISTER OF DEFENCE	DEVELOPMENT, COMPETITIVENESS, INFRASTRUCTURE TRANSPORTATIONS AND NETWORKS
CHRISTOS STAIKOURAS	**PANAYOTIS KARABELLAS**	**CONSTANTINOS CHATZIDAKIS**

EDUCATION AND RELIGION CULTURE AND SPORTS	ALTERNATE MINISTER OF HEALTH	JUSTICE, TRANSPARENCY AND HUMAN RIGHTS
CONSTANTINOS ARVANITOPOULOS	**MARIOS SALMAS**	**ANTONIOS ROUPAKIOTIS**