TEMPLATE CLINICAL TRIAL AGREEMENT 2013 – THE NETHERLANDS

CLINICAL TRIAL AGREEMENT

(Template agreement for industry initiated and sponsored Clinical Trials, with human subjects, conducted by academic centres in The Netherlands)

Clinical Trial: [insert title]
Protocol: [insert EUDRACT number or Dutch Registration NL-number and date]
Trial Site: [insert site number or location]
Investigational Product: [insert name]
Effective date of agreement: __/__/____ (dd-mm-yyyy)

Scope of use:
This template clinical trial agreement is designed and supported by the Nationale Federatie van Universitair Medische Centra and Nefarma to facilitate conducting clinical trials in The Netherlands in case the agreement is entered into by a pharmaceutical company as Sponsor and an academic hospital as Institution, which employs the Principal Investigator.

In case a Clinical Trial Organisation (CRO) is signing this agreement on behalf of the Sponsor, please note that a separate indemnity letter must be signed by the Sponsor.
The Parties,

A. [insert name of Sponsor], whose registered office is at [insert address], lawfully represented by [insert name(s) and function(s)] (hereinafter referred to as “Sponsor”) and

B. [insert name of Institution], whose address is at [insert address], lawfully represented by [insert name(s) and function(s)] (hereinafter referred to as “Institution”)

(each hereinafter referred to as “Party” or collectively as “Parties”)

in the presence of

[insert investigator’s title, name and department of Institution where the investigator is employed], the supervisor under whose responsibility the conduct of the clinical trial will be carried out [on behalf of Institution] (hereinafter referred to as “the Principal Investigator”),

WHEREAS:

a. Sponsor is a pharmaceutical company involved in research, development, registration, manufacture and/or sale of medicines for use in humans;

b. Sponsor wishes to investigate and evaluate the safety and/or efficacy of the investigational product (as defined hereinafter);

c. Institution and the Principal Investigator are concerned with the diagnosis, treatment and prevention of disease and/or clinical research for the improvement of healthcare;

d. the Principal Investigator has obtained from Sponsor and has had sufficient time to review and evaluate the Protocol (as defined hereinafter), the investigator brochure (“IB”), the product information and other information sources regarding the investigational product, in order to become thoroughly familiar with the appropriate use of the investigational product and to determine his/her interest in participating in the clinical trial;

e. Institution has facilities and personnel with the requisite skills, experience, and knowledge to participate in the clinical trial as a clinical trial site in accordance with the Protocol and Institution and Principal Investigator are willing to conduct the clinical trial at the trial site pursuant to the Protocol and the terms and conditions set forth in this Agreement; and
f. the Parties wish to provide the terms and conditions according to which Sponsor, Institution and the Principal Investigator shall participate in and perform the clinical trial;

NOW THEREFORE it has been agreed as follows:

1. DEFINITIONS

1.1. The following capitalised words and phrases have the meaning assigned thereto:

a. “Affiliate” means any business entity which controls, is controlled by, or is under the common control with Sponsor. For the purposes of this definition, a business entity shall be deemed to control another business entity if it owns, directly or indirectly, in excess of 50% of the voting interest in such business entity or the power to direct the management of such business entity or to elect or appoint 50% or more of the members of the management of such business entity;

b. “Agent” shall include, but shall not be limited to, any person providing services to a Party under a contract for services or otherwise, to include without limitation any pharmacist, clinical chemist, nurse or other health professional.

c. “Agreement” means this agreement comprising its clauses, schedules and any appendices attached to it and all amendments thereto agreed to in writing by Parties;

d. “Auditor” means a person who is authorised to carry out a systematic review and independent examination of Clinical Trial related activities and documents to determine whether the evaluated Clinical Trial related activities were conducted, and the data were recorded, analysed and accurately reported according to the Protocol, Standard Operating Procedures, ICH GCP, this Agreement and the applicable regulatory requirements;

e. “Clinical Trial” means the investigation (to be) conducted at the Trial Site in accordance with the Protocol;

f. “Clinical Trial Subject” means a person recruited to participate in the Clinical Trial;

g. “Clinical Trial Authorisation” means a Clinical Trial authorised in accordance with article 2 and 13i of the Dutch Medical Research Involving Human Subjects Act);

h. “Competent Authority” means the authority appointed to evaluate the Clinical Trial in accordance with article 13i of the Dutch Medical Research Involving Humans Subjects Act, based on article 9 of the European Clinical Trial Directive 2001/20/EC;

i. “Confidential Information” means any and all information, data and material of any nature belonging or entrusted to Institution or to Sponsor and/or its Affiliates which either Party may receive or obtain in connection with or as a consequence of this Agreement (1) which is Personal Data (as such term is defined in the
Dutch *Personal Data Protection Act* of 2000) which relates to any patient of Institution or his or her treatment or medical history, or (2) other information, the release of which is likely to prejudice the non-commercial or commercial interests of Institution or Sponsor respectively, or which is a trade secret, including Know How;

j. “CRF” means the case report form in a format prepared by Sponsor and documenting the administration of the Investigational Product to Clinical Trial Subjects as well as all tests and observations related to the Clinical Trial;

k. “eCRF” means a CRF in electronic form;

l. “DSMB” means a group of individuals with pertinent expertise that have oversight of and reviews on a regular basis accumulating data from one or more ongoing clinical trials and that advise the Sponsor regarding the continuing safety of Clinical Trial Subjects and those to be recruited to the Clinical Trial, as well as the continuing validity and scientific merit of the Clinical Trial.

m. “Effective Date” means the date first written above, being the date this Agreement comes into effect;

n. “Ethics Committee” means the accredited medical research ethics committee competent to review the Clinical Trial in accordance with article 2 of the Dutch *Medical Research Involving Human Subjects Act*, and to which the Protocol has been submitted for review and approval;

o. “ICH GCP” means the ICH Harmonised Tripartite Guideline for Good Clinical Practice (CPMP/ICH/135/95) together with such other good clinical practice requirements as are specified in Directives 2001/20/EC and 2005/28/EC of the European Parliament and the Council relating to medicinal products for human use and in guidance published by the European Commission pursuant to such Directives;

p. “Indemnitees” means the persons and entities defined in clause 4.1;

q. “Intellectual Property Rights” means patents, trade marks, trade names, service marks, domain names, copyrights, moral rights, rights in and to databases (including rights to prevent the extraction or reutilisation of information from a database), design rights, topography rights and all rights or forms of protection of a similar nature or having equivalent or the similar effect to any of them which may subsist anywhere in the world, whether or not any of them are registered and including applications for registration of any of them;

r. “Investigational Product” means the study drug or control material as defined in the Protocol;

s. “Know How” means all technical and other information which is not in the public domain (other than as a result of a breach of confidence), including but not limited to information comprising or relating to concepts, discoveries, data, designs, formulae, ideas, inventions, methods, models, procedures, designs for experiments and tests and results of experimentation and testing, processes, specifications and techniques, laboratory records, clinical data, manufacturing data and information contained in submissions to regulatory authorities, whether
or not protected by Intellectual Property Rights or any applications for such rights;

t. “Party” means the Sponsor or the Institution and “Parties” shall mean both of them;

u. “Principal Investigator” means the person who will take primary responsibility for the conduct of the Clinical Trial at the Trial Site [on behalf of Institution] or any other person as may be agreed between the Parties as a replacement;

v. “Protocol” means the description of the Clinical Trial that is fully recorded in the protocol identified on page 1 of this Agreement and all amendments thereto (including any substantial amendments for which Clinical Trial Authorisation has been obtained);

w. “Rate” means the rate of inclusion of Clinical Trial Subjects per designated time period as referred to in clause 5.3;

x. “Research Staff” means the persons who will undertake the conduct of the Clinical Trial at the Trial Site on behalf of Institution under the supervision of the Principal Investigator;

y. “Sponsor” means the Party commissioning for the Clinical Trial to be done, acting as "verrichter" as defined in Article 1.1.f of the Dutch Medical Research Involving Human Subjects Act WMO (Dutch: "Wet medisch-wetenschappelijk onderzoek met mensen");

z. “Standard Operating Procedures” means the procedures or (abbreviated) SOPs describing in detail how to conduct and document the Clinical Trial;

aa. “Target” means the number of Clinical Trial Subjects to participate in the Clinical Trial as described in clause 5.2;

bb. “Thresholds” means one or more series of Clinical Trial Subjects (to be) enrolled within specified Timeline(s) as referred to in clause 5.3, and Threshold shall mean any one of such thresholds;

cc. “Timelines” means the dates set out in Exhibit 1 hereto as may be amended by agreement between the Parties and Timeline shall mean any one of such dates;

dd. “Trial Monitor” means one or more persons appointed by Sponsor to monitor compliance of the Clinical Trial with ICH GCP and the Protocol and to conduct source data verification;

ee. “Trial Site(s)” means the premises at the department [insert department of Institution] of the [insert location] where Clinical Trial will be conducted.

1.2. Any reference to a law, regulation, code or guidance shall be deemed to include reference to any subsequent modification or re-enactment of it.

2. PRINCIPAL INVESTIGATOR AND RESEARCH STAFF

2.1. Institution represents that it is entitled to and will procure the services of the Principal Investigator to act as Principal Investigator and shall ensure the performance of the obligations of the Principal Investigator set out in the Agreement.
2.2. Institution represents that the Principal Investigator holds the necessary registration and has the necessary qualifications, expertise, time and resources to perform the Clinical Trial. The Principal Investigator is made aware of the obligations applicable to the Principal Investigator set out in this Agreement and acknowledges his/her acceptance of said obligations by co-signing this Agreement.

2.3. The Institution shall notify the Sponsor if the Principal Investigator ceases to be employed by or associated with the Institution or is otherwise unavailable to continue as Principal Investigator, and shall use all reasonable endeavours to find a replacement capable of continuing the Clinical Trial without undue delay and acceptable to both the Sponsor and the Institution, subject always to the Institution’s overriding obligations in relation to Clinical Trial Subjects and individual patient care. The Institution’s proposal for the Principal Investigator’s replacement shall not be rejected unreasonably by the Sponsor. If no mutually acceptable replacement can be found the Sponsor and the Institution may each terminate this Agreement pursuant to clause 12 below.

2.4. The Institution shall procure and shall ensure that the Principal Investigator procures the performance of the obligations of the Research Staff as set out in this Agreement. All matters, terms and payment of compensation, benefits and other conditions of engagement of any nature for the Principal Investigator and any member of the Research Staff used in the Clinical Trial shall be solely a matter between the Institution and such individuals, regardless of whether such individuals are considered employees, agents or independent contractors of the Institution. The Institution will take appropriate steps to inform each such person of his/her obligations hereunder and to obtain his/her agreement to abide by the terms and conditions of this Agreement.

2.5. The Institution represents that the Principal Investigator is free to participate in the Clinical Trial and there are no rights which may be exercised by or obligations owed to any third party which might prevent or restrict the Principal Investigator’s performance of his/her obligations set out in this Agreement.

2.6. Subject to Institution’s and the Principal Investigator’s overriding obligations in relation to Clinical Trial Subjects and individual patient care, neither Institution, the Principal Investigator or any other member of the Research Staff shall during the term of this Agreement conduct any other trial which might hinder Institution’s or Principal Investigator’s ability to recruit and study the required cohort of Clinical Trial Subjects.

3. CLINICAL TRIAL GOVERNANCE AND COMPLIANCE

3.1. Sponsor shall be responsible for obtaining and maintaining Clinical Trial Authorization for the conduct of the Clinical Trial and substantial amendments to the Protocol. Sponsor may require Institution and Principal Investigator to apply for the Clinical Trial Authorisation, in which case the Principal Investigator shall
keep Sponsor fully apprised of the progress of the Ethics Committee submissions and shall upon request provide Sponsor with all correspondence relating to such submissions.

3.2. The Principal Investigator shall not consent to any change in the Protocol requested by an Ethics Committee or Competent Authority nor implement any deviation from, or changes of the Protocol without the prior written consent of and as required by Sponsor and, to the extent required by applicable law or ICH GCP, the prior review and documented approval of the competent authority(ies) and the favourable opinion from the Ethics Committee.

3.3. Sponsor shall submit the Clinical Trial for listing in a free, publicly accessible clinical trial registry after Clinical Trial Authorisation.

3.4. Neither Institution nor the Principal Investigator shall register either the Clinical Trial, or the results, on any publicly accessible clinical trial registry, unless otherwise agreed with the Sponsor.

3.5. Sponsor shall inform Institution and the Principal Investigator about the name and telephone number of the Trial Monitor and the name of the person who will be available as a point of contact. Sponsor shall also provide the Principal Investigator with an emergency number to enable adverse event reporting at any time.

3.6. The Parties and the Principal Investigator shall conduct the Clinical Trial in accordance with:
   a. the Protocol;
   b. the terms and conditions of the Clinical Trial Authorisation granted by the Ethics Committee and Competent Authority; and
   c. the applicable legal and regulatory requirement(s).

3.7. The Parties and the Principal Investigator shall comply with all relevant laws and regulations of the EU if directly applicable or of direct effect and all relevant laws and regulations of The Netherlands including but not limited to, the (Dutch) Medical Research Involving Human Subjects Act (“WMO”), the (Dutch) Personal Data Protection Act (“Wbp”), the (Dutch) Act on the Agreement regarding Medical Treatment (“WGBO”), the (Dutch) law on Safety and Quality of Human Material (“Wet Veiligheid en Kwaliteit Lichaamsmateriaal”) and with all relevant guidance relating to medicines, use of human tissue and clinical trials from time to time in force including, but not limited to, the ICH GCP and the Code for Proper Use of Human Tissue 2011.

4. LIABILITIES, INDEMNIFICATION AND INSURANCE

4.1. Subject to the limitations set out hereinafter, Sponsor shall indemnify and hold harmless Institution, members of the Research Staff and any other employees including the Principal Investigator (the “Indemnitees”) against all claims, demands, actions or proceedings (to include any settlements or ex gratia payments made with the consent of the Parties hereto and reasonable legal and
expert costs and expenses) made or brought (whether successfully or otherwise): (i) by or on behalf of any Clinical Trial Subject for personal injury or death arising out of the administration or use of the Investigational Product during or as a result of the Clinical Trial, or to any clinical intervention or procedure provided for or required by the Protocol, to which the Clinical Trial Subject would not have been exposed but for its participation in the Clinical Trial; (ii) by Institution, its employees or by or on behalf of a Clinical Trial Subject for compensation of reasonable and necessary medical costs and expenses incurred by the Clinical Trial Subject who has suffered such personal injury as a direct result of the treatment or adverse reaction from the Investigational Product used in accordance with the Protocol.

4.2. Sponsor’s indemnification and defence of the Indemnitees under clause 4.1 shall not apply to any claim or proceeding pursuant to clause 4.1, and Sponsor shall not be liable:

(a) to the extent that said personal injury (including death) is caused by any of the Indemnitees’ failure to comply with this Agreement including but not limited to any failure of one or more of the Indemnitees to obtain the Clinical Trial Subject’s informed consent or other failure to conduct the Clinical Trial in accordance with the Protocol, applicable laws, regulations, ICH GCP, or the written instructions of Sponsor; or

(b) to the extent that said personal injury (including death) is caused by (medical or other) professional malpractice, negligence, recklessness or deliberate misconduct (in Dutch: beroepsfout, nalatigheid, roekeloosheid of opzettelijk handelen of nalaten) of any of the Indemnitees;

(c) unless as soon as reasonably practicable following receipt of notice of such claim or proceeding, Institution or Principal Investigator shall have notified Sponsor in writing of it and shall, upon Sponsor’s request and at Sponsor’s cost, have permitted Sponsor to have full care and control of the claim or proceeding using legal representation of its own choosing, and

(d) if any of the Indemnitees shall have made any admission in respect of such claim or proceeding or taken any action relating to such claim or proceeding prejudicial to the defence of it, without the written consent of Sponsor, such consent not to be unreasonably withheld, provided that this condition shall not be treated as breached by any statement properly made by any of the Indemnitees in connection with the operation of Institution’s internal complaint procedures, accident reporting procedures or disciplinary procedures or where such a statement is required by law.

4.3. Sponsor shall keep Institution reasonably informed of the progress of any such claim or proceeding. Sponsor will consult with Institution on the nature of any defence to be advanced.

4.4. Without prejudice to the provisions of clause 4.2 above, Institution and Principal Investigator each will use its reasonable endeavours to inform Sponsor promptly of any circumstances reasonably thought likely to give rise to any such claim or
proceeding of which it is directly aware and shall keep Sponsor reasonably informed of developments in relation to any such claim or proceeding even where one or more of the Indemnitees decides not to make a claim for indemnification under clause 4.1. Likewise, Sponsor shall use its reasonable endeavours to inform Institution of any circumstances and shall keep Institution reasonably informed of developments in relation to any such claim or proceeding made or brought against Sponsor alone.

4.5. Institution, Principal Investigator and Sponsor will each give to the other such help as may reasonably be required for the efficient conduct and prompt handling of any claim or proceeding made or brought by or on behalf of Clinical Trial Subjects (or their dependants).

4.6. Nothing in this clause 4 shall operate so as to restrict or exclude the liability of any Party vis-à-vis the Clinical Trial Subjects in relation to their death or personal injury caused by the negligence of that Party or its servants or employees or to restrict or exclude any other liability of either Party or the Principal Investigator which cannot be so restricted or excluded in law.

4.7. In no circumstances shall any Party be liable to the other in contract, tort or otherwise howsoever arising or whatever the cause thereof, for any indirect or consequential damages of any nature, such as but not limited to any loss of profit, business, goodwill, reputation, contracts, revenues or anticipated savings which arise directly or indirectly from any default on the part of Sponsor, Institution or the Principal Investigator, except and to the extent such damages (a) shall be covered under and paid out of any insurance policy of the liable party, or (b) result from negligence, recklessness or deliberate misconduct of the liable party or their employees, officers, Agents or other auxiliary persons (in Dutch: hulppersonen).

4.8. The liability of the Institution for a claim or proceeding of Sponsor under clause 4.7 shall be limited to the maximum amount covered under the insurance policy as generally applicable for such claim or proceeding or to euro one million (€1,000,000), whichever amount is the highest.

4.9. In the case of equipment loaned or otherwise made available by or on behalf of Sponsor to Institution for the purposes of the Clinical Trial, Institution’s liability for damages or loss of the equipment arising from its negligence or from negligence of its Agents or auxiliary persons shall exclude fair wear and tear and shall not exceed the value of the equipment.

4.10. Sponsor will take out or maintain (a) insurance cover in respect of its potential liability for damages to Clinical Trial Subjects resulting from the Clinical Trial in accordance with the requirements set out in the (Dutch) Medical Research Involving Human Subjects Act and the Decree on Obligatory Insurance for Medical Studies involving Human Subjects unless this requirement has been waived by the Ethics Committee, and (b) further appropriate insurance cover in respect of its other potential liability under this Agreement. Sponsor shall produce to Institution, on request, copies of such insurance certificates, together
with evidence that the policies to which they refer remain in full force and effect during the term of this Agreement and any period thereafter as may be required by mandatory law. The terms of any insurance or the amount of cover shall not relieve Sponsor of any liabilities under this Agreement.

4.11. Institution will take out or maintain an insurance cover in respect of the potential liability of Institution, members of the Research Staff (including the Principal Investigator) and any other employees involved with the conduct of the Clinical Trial pursuant to this Agreement. Institution shall produce to Sponsor, on request, copies of insurance certificates, together with evidence that the policies to which they refer remain in full force and effect during the term of this Agreement and any period thereafter as may be required by mandatory law. The terms of any insurance or the amount of cover shall not relieve Institution or the Principal Investigator of any liabilities under this Agreement.

5. **CLINICAL TRIAL SUBJECT RECRUITMENT AND ENROLLMENT**

5.1. Institution shall make sure or cause the Principal Investigator to make sure that in accordance with applicable legislation and the ICH GCP, the Clinical Trial Subjects and, if required by law, their legal representatives, prior to the Clinical Trial Subjects’ participation in the Clinical Trial (a) will be duly informed, in a language the Clinical Trial Subjects and their legal representatives can fully understand, on all aspects of the Clinical Trial which are required or deemed relevant in their decision to participate, and (b) each give their informed consent.

5.2. Institution shall use reasonable endeavours to recruit or cause the Principal Investigator to use reasonable endeavours to recruit the Target number of Clinical Trial Subjects in accordance with the Timelines, all as specified in Exhibit 1.

5.3. Furthermore, Sponsor may (1) advise a Rate of Clinical Trial Subjects by a designated time period (day, week or month), and/or (2) determine one or more Thresholds either up to or beyond the Target, each (1) and (2) to allow for and ensure the close monitoring of the progress of the Clinical Trial, the proper collection and recording of trial data, the welfare of the Clinical Trial Subjects, and altogether the good quality of the Clinical Trial and compliance with ICH GCP and applicable laws and regulations. The recruitment and inclusion of Clinical Trial Subjects by the Principal Investigator above and beyond the Target or Threshold(s), or any adjustment of the Target or Threshold(s), shall be subject to prior written approval of Sponsor. As soon as the Principal Investigator expects to reach a Target or Threshold, he/she shall notify Sponsor.

5.4. If circumstances or events have occurred or will occur that will substantially delay or that are likely to substantially delay the progress of recruitment or enrolment of the Clinical Trial Subjects, the Institution shall without any undue delay inform the Sponsor in writing. In each such event the Parties shall discuss the consequences of the delay and each Party shall undertake reasonable endeavours to agree on measures to overcome the delay or to agree such other
arrangements that the Parties and the Principal Investigator consider appropriate for the further implementation of the Clinical Trial.

5.5. If Institution has received from Sponsor all Investigational Product, means, information and Clinical Trial Authorisation necessary to perform the Clinical Trial and it has not recruited any Clinical Trial Subject within a reasonable period of time as mutually agreed by Parties in the Protocol or in other written documents, Sponsor is entitled to exclude the Trial Site from the Clinical Trial. Upon Sponsor’s decision to exclude the Trial Site, it shall notify Institution without delay.

5.6. In the event that the Clinical Trial is part of a multi-centre clinical trial (which for the purposes of this Agreement shall mean that at least one other institution is taking part) Sponsor may amend the number of Clinical Trial Subjects to be recruited pursuant to clause 5.2 above subject to the following, and always based on timely and adequate exchange of information:

(a) If in the reasonable opinion of Sponsor recruitment of Clinical Trial Subjects at Institution will not meet or will not likely meet the Target within the Timelines or is proceeding at a rate below that required to enable the relevant Timeline to be met, Sponsor may request Institution to increase the number and rate of Clinical Trial Subjects to be recruited and enrolled at the Trial Site. If Institution is unable to do so, Sponsor may (i) by notice to Institution require recruitment at the Trial Site to cease, or (ii) with the agreement of Institution decrease the number of Clinical Trial Subjects to be recruited at Institution subject to Clinical Trial Authorization;

(b) If recruitment of Clinical Trial Subjects is proceeding at a rate above that required to meet the relevant Timelines, Sponsor may, with the agreement of Institution, increase the number and the rate of Clinical Trial Subjects to be recruited and enrolled at the Trial Site; or

(c) If the overall recruitment target for all clinical centers that are part of the multi-centre clinical trial of Sponsor and its Affiliates has been reached, Sponsor may by notice to Institution require recruitment at the Trial Site to cease.

The Principal Investigator shall upon receipt of a notice to cease the recruitment immediately stop further recruitment and inclusion of Clinical Trial Subjects and the terms of the Agreement shall relate thereafter to the number of Clinical Trial Subjects who have been enrolled in the Clinical Trial at the date of such notice. Payments shall only be made according to the number of Clinical Trial Subjects recruited up to the date of receipt of the notice and include non-cancellable expenses reasonably and necessarily incurred by or on behalf of Institution to perform its duties under this Agreement. Sponsor acknowledges that Institution’s cancellation of anticipated inclusions of Clinical Trial Subjects should be avoided as much as possible. Sponsor will have no duty to make any payment for Clinical Trial Subjects recruited after the date of receipt of its notice.
6. QUALITY ASSURANCE AND CONTROL

6.1. Institution and Principal Investigator shall permit the Trial Monitor and any Auditor direct access to all relevant clinical data of Clinical Trial Subjects for monitoring and source data verification, such direct access to be arranged at mutually convenient times and on reasonable notice. Such monitoring may take such form as Sponsor reasonably thinks appropriate including the right to inspect any facility being used for the conduct of the Clinical Trial and to examine any procedures or records relating to the Clinical Trial. Sponsor will alert Institution promptly to significant issues relating to the conduct of the Clinical Trial.

6.2. Institution shall permit authorized representatives of the Ethics Committee and Competent Authority or any other regulatory authority access to, copy and verify information relating to the Clinical Trial, as required by applicable legislation or requested by Sponsor.

6.3. In the event that the Sponsor reasonably believes there has been any research misconduct in relation to the Clinical Trial, the Institution and the Principal Investigator shall provide all reasonable assistance to any investigation into any alleged research misconduct undertaken by or on behalf of the Sponsor, the results of which the Party on whose behalf the investigation was undertaken shall, subject to any obligations of confidentiality, communicate to the Institution. In the event that the Institution reasonably believes there has been any research misconduct in relation to the Clinical Trial, the Sponsor shall provide all reasonable assistance to any investigation undertaken by or on behalf of the Institution or Principal Investigator, the results of which shall, subject to any obligations of confidentiality, be communicated to the Sponsor.

6.4. The Institution shall promptly inform Sponsor of any intended or actual inspection, written enquiry and/or visit to the Trial Site by any regulatory authority in connection with the Clinical Trial and forward to Sponsor copies of any correspondence from any such regulatory authority relating to the Clinical Trial. Institution and Principal Investigator shall allow Sponsor representatives to be present during any such visit.

6.5. Institution will permit Sponsor to examine the conduct of the Clinical Trial and the Trial Site upon reasonable advance notice and in the company of an employee of Institution during regular business hours to determine that the Clinical Trial is being conducted in accordance with the Protocol, ICH GCP, the applicable regulatory requirements.

6.6. Institution shall inform or cause the Principal Investigator to inform Sponsor of any significant problem which might occur or be found during the course of the Clinical Trial and which might hinder or adversely affect the proper performance of the Clinical Trial. Institution shall immediately inform or cause the Principal Investigator to immediately inform Sponsor of any serious adverse event (“SAE”) in accordance with the (Dutch) Medical Research Involving Human
Subjects Act. Institution or the Principal Investigator shall report adverse events ("AE") to Sponsor in accordance with the procedures outlined in the Protocol.

6.7. Institution shall take such measures and actions as any regulatory authority or Sponsor may reasonably require for solving problems and issues reported by the Trial Monitors, the Auditor or any representative of the Ethics Committee, the Competent Authority or other regulatory authority in order to comply with the Protocol, ICH GCP, the applicable regulatory requirements.

6.8. Upon completion of the Clinical Trial (whether prematurely or otherwise) the Principal Investigator and Sponsor shall co-operate in producing a report of the Clinical Trial detailing the methodology, results and containing an analysis of the results and drawing appropriate conclusions.

6.9. It is expressly understood and accepted by Institution and the Principal Investigator that Sponsor will not separately compensate Institution or the Principal Investigator nor any member of the Research Staff for (a) the assistance or guidance of representatives of the Ethics Committee, Competent Authority or other regulatory authority and (b) the assistance or guidance of Trial Monitors or Sponsor’s auditors by Institution, Principal Investigator and the Research Staff. Compensation for such activities shall be deemed included in the remuneration to be paid pursuant to clause 13 hereinafter, unless expressly agreed otherwise in writing or laid down in Exhibit 2.

6.10. The Institution shall submit CRF or CRFs to the Sponsor, completed, fully and truly, by or on behalf of the Principal Investigator. The Sponsor may agree with the Institution to (a) train the Principal Investigator and selected members of the Research Staff to learn about the use of eCRFs and the duties relative to the eCRF process, and (b) make a computer and/or internet connection available to the Institution to enable the Research Staff to submit eCRFs for the Clinical Trial to the Sponsor.

6.11. The Institution shall ensure or cause the Principal Investigator to ensure that all procedures defined in the Protocol are complied with, that all data coming from the Trial Site are reliable and have been processed correctly (especially the randomization lists and the blind character of the Clinical Trial as the case may be) and that the content of CRFs or e-CRFs will accurately reflect source documents.

7. INVESTIGATIONAL PRODUCTS AND EQUIPMENT

7.1. Sponsor will provide Institution, Principal Investigator and Research Staff with a) all necessary information on the Investigational Product(s), quality and handling instructions thereof and b) sufficient quantities of the Investigational Product needed to conduct the Clinical Trial at no costs, including, unless otherwise agreed, placebo or comparator if required by the Protocol.

7.2. Neither Institution nor the Principal Investigator shall permit the Investigational Product to be used for any purpose other than the conduct of the Clinical Trial.
and upon termination or expiration of this Agreement all unused Investigational Product shall, at Sponsor’s option, either be returned to Sponsor or disposed of in accordance with the Protocol or Sponsor’s written instructions.

7.3. Any equipment provided by Sponsor to Institution or the Principal Investigator for the conduct of the Clinical Trial at the Trial Site will remain the property of Sponsor, and, unless otherwise agreed, may be used at the Trial Site for purposes of the Clinical Trial only. Such equipment shall promptly be returned by the Principal Investigator or, as the case may be, Institution upon the earlier of (a) the date agreed between the Parties, (b) the date of expiry or termination of this Agreement, or (c) the date requested by Sponsor.

8. CONFIDENTIALITY

8.1 The Parties and the Principal Investigator agree to adhere to the principles of medical confidentiality in relation to Clinical Trial Subjects involved in the Clinical Trial. Personal Data (as defined in the Dutch Personal Data Protection Act) shall not be disclosed to Sponsor by Institution or Principal Investigator unless this is required to satisfy the requirements of the Protocol or for the purpose of monitoring or adverse event reporting, or in relation to a claim or proceeding brought by the Clinical Trial Subject in connection with the Clinical Trial. The Parties and the Principal Investigator shall not disclose the identity of Clinical Trial Subjects to third parties without prior written consent of the Clinical Trial Subject, except in accordance with the provisions of the Personal Data Protection Act, as appropriated with respect to the handling of a claim or proceeding brought by the Clinical Trial Subject in connection with the Clinical Trial.

8.2 Institution and Sponsor shall ensure that only those of its officers, Agents and employees (and those of its Affiliates) directly concerned with the carrying out of this Agreement (the “Recipients”) have access to the Confidential Information of the other Party and that any third party Recipients shall be bound by confidentiality and user undertakings and limitations substantially similar and no less stringent than those provided for in this Agreement. Each Party and the Principal Investigator undertakes to treat as strictly confidential and not to disclose to any third party any Confidential Information of the other Party (the “Disclosing Party”) or the terms and conditions of this Agreement, except where disclosure is (a) required by the Competent Authority, the appropriate Ethics Committee or other regulatory authority or by law or to comply with ICH GCP, or (b) permitted under article 8.3 and article 10.2, or (c) made to any third party Recipients, or (d) expressly agreed to in writing by the Disclosing Party. The Party or the Principal Investigator required to make the disclosure shall inform the other(s) within a reasonable time prior to being required to make the disclosure, of the requirement to disclose and the information required to be disclosed. Each Party and the Principal Investigator undertakes not to make use
of any Confidential Information of the Disclosing Party, other than in accordance with and as permitted under this Agreement or as and when approved in writing by the Disclosing Party.

8.3 The obligations of confidentiality set out in clause 8 shall not apply to information which:

a. is or becomes part of the public domain by any other means than a wrongful act or breach of this Agreement by the Parties;
b. was or becomes in the receiving Party’s possession prior to its receipt from the Disclosing Party, as evidenced by contemporaneous written evidence, and is not subject to a duty of confidentiality;
c. has been independently developed by the receiving Party without the use of Confidential Information of the other Party and is not subject to a duty of confidentiality;
d. has been obtained by the receiving Party from a third party who is not subject to a duty of confidentiality.

9. INTELLECTUAL PROPERTY

9.1. All Intellectual Property Rights and Know How owned by or licensed to any of the Parties prior to and after the date of this Agreement other than any Intellectual Property Rights and Know How arising from the Clinical Trial are and shall remain the property of that Party or its licensor.

9.2. All Intellectual Property Rights and Know How arising from and relating to the Clinical Trial, the Investigational Product (including but not limited to its formulation and use alone or in combination with other drugs) or the Protocol, shall vest in the Sponsor in accordance with clause 9.3 and 9.4, except for (1) any Know How concerning clinical procedure and improvements thereto that are clinical procedures of the Institution, which Know How shall vest in the Institution, and (2) copyrights on work published by the Principal Investigator in accordance with clause 11 hereinafter, which copyrights shall either vest in the Institution or, if made by the Principal Investigator and other authors, in the Institution and the other co-author(s) in accordance with applicable copyright laws or as mutually agreed between the Parties, or shall vest in the publisher of such work upon the transfer of copyrights by the author(s). Notwithstanding the previous sentence the Parties shall consult each other in case of doubt that the Intellectual Property Rights and/or Know How arise from and/or relate to the Clinical Trial, the Investigational Product (including but not limited to its formulation and use alone or in combination with other drugs) or the Protocol and reach agreement on the subject matter.

9.3. In accordance with clause 9.2 above, the Institution hereby assigns, and shall procure that the Research Staff members and the Principal investigator assign, its/their rights in relation to all Intellectual Property Rights and in all Know How, falling within clause 9.2 above, to the Sponsor and at the request and expense of
the Sponsor, the Institution shall execute, and shall procure that its Research Staff members and the Principal investigator execute, all such documents and do all such other acts as the Sponsor may reasonably require in order to vest, maintain and defend fully and effectively all such Intellectual Property Rights and Know How in the Sponsor or its nominee.

9.4. The Institution and the Principal Investigator shall promptly disclose to the Sponsor any Know How generated to this Agreement and falling within clause 9.2 above and undertake not to disclose such Know How other than for the purpose of this Agreement.

9.5. Nothing in this clause 9 shall be construed so as to prevent or hinder the Institution from using Know How gained during the performance of the Clinical Trial in the furtherance of its normal hospital and (non-commercial) research activities, to the extent such use does not result in the disclosure or misuse of Confidential Information or the infringement of any Intellectual Property Rights of the Sponsor.

9.6 In case a third party brings a claim or initiate proceedings against the Institution for the use of Intellectual Property of Sponsor in conducting the Clinical Trial, Sponsor shall indemnify Institution against such claims or proceedings, provided the Institution shall have notified Sponsor promptly in writing of it and shall, upon Sponsor’s request and at Sponsor’s costs, have permitted Sponsor to have full care and control over the claim or proceeding using legal representation of its own choosing.

10. PUBLICITY

10.1 Sponsor will not use the logo or name of Institution, nor of any member of Institution's Research Staff, for promotional purposes, in any publicity, advertising or news release without the prior written approval of an authorised representative of Institution, such approval not to be unreasonably withheld. Institution will not, and will ensure that the Principal Investigator and Research Staff will not, use the name or logo of Sponsor or of any of its employees, nor the name of the Clinical Trial, nor the name of the Investigational Product, in any publicity, advertising or news release without the prior written approval of Sponsor, such approval not to be unreasonably withheld.

10.2 Except and to the extent the disclosure of information is permitted in accordance with clause 8.2, or is required by the Competent Authority or any other regulatory authority pursuant to mandatory law, neither the Institution nor the Principal Investigator will issue any information or statement to the press or public, including but not limited to advertisements for the enrolment of Clinical Trial Subjects, without, where appropriate, its review and the delivery of the opinion or, where required, an approval by the Ethics Committee and the prior written permission of Sponsor.
11. PUBLICATION

11.1 Sponsor, Institution and the Principal Investigator each acknowledge the importance of public disclosure of information collected or generated as a result of or related to the Clinical Trial, subject to the provisions of this clause 11.

11.2 Sponsor agrees, that the Principal Investigator alone or jointly with members of the Research Staff present at symposia, national or regional professional meetings, and to publish in journals, theses or dissertations, or otherwise of their own choosing, methods and results of the Clinical Trial, subject to this clause 11 and any publication policy described in the Protocol, to the extent such policy does not obstruct or restrict said publication or presentation unreasonably. If it is a multi-centre Clinical Trial (as defined in clause 5.6), any publication based on the results obtained at the Trail Site (or a group of sites) shall not be made before the first multi-centre publication or presentation unless otherwise agreed in writing. If a publication concerns the analysis of subsets of data from a multi-centred Clinical Trial, the publication or presentation shall make reference to the relevant multi-centre publication(s) or presentation(s).

11.3 Upon completion of the Clinical Trial, and any prior publication of multi-centre data, or when the Clinical Trial data are adequate (in Sponsor's reasonable judgement), the Institution and/or the Principal Investigator may prepare the data derived from the Clinical Trial for publication or presentation. In order to ensure that the Sponsor will be able to make comments and suggestions where pertinent and for the Sponsor to determine whether or not its Confidential Information or Know How will be permitted in the proposed publication or presentation, material for public dissemination will be submitted to the Sponsor for review at least ninety (90) days prior to any presentation, submission for publication, public dissemination, or review by a publication committee. Within forty-five (45) days following receipt the Sponsor shall make its comments and suggestions to the Institution and/or the Principal Investigator.

11.4 If a multi-centre publication is not published within 12 months after completion of the Clinical Trial and lock of the database at all research sites that are part of a multi-centre clinical trial (as referred to in clause 5.2) or any earlier termination or abandonment of the Clinical Trial, or if Sponsor informs the Principal Investigator that no multi-centre publication shall take place – whichever is the first -, Institution and the Principal Investigator shall have the right to publish or present the Results of Institution’s and Principal Investigator’s activities conducted under this Agreement, including Clinical Trial data, independently and solely in accordance with the provisions of this clause 11.

11.6 The Institution and the Principal Investigator agree that all reasonable comments made by the Sponsor in relation to a proposed publication or presentation will be incorporated or appropriately reflected into respectively the publication or presentation. Reasonable comments for the purposes of this clause 11 shall mean such comments and suggestions that, with a view to the scientific interest or the
treatment of patients, will clarify or improve the proposed publication or presentation of the results of the Clinical Trial or the conclusions drawn from such results, and such other comments that aim to avoid that such publication or presentation will misrepresent the results.

11.7 The Institution and the Principal Investigator each acknowledge that the Sponsor may present at symposia, national or regional professional meetings, and publish in journals, theses or dissertations, or otherwise of their own choosing, methods and results of the Clinical Trial and in particular, but without limiting the foregoing, post a summary of Clinical Trial results in on-line clinical trials register(s) before or after publication by any other method. In the event the Sponsor coordinates a multi-centre publication, the participation of the Principal Investigator or other representatives of the Institution as a named author shall be determined in accordance with generally accepted academic standards for authorship. If the Principal Investigator or other representative of the Institution is a named author of the multi-centre publication, such person shall have access to the Clinical Trial data from all Clinical Trial sites as necessary to participate fully in the development of the multi-centre publication.

11.8 During the period for review of a proposed publication or presentation referred to in clause 11.3 above, the Sponsor shall be entitled to make a reasoned request to the Institution and Principal Investigator that publication or presentation be delayed for a period of up to 90 days from the date of first submission to the Sponsor in order to enable the Sponsor to take steps to protect its Confidential Information and/or Intellectual Property Rights and Know How and the Institution and Principal Investigator shall not unreasonably withhold its consent to such a request. The Institution shall not unreasonably withhold or delay its consent to the reasoned request from the Sponsor in case of exceptional circumstances such as the Sponsor’s Confidential Information and/or Intellectual Property Rights and Know How might otherwise be compromised or lost.

12 TERM AND TERMINATION

12.1 This Agreement commences on the Effective Date and shall continue in force until the earlier of:
   a. completion of the Clinical Trial, close-out of the Trial Site and completion of the obligations of the Parties under this Agreement; or
   b. early termination in accordance with clauses 12.2, 12.3 or 12.5 of this Agreement;

12.2 Each Party may terminate this Agreement upon written notice to the other Parties with immediate effect in the following events:
   a. if the approval by the Ethics Committee in charge of the Clinical Trial is irrevocably revoked;
   b. if it can be reasonably assumed that the Clinical Trial must be terminated in the interests of the health of the Clinical Trial Subjects;
c. If it becomes apparent, following confirmation of the Ethics Committee or the DSMB, that continuation of the Clinical Trial cannot serve a scientific purpose, and this is notified to the Ethics Committee;
d. if the Sponsor and/or the Institution become or are declared insolvent or a petition in bankruptcy has been filed against it or if one of them is dissolved;
e. if circumstances beyond a Party’s control occur that render continuation of the Clinical Trial unreasonable;
f. if one of the parties fails to comply with the obligations arising from the Agreement and, if capable of remedy, is not remedied within 30 days after receipt of notice from the other Party specifying the non compliance and requiring its remedy, unless failure to comply is not in reasonable proportion to the premature termination of the Clinical Trial.

12.3 Either Party may terminate this Agreement if the Principal Investigator is no longer able (for whatever reason) to act as Principal Investigator and no mutually acceptable replacement has been found in accordance with clause 2.3.

12.4 In all circumstances causing the early termination of this Agreement pursuant to clauses 12.2 or 12.3 above, the Sponsor shall confer with the Principal Investigator and use their best endeavours to minimise any inconvenience or harm to Clinical Trial Subjects caused by the premature termination of the Clinical Trial.

12.5 Sponsor may terminate this Agreement upon written notification to the Principal Investigator and the Institution, with immediate effect, in the following events:
   a. for lack of recruitment at the Trial Site in case the Clinical Trial is conducted at one Site only; or
   b. in case of a multicentre trial, if termination at the Trial Site does not affect performance of the Protocol.

The foregoing provided however, that this clause 12.5 shall not apply and Sponsor shall have no right to terminate this Agreement if any Clinical Trial Subject has undergone treatments or conduct has been imposed on the Clinical Trial Subject as per the Protocol, at the Trial Site.

12.6 If the Agreement is terminated for one of the reasons in clauses, 12.2, 12.3 or 12.5, except for material breach by the Institution and/or the Principal Investigator under clause 12.2 (f), and subject to an obligation on the Institution and the Principal Investigator to mitigate any loss, the Sponsor shall pay all fees and expenditures falling due for payment by the Institution up to the date of termination, and also all expenditure falling due for payment after the date of termination which arises from commitments reasonably and necessarily incurred by the Institution for the performance of the Clinical Trial prior to the date of termination, and agreed with the Sponsor and which cannot be cancelled.

12.7 In the event of early termination if payment (whether for salaries or otherwise) has been made by the Sponsor to the Institution in advance for work not completed, such monies shall be applied to termination related costs and the Institution shall issue a credit note and repay the remainder of the monies within 45 days of receipt of written notice from the Sponsor.
12.8 At close-out of the Trial Site following termination or expiration of this Agreement the Principal Investigator and the Institution shall immediately deliver to the Sponsor all Confidential Information and any equipment provided to the Institution and/or the Principal Investigator pursuant to this Agreement, except for copies to be retained in order to comply with Institution’s archiving obligations or for evidential purposes.

12.9 Termination of this Agreement will be without prejudice to the accrued rights and liabilities of the Parties under this Agreement.

13 FINANCIAL PROVISIONS

13.1 Arrangements relating to the financing of this Clinical Trial by Sponsor are set out in Exhibit 2.

13.2 In the event that amendments to the Protocol require changes to the Clinical Trial financing arrangements, an amended financial schedule will be agreed upon and signed by the Parties and attached as a supplement at Exhibit 2 of this Agreement.

13.3 All payments will be made according to the schedule and conditions contained in Exhibit 2.

13.4 If the Agreement is terminated prematurely, Sponsor shall pay all costs, including non-cancellable costs, incurred and falling due for payment by Institution up to the date of termination, and also all expenditure falling due for payment after the date of termination which arises from commitments reasonably and necessarily incurred by the Institution for the performance of the Clinical Trial. For the avoidance of doubt; it is understood by the Parties, that the full costs of staff which was hired and/or employed by Institution for the performance of the Clinical Trial, are non-cancellable commitments of Institution. Institution will do it’s utmost best to limit the costs as meant above.

13.5 Sponsor shall make payment within 45 days of receipt of an invoice from Institution or Principal Investigator, supplemented by, when applicable, the rate of VAT in effect on the date of the invoice. Any delay in the payment of the payee invoices by Sponsor will incur an interest charge on any amounts overdue of one (1) per cent per month above the monthly Euro Inter Bank Offered Rate (Euribor) rate prevailing on the date the payment is due.

13.6 For the avoidance of doubt, the sums paid under Exhibit 2 of the Agreement to Institution shall be an all-inclusive remuneration for the performance of the Clinical Trial carried out at the Trial Site, to the exclusion of any other payment by Sponsor to Institution or to any person hired or engaged by Institution or the Principal Investigator such as but not limited to sub-investigators, hospital pharmacists, clinical chemists, other Research Staff or third parties unless expressly agreed otherwise in writing. Institution shall arrange and pay for all necessary laboratory and other facilities, equipment, supplies (other than the Investigational Product), and physicians and clinical support staff required to comply with its obligations with
respect to the Clinical Trial unless expressly agreed otherwise in writing between Sponsor and Institution.

13.7 Should this Agreement be terminated prior to the actual start of the Clinical Trial, Sponsor shall owe and pay Institution the set-up costs to the extent the Institution is obliged to pay such costs for the preparation of the Clinical Trial, as defined in Exhibit 2.

14 MISCONDUCT AND DEBARMENT

14.1 Institution certifies to Sponsor, and Principal Investigator certifies to Institution, that it has never been and, to the best of its knowledge after reasonable inquiry, any other member of the Research Staff or any other individual who will be involved in conducting the Clinical Trial has never been (i) involved in any regulatory or misconduct litigation or investigation by the Competent Authority, the European Medicines Agency, the (US) Food and Drug Administration or other regulatory authorities, or (ii) debarred, excluded, disqualified or restricted in their ability to practice medicine, to participate in a clinical trial or to perform services in connection with the evaluation of a pharmaceutical product under any laws, regulations or professional code of conduct.

14.2 Institution and the Principal Investigator shall immediately notify Sponsor in the event of any such debarment, exclusion, disqualification or restriction, or should litigation or investigation be initiated against any of them that could result in their being debarred, excluded, disqualified or restricted, at any time during the term of this Agreement and during the twelve months following the expiry or termination of the Agreement.

15 DISCLOSURE OF FINANCIAL INTEREST

15.1 Institution shall make any necessary disclosures of financial interests and arrangements and cause the Principal Investigator to make any necessary disclosures of financial interests and arrangements as required by regulations and for the purposes of these obligations Sponsor shall advise the Principal Investigator and Institution in writing of the completion date of the Clinical Trial.

15.2 The Institution shall ensure that Principal Investigator, the Research Staff and collaborators involved in the Clinical Trial at the Trial Site provide Sponsor with the appropriate financial disclosures required by the U.S. Food and Drug Administration for compliance with CFR title 21 part 54 (Financial disclosures by clinical investigators) on such forms as Sponsor may supply or approve. During the term of this Agreement and for one (1) year following termination or completion of the Clinical Trial, Principal Investigator shall promptly notify Sponsor of any material change in the information disclosed on any previous form.
16 FORCMAJEURE

16.1 Neither Party shall be liable to the other Party or shall be in default of its obligations hereunder if such default is the result of war, hostilities, terrorist activity, revolution, civil commotion, strike, excluded strikes within the company of Parties, and epidemic or because of any other cause beyond the reasonable control of the Party affected. The Party affected by such circumstances shall promptly notify the other Party in writing when such circumstances cause a delay or failure in performance ("a Delay") and where they cease to do so.

16.2 In the event of a Delay lasting for 8 weeks, or such other period that would reasonably be required to safeguard the wellbeing and safety of the Clinical trial Subject, the non-affected Party shall have the right to terminate this Agreement immediately by notice in writing to the other Party.

17 GOVERNING LAW AND DISPUTE RESOLUTION

The Agreement shall be governed by, and construed in all respects in accordance with the laws of The Netherlands without regard to its conflict of laws rules. Any claims, controversies or disputes arising out of or in connection with the Agreement which cannot be settled amicably between the Parties, shall be subject to the exclusive jurisdiction of the competent court of [insert city where court is located].

18 MISCELLANEOUS

18.1 Sponsor shall have the right to assign this Agreement to an Affiliate upon prior written notice to Institution. Institution shall have the right to assign this Agreement to an Affiliate upon prior written notice to Sponsor. In all other circumstances, neither Party shall assign its rights or duties under this Agreement to another party without prior written consent of the other Party. Any approval by a Party of an assignment, transfer or encumbrance by the other Party shall not release the assigning Party of any of its obligations under this Agreement due up until such assignment. Subject to the foregoing, this Agreement shall bind and inure to the benefit of the respective Parties and their successors and assignees.

18.2 Neither Party may sub-contract the performance of all or any of its obligations under this Agreement without the prior written consent of the other Party, such consent not to be unreasonably withheld or delayed. Any party who so sub-contracts shall be responsible for the acts and omissions of its sub-contractors as though they were its own.

18.3 Nothing shall be construed as creating a joint venture, partnership or contract of employment between the Parties.
18.4 Any agreement to amend, vary or modify the terms of the Agreement in any manner shall be valid only if effected in writing and signed by duly authorized representatives of each of the Parties hereto.

18.5 If any term or provision or any part thereof contained in the Agreement shall be declared or become unenforceable, invalid or illegal in any respect, under the law of any relevant jurisdiction, such term or provision or part thereof shall be deemed to have been severed from the remaining terms of the Agreement and the terms and conditions hereof shall remain in full force and effect as if the Agreement had been executed without the offending provision appearing.

18.6 Should there be any inconsistency between the Protocol and the terms of this Agreement, or any other document incorporated therein, the Protocol shall prevail in case such inconsistency concerns clinical matters and the Agreement shall prevail the inconsistency concerns non-clinical matters.

18.7 The clauses 3.4 to 3.8 (inclusive), 4, 6, 10, 11, 12, 13, 14, 15, 16, 17, and 18 shall survive the termination or expiry of this Agreement. The provision of clause 8 remain in force for a period of 5 years after the termination or expiry of the Agreement.

[This part of page is intentionally left blank; for signatures, see next page]
Signed on behalf of Sponsor

Signature: ......................................................
Name: .................................
Title: .................................
Date: .................................

Signed on behalf of Institution

Signature: ......................................................
Name: .................................
Title: .................................
Date: .................................

The undersigned Principal Investigator hereby declares that he/she has read the above Agreement between the Parties and that he/she agrees with the provisions of the Agreement relative to his/her role, responsibilities and duties concerning the Clinical Trial:

Signed by the Principal Investigator

Signature: ......................................................
Name: .................................
Title: .................................
Date: .................................

APPENDICES:

Exhibit 1: Timelines
Exhibit 2: Financial arrangements
EXHIBIT 1

TIMELINES

Reference: clause 5.

*[Sample; modify as appropriate]*

<table>
<thead>
<tr>
<th>Milestone</th>
<th>Sponsor responsibility</th>
<th>Site responsibility</th>
<th>Target Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>[Provision of materials for Ethics Committee submission]</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>[Ethics Committee submission]</td>
<td>[X]</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Trial Site initiation visit</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>First Clinical Trial Subject recruited</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Last Clinical Trial Subject recruited</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>All (e)CRF queries submitted</td>
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<td></td>
</tr>
<tr>
<td>All (e)CRF queries completed</td>
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<td></td>
</tr>
</tbody>
</table>

Duration of the Clinical Trial:
*The Parties estimate that the whole Clinical Trial will be completed approximately by: [insert date]*

Target:
*Clinical Trial Subjects’ Target is: [insert number]*

Rate (if any):
*Clinical Trial Subjects to be included per [insert day/ week/month/ year] is: [insert number].*

Threshold(s) (if any):
*In accordance with clause 5.3 Sponsor may (pre-) determine one Threshold or more Thresholds, each within a defined period of time. Sponsor allows Institution to include: [insert number] Clinical Trial Subjects as a maximum number of Clinical Trial Subjects to be enrolled within [insert Timeline(s)].*
EXHIBIT 2
FINANCIAL ARRANGEMENTS


Schedule of payments:

[Sample; modify as appropriate]

[Insert details of financial arrangements e.g.
(B) investigator standard fees;
(C) special fees like fees for review by the Ethics Committee, Institution’s handling or administrative fees, fees for (start-up) investigator meetings, home care visits, consulting by telephone, pharmacy fees and expenses;
(D) reimbursement of trial subjects’ travel expenses, reimbursement of (pre-agreed) expenses made by the Investigator and the Research staff;
(E) invoicing and bank account details;
(F) conditions to (final) payment, if any, like the accurate and complete delivery of queries, CRFs, DRFs and final trial data, satisfactory compliance with trial data retention requirements and return of remaining Investigational Product]

Final invoice:
Sponsor shall promptly respond to any reasonable request for invoicing data received from Institution within 45 days of the close-out of the Trial Site. Institution will send its final invoice, (or, as the case may be, issue a credit note and make repayment of any monies previously paid for work not completed), to Sponsor as soon as possible and, in any event, within 45 days of receipt of the said data where such a request has been made, or within 45 days of study close-out in all other circumstances unless there is a written agreement between Institution and Sponsor to extend these periods.