SUBSIDIARY LEGISLATION 458.43

CLINICAL TRIALS REGULATIONS

26th November, 2004

LEGAL NOTICE 490 of 2004, as amended by Legal Notice 248 of 2007.

Citation.

1. The title of these regulations is the Clinical Trials Regulations.

Scope.

Cap. 458.

2. (1) These regulations apply Directive 2001/20/EC and shall regulate the conduct of clinical trials, including multi-centre trials, in Malta on human subjects involving medicinal products as defined under the Medicines Act and in particular relating to the implementation of good clinical practice. These regulations shall not apply to non-interventional trials.

(2) All clinical trials including bioavailability and bioequivalence studies shall be designed, conducted and reported in accordance with the principles of good clinical practice. The various aspects associated with submissions including notifications and requests to the Licensing Authority and the Ethics Committee and any other procedures and requirements related to clinical trials as deemed necessary by the Licensing Authority, shall be in accordance with the publications related to clinical trials published and, or adopted periodically by the Commission as deemed necessary by the Licensing Authority.

Definitions.

3. In these regulations, unless the context otherwise requires -

"adverse event" means any untoward medical occurrence in a patient or clinical trial subject who is administered a medicinal product and which does not necessarily have a causal relationship with this treatment;

"adverse reaction" means all untoward and unintended responses to an investigational medicinal product related to any dose administered;

"Agency" means the European Medicines Agency established by Council Regulation (EC) No 726/2004;

"clinical trial" means any investigation in human subjects intended to discover or verify the clinical, pharmacological and, or other pharmacodynamic effects of any investigational medicinal product and, or to identify any adverse reactions to any investigational medicinal product and, or to study absorption, distribution, metabolism and excretion of any investigational medicinal product with the object of ascertaining its safety and, or efficacy. This includes clinical trials carried out in either one site or multiple sites, whether in one or more than one Member State;

"the Ethics Committee" means an independent body, consisting of healthcare professionals and non-medical members, whose responsibility is to protect the rights, safety and well-being of human subjects involved in a trial and to provide public assurance

of that protection, by, among other things, expressing an opinion on the trial protocol, the suitability of the investigators and the adequacy of facilities, and on the methods and documents to be used to recruit and inform trial subjects and obtain their informed consent;

"good clinical practice" means a set of internationally recognized ethical and scientific quality requirements which must be observed for designing, conducting, recording and reporting clinical trials that involve the participation of human subjects. Compliance with this good practice provides assurance that the rights, safety and well being of trial subjects are protected and that the results of the clinical trials are credible;

"informed consent" means a decision, which must be written in one of the official languages of Malta or in a language understandable to the clinical trial subject and, or his legal representative, dated and signed, to take part in a clinical trial, taken freely after being duly informed of its nature, significance, implications and risks and appropriately documented, by any person capable of giving consent or, where the person is not capable of giving consent, by his or her legal representative[if such person is unable to write, oral consent may be given in the presence of at least one witness;

"inspection" means the act by the Licensing Authority of conducting an official review of documents, facilities, records, quality assurance arrangements, and any other resources deemed to be related to the clinical trial and that may be located at the site of the trial, at the sponsor's and, or contract research organisation's facilities, or at other establishments which the Licensing Authority sees fit to inspect;

"investigational medicinal product" means a pharmaceutical form of an active substance or placebo being tested or used as a reference in a clinical trial, including products already with a marketing authorisation but used or assembled (formulated or packaged) in a way different from the authorised form, or when used for an unauthorised indication, or when used to gain further information about the authorised form;

"investigator" means a doctor or a person who is suitably qualified approved by the Licensing Authority for investigations because of the scientific background and the experience in patient care such investigation requires. The investigator is responsible for the conduct of a clinical trial at a trial site. If a trial is conducted by a team of individuals at a trial site, the investigator is the leader responsible for the team and may be called the principal investigator;

"investigator's brochure" means a compilation of the clinical and non-clinical data on the investigational medicinal product or products which are relevant to the study of the product or products in human subjects;

"multi-centre clinical trial" means a clinical trial conducted according to a single protocol but at more than one site, and therefore by more than one investigator, in which the trial sites may

be located in a single Member State, in a number of Member States and, or in Member States and third countries;

"non-interventional trial" means a study where a medicinal product is, prescribed in the usual manner in accordance with the terms of the marketing authorisation. The assignment of the patient to a particular therapeutic strategy is not decided in advance by a trial protocol but falls within current practice and the prescription of the medicine is clearly separated from the decision to include the patient in the study. No additional diagnostic or monitoring procedures shall be applied to the patients and epidemiological methods shall be used for the analysis of collected data;

"protocol" means a document that describes the objective or objectives, design, methodology, statistical considerations and organisation of a trial. The term protocol refers to the protocol, successive versions of the protocol and protocol amendments;

"serious adverse" event or "serious adverse reaction" means any untoward medical occurrence or effect where any dose results in death, is life-threatening, requires hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability or incapacity, or is a congenital anomaly or birth defect;

"sponsor" means an individual, company, institution or organisation or its legal representative who must be established in the Community and who takes responsibility for the initiation, management and, or financing of a clinical trial;

"subject" means an individual who participates in a clinical trial as either a recipient of the investigational medicinal product or a control;

"unexpected adverse reaction" means an adverse reaction, the nature or severity of which is not consistent with the relevant product information (e.g. investigator's brochure for an unauthorised investigational product or summary of product characteristics for an authorised product).

Protection of clinical trial subjects.

4. (1) A clinical trial may be undertaken only if, in particular -

(*a*) the foreseeable risks and inconveniences have been weighed against the anticipated benefit for the individual trial subject and other present and future patients. A clinical trial may be initiated only if the Ethics Committee and, or the Licensing Authority comes to the conclusion that the anticipated therapeutic and public health benefits justify the risks and may be continued only if compliance with this requirement is permanently and continuously monitored;

(*b*) the trial subject or, when the person is not able to give informed consent, his legal representative, has had the opportunity, in a prior interview with the investigator or a member of the investigating team, to understand the objectives, risks and inconveniences of the trial, and the conditions under which it is to be conducted

and has also been informed of his right to withdraw from the trial at any time by revoking his informed consent without suffering any detriment;

(*c*) the rights of the subject to physical and mental integrity, to privacy and to the protection of the data concerning him in accordance with the Data Protection Act and any amendments thereto, are safeguarded;

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(*d*) the trial subject or, when the person is not able to give informed consent, his legal representative has given his written consent after being informed of the nature, significance, implications and risks of the clinical trial. However if the individual is unable to write, oral consent may be given in the presence of at least one witness;

(*e*) provision has been made for insurance or indemnity to cover the liability of the investigator and sponsor.

(2) It shall be the responsibility of an appropriately named qualified doctor or, where appropriate, of a named qualified dentist or other named person with appropriate qualifications as the case may be, to provide at all times the necessary medical care and make medical decisions on behalf of the subjects.

(3) The subject shall be provided with a contact point where he may obtain further information.

Clinical trials on minors.

5. Without prejudice to any other relevant restriction, a clinical trial on minors may only be undertaken if -

(*a*) the informed consent of the parents or legal representative has been obtained; consent must represent the minor's presumed will and may be revoked at any time, without detriment to the minor;

(*b*) the minor has received information according to his capacity of understanding, from staff with experience with minors, regarding the trial, the risks and the benefits;

(*c*) the explicit wish of a minor who is capable of forming an opinion and assessing this information to refuse participation or to be withdrawn from the clinical trial at any time is given due consideration by the investigator or, where appropriate, the principal investigator;

(*d*) no incentives or financial inducements are given except agreed compensation;

(*e*) some direct benefit for the group of patients is expected from the clinical trial and only where such research is essential to validate data obtained in clinical trials on persons able to give informed consent or by other research methods; additionally, such research should either relate directly to a clinical condition from which the minor concerned suffers or be of such a nature that it can only be carried out on

minors;

(*f*) the corresponding scientific guidelines of the Agency have been followed;

(*g*) clinical trials have been designed to minimise pain, discomfort, fear and any other foreseeable risk in relation to the disease and developmental stage[both the risk threshold and the degree of distress have to be specially defined and constantly monitored;

(*h*) the Ethics Committee, with pediatric expertise or after taking advice in clinical, ethical and psychosocial problems in the field of pediatrics, has endorsed the protocol; and

(*i*) the interests of the patient always prevail over those of science and society.

Clinical trials on incapacitated adults not able to give informed legal consent.

6. (1) For the performance of clinical trials on persons incapable of giving informed legal consent, all relevant requirements listed for persons capable of giving such consent shall also apply. Furthermore, clinical trials on incapacitated adults who have not given and not refused informed consent before the onset of their incapacity, shall only be allowed if:

(*a*) the informed consent of the legal representative has been obtained; consent must represent the subject's presumed will and may be revoked at any time, without detriment to the subject;

(*b*) the person not able to give informed legal consent has received information according to his capacity of understanding regarding the trial, the risks and the benefits;

(*c*) the explicit wish of a subject who is capable of forming an opinion and assessing this information to refuse participation in, or to be withdrawn from, the clinical trial at any time is given due consideration by the investigator or where appropriate the principal investigator;

(*d*) no incentives or financial inducements are given except agreed compensation;

(*e*) such research is essential to validate data obtained in clinical trials on persons able to give informed consent or by other research methods and relates directly to a life-threatening or debilitating clinical condition from which the incapacitated adult concerned suffers;

(*f*) clinical trials have been designed to minimise pain, discomfort, fear and any other foreseeable risk in relation to the disease and developmental stage; both the risk threshold and the degree of distress shall be specially defined and constantly monitored;

(*g*) the Ethics Committee, with expertise in the relevant disease and the patient population concerned or after taking advice in clinical, ethical and psychosocial

questions in the field of the relevant disease and patient population concerned, has endorsed the protocol;

(*h*) the interests of the patient always prevail over those of science and society; and

(*i*) there are grounds for expecting that administering the medicinal product to be tested will benefit the patient outweighing the risks or produce no risk at all.

Ethics Committee.

7. (1) The Licensing Authority shall set up an Ethics Committee which shall give its opinion, before a clinical trial commences, on any issue requested.

(2) In preparing its opinion, the Ethics Committee shall consider, in particular -

(*a*) the relevance of the clinical trial and the trial design;

(*b*) whether the evaluation of the anticipated benefits and risks as required under regulation 4(1)(*a*) is satisfactory and whether the conclusions are justified;

(*c*) the protocol;

(*d*) the suitability of the investigator and supporting staff;

(*e*) the investigator's brochure;

(*f*) the quality of the facilities;

(*g*) the adequacy and completeness of the written information to be given and the procedure to be followed for the purpose of obtaining informed consent and the justification for the research on persons incapable of giving informed consent as regards the specific restrictions laid down in regulation 4;

(*h*) provision for indemnity or compensation in the event of injury or death attributable to a clinical trial;

(*i*) any insurance or indemnity to cover the liability of the investigator and sponsor;

(*j*) the amounts and, where appropriate, the arrangements for justly rewarding investigators and compensating trial subjects and the relevant aspects of any agreement between the sponsor and the site;

(*k*) the arrangements for the recruitment of subjects.

(3) (*a*) The Ethics Committee shall within a maximum of sixty days from the date of receipt of a valid application give its reasoned opinion to the applicant and the Licensing Authority.

(*b*) Within the period of examination of the application for an opinion, the Ethics Committee may send a single request for information supplementary to that already supplied by the applicant. The period mentioned in paragraph (*a*) shall be suspended until receipt of the supplementary information.

(4) No extension to the sixty-day period referred to in subregulation (3) shall be permissible except in the case of trials involving medicinal products for gene therapy or somatic cell therapy or medicinal products containing genetically modified organisms. In this case, an extension of a maximum of thirty days shall be permitted. For these products, this ninety-day period may be extended by a further ninety days in the event of consultation of a group or committee. In the case of xenogenic cell therapy, there shall be no time limit to the authorisation period.

Single opinion.

8. (1) In the case of multi-centre clinical trials limited to the territory of Malta there shall only be in respect of such trials a single opinion by the Ethics Committee.

(2) In the case of multi-centre clinical trials which are carried out in more than one Member State simultaneously, a single opinion shall be given by the Ethics Committee for each Member State concerned by the clinical trial.

Commencement of a clinical trial.

9. (1) It shall be an offence for the sponsor to start a clinical trial in Malta unless the Ethics Committee has issued a favourable opinion and the Licensing Authority has not informed the sponsor of any grounds for non-acceptance. The procedures to reach these decisions can be run in parallel or not, depending on the sponsor.

(2) Before commencing any clinical trial in Malta, the sponsor shall submit a valid request for authorisation to conduct the clinical trial to the Licensing Authority.

(3) If the Licensing Authority notifies the sponsor of grounds for non-acceptance, the sponsor may, on one occasion only, amend the content of the request referred to in subregulation (2) in order to take due account of the grounds given. If the sponsor fails to amend the request accordingly, the request shall be considered rejected and the clinical trial may not commence.

(4) (*a*) Consideration of a valid request for authorisation by the Licensing Authority shall be carried out as rapidly as possible and may not exceed sixty days.

(*b*) No further extensions to the period referred to in paragraph (*a*) shall be permissible except in the case of trials involving the medicinal products listed in subregulation (6), for which an extension of a maximum of thirty days shall be permitted. For these products, this ninety-day period may be extended by a further ninety days in the event of consultation of a group or of the Ethics Committee. In the case of xenogenic cell therapy there shall be no time limit to the authorisation period.

(*c*) Within the period of examination of the application the Licensing Authority may request information supplementary to that already supplied by the applicant. The period laid down in paragraphs (*a*) and (*b*) shall be suspended until receipt of the supplementary information.

(5) Without prejudice to subregulation (6), written authorisation may be required before the commencement of clinical trials for such trials on medicinal products which do not have a marketing authorisation within the meaning of the Medicines Act, Cap. 458. and any regulations thereunder, and are referred to in Part A of the Annex to Regulation (EEC) No 2309/93, and other medicinal products with special characteristics, such as medicinal products the active ingredient or active ingredients of which is or are a biological product or biological products of human or animal origin, or contain biological components of human or animal origin, or the manufacturing of which requires such components.

(6) Written authorisation shall be required before commencing clinical trials involving medicinal products for gene therapy, somatic cell therapy including xenogenic cell therapy and all medicinal products containing genetically modified organisms. No gene therapy trials may be carried out which result in modifications to the subject's germ line genetic identity.

(7) This authorisation shall be issued without prejudice to the application of Council Directives 90/219/EEC of the 23rd April, 1990 on the contained use of genetically modified micro-organisms and 2001/18/EEC of the 12th March, 2001 on the deliberate release into the environment of genetically modified organisms.

Conduct of a clinical trial.

10. Amendments may be made to the conduct of a clinical trial following the procedure described hereinafter:

(*a*) (i) after the commencement of the clinical trial, the sponsor may make amendments to the protocol. If those amendments are substantial and are likely to have an impact on the safety of the trial subjects or to change the interpretation of the scientific documents in support of the conduct of the trial, or if they are otherwise significant, the sponsor shall preferably prior to implementation notify the Licensing Authority and the competent authorities of the Member States concerned of the reasons for, and content of, these amendments and shall inform the Ethics Committee or committees concerned in accordance with regulations 7 and 9, and where necessary;

(ii) a new informed consent has to be obtained from the trial subjects if so required by the Ethics Committee;

(*b*) the Ethics Committee shall, on the basis of the details referred to in regulation 7(2) and in accordance with regulation 8, give an opinion within a maximum of thirty-five days of the date of receipt of the proposed amendment in good and due form. If this opinion is unfavourable, the sponsor may not implement the amendment to the protocol. If the opinion of the Ethics Committee is favourable and the Licensing Authority has raised no grounds for non-acceptance of the above-

mentioned substantial amendments, the sponsor shall proceed to conduct the clinical trial following the amended protocol. Should this not be the case, the sponsor shall either take account of the grounds for non-acceptance and adapt the proposed amendment to the protocol accordingly or otherwise withdraw the proposed amendment;

(*c*) without prejudice to paragraphs (*a*) and (*b*), in the light of the circumstances, notably the occurrence of any new event relating to the conduct of the trial or the development of the investigational medicinal product where that new event is likely to affect the safety of the subjects, the sponsor and the investigator shall take appropriate urgent safety measures which include information to the subjects, in order to protect the subjects against any immediate hazard. The sponsor shall forthwith inform the Licensing Authority and the competent authorities of the Member States concerned of those new events and the measures taken and shall ensure that the Ethics Committee is notified at the same time; and

(*d*) within ninety days of the end of a clinical trial the sponsor shall notify the Licensing Authority and the competent authorities of the Member States concerned and the Ethics Committee, that the clinical trial has ended. If the trial has to be terminated early, this period shall be reduced to fifteen days and the reasons clearly explained.

Exchange of information. *Amended by: L.N. 248 of 2007.*

11. (1) When the clinical trial is taking place in Malta, the Licensing Authority shall enter in a European database, accessible only to the competent authorities of the Member States, the Commission and the Agency -

(*a*) extracts from the request for authorisation referred to in regulation 9(2);

(*b*) any amendments made to the request, as provided for in regulation 9(3);

(*c*) any amendments made to the protocol, as provided for in regulation 10(*a*) and (*b*);

(*d*) the favourable opinion of the Ethics Committee;

(*e*) the declaration of the end of the clinical trial; and

(*f*) a reference to the inspections carried out on conformity with good clinical practice.

(2) At the substantiated request of any Member State, the Agency or the Commission, the Licensing Authority shall supply all further information concerning the clinical trial in question other than the data already in the European database.

(3) By way of derogation from subregulation (1), the Agency shall make public part of the information on paediatric clinical trials entered in the European database in accordance with the

provisions of Regulation (EC) No. 1901/2006 of the European Parliament and of the Council of the 12th December, 2006 on medicinal products for paediatric use.

Suspension of the trial or infringements.

12. (1) Where the Licensing Authority has objective grounds for considering that the conditions in the request for authorisation referred to in regulation 9(2) are no longer met or has information raising doubts about the safety or scientific validity of the clinical trial, it may suspend or prohibit the clinical trial and shall notify the sponsor thereof. Before the Licensing Authority reaches its decision it shall, except where there is imminent risk, ask the sponsor and, or the investigator for their opinion, to be delivered within one week. The Licensing Authority shall forthwith inform the other competent authorities, the Ethics Committee concerned, the Agency and the Commission of its decision to suspend or prohibit the trial and of the reasons for the decision.

(2) Where the Licensing Authority has objective grounds for considering that the sponsor or the investigator or any other person involved in the conduct of the trial no longer meets the obligations laid down, it shall forthwith inform him thereof, indicating the course of action which he must take to remedy this state of affairs. The Licensing Authority shall forthwith inform the Ethics Committee, the other competent authorities and the Commission of this course of action.

Authorisation for the manufacture and import of investigational medicinal products.

13. (1) It shall not be lawful to manufacture or import any investigational medicinal product unless there is in respect of such an activity an authorisation issued by the Licensing Authority:

Provided that the authorisation shall be conditional to the carrying out of such obligations as may be imposed therein. This authorization shall also be required if the investigational medicinal product or products is, are intended for export.

(2) (*a*) The authorisation shall be required for both total and partial manufacture and for the various processes of dividing up, packaging or presentation.

(*b*) However, the Licensing Authority may exclude from subregulation (1) the process of making changes to the packaging of investigational medicinal products where this process is carried out by pharmacists or persons authorised to carry out such processes in hospital, health centre or clinic within which solely such investigational medicinal products are intended for use.

(3) The holder of the authorisation shall dispose of investigational medicinal products in terms of the conditions imposed by the Licensing Authority.

Manufacture and import of investigational medicinal products. S.L. 458.36

14. (1) The holder of the authorisation referred to in regulation 13 shall have at his continuous and permanent disposal the services of at least one qualified person having the qualifications and experience defined under the Manufacture of Medicinal Products for Human Use Regulations, and he shall be

responsible for carrying out the duties specified in subregulation (2).

(2) In addition to his duties defined under the Manufacture of Medicinal Products for Human Use Regulations, the qualified person shall also, for the purposes of these regulations, be responsible for ensuring that: S.L. 458.36

(*a*) in the case of investigational medicinal products manufactured in Malta, each batch of medicinal products has been manufactured and checked in compliance with the principles and guidelines of good manufacturing practice laid down by the law in force, the product specification file and the information notified pursuant to regulation 9(2);

(*b*) in the case of investigational medicinal products manufactured in a third country, each production batch has been manufactured and checked in accordance with standards of good manufacturing practice at least equivalent to those laid down by the law in force, in accordance with the product specification file, and that each production batch has been checked in accordance with the information notified pursuant to regulation 9(2);

(*c*) in the case of an investigational medicinal product which is a comparator product from a third country, and which has a marketing authorisation, where the documentation certifying that each production batch has been manufactured in conditions at least equivalent to the standards of good manufacturing practice referred to above cannot be obtained, each production batch has undergone all relevant analyses, tests or checks necessary to confirm its quality in accordance with the information notified pursuant to regulation 9(2).

(3) Insofar as the provisions laid down in subregulation (2)(*a*), (*b*), or (*c*) are complied with, investigational medicinal products shall not have to undergo any further checks if they are imported into another Member State together with batch release certification signed by the qualified person.

(4) In all cases, the qualified person shall certify in a register or equivalent document that each production batch satisfies the provisions of this regulation. The said register or equivalent document shall be kept up to date as operations are carried out and shall remain at the disposal of the Licensing Authority for a period of five years.

15. The particulars on the outer packaging of investigational medicinal products or, where there is no outer packaging, on the immediate packaging shall appear in at least one of the official languages of Malta and shall comply with the guidelines of good manufacturing practice for investigational medicinal products published by the Commission. Labelling.

Verification of compliance of investigational medicinal products with good clinical and manufacturing practice.

16.(1)(*a*) To verify compliance with the provisions on good clinical and manufacturing practice, the Licensing Authority shall appoint inspectors who shall on behalf of the Community carry out inspections and inspect the sites concerned by any clinical trial conducted, particularly the trial site or sites, the manufacturing site of the investigational medicinal product, any laboratory used for analyses in the clinical trial and, or the sponsor's premises.

(*b*) The Licensing Authority shall inform the Agency of the inspections carried out and the results shall be recognised by all the other Member States.

(*c*) These inspections shall be coordinated by the Agency, within the framework of its powers as provided for in Regulation (EEC) No 2309/93. A Member State may request assistance from another Member State in this matter.

(2) After an inspection is performed an inspection report shall be drawn up. The report shall be made available to the sponsor while safeguarding confidential aspects. It may be made available to the other Member States, to the Ethics Committee and to the Agency, at their reasoned request.

Notification of adverse events.

17. (1) The investigator shall report all serious adverse events immediately to the sponsor except for those that the protocol or investigator's brochure identifies as not requiring immediate reporting. The immediate report shall be followed by detailed, written reports. The immediate and follow-up reports shall identify subjects by unique code numbers assigned to the latter.

(2) Adverse events and, or laboratory abnormalities identified in the protocol as critical to safety evaluations shall be reported to the sponsor according to the reporting requirements and within the time periods specified in the protocol.

(3) For reported death of a subject, the investigator shall supply the sponsor and the Ethics Committee with any additional information requested.

(4) The sponsor shall keep detailed records of all adverse events which are reported to him by the investigator or investigators. These records shall be submitted to the Member States in whose territory the clinical trial is being conducted, if they so request.

Notification of serious adverse reactions.

18.(1)(*a*) The sponsor shall ensure that all relevant information about suspected serious unexpected adverse reactions that are fatal or life-threatening is recorded and reported as soon as possible to the competent authorities in all the Member States concerned, and to the Ethics Committee, and in any case no later than seven days after knowledge by the sponsor of such a case, and that relevant follow-up information is subsequently communicated within an additional eight days.

(*b*) All other suspected serious unexpected adverse reactions shall be reported to the competent authorities concerned and to the Ethics Committee concerned as soon as possible but within a maximum of fifteen days of first knowledge by the sponsor.

(*c*) The Licensing Authority shall ensure that all suspected unexpected serious adverse reactions to an investigational medicinal product which are brought to its attention, shall be recorded.

(*d*) The sponsor shall also inform all investigators.

(2) Once a year throughout the clinical trial, the sponsor shall provide the Member States in whose territory the clinical trial is being conducted and to the Ethics Committee, with a listing of all suspected serious adverse reactions which have occurred over this period and a report of the subjects' safety.

(3) The Licensing Authority shall ensure that all suspected unexpected serious adverse reactions to an investigational medicinal product which are brought to its attention are immediately entered in a European database to which, only the competent authorities of the Member States, the Agency and the Commission shall have access in accordance with regulation 11(1).

(4) The collection, verification and presentation of adverse event or reaction reports together with the decoding procedures for unexpected serious adverse reactions shall be carried out in accordance with the detailed guidance published by the Commission.

General provisions.

19. (1) These regulations are without prejudice to the civil and criminal liability of the sponsor or investigator. To this end, the sponsor or a legal representative of the sponsor must be established in the Community.

(2) Unless the Licensing Authority has established precise conditions for exceptional circumstances, investigational medicinal products and, or the devices used for their administration shall be made available free of charge by the sponsor to the trial subjects.