

## **CLINICAL TRIALS ON MEDICINAL PRODUCTS IN HUMAN SUBJECTS**

Unofficial translation

### **Legal bases**

Medicines Act, sections 87 and 15a  
Act on Medical Research, section 10i

### **Target groups**

Those performing clinical trials

### **Period of validity**

1 December 2007 – 30 November 2012

### **Regulations repealed**

Regulation 2/2004  
Regulation 1/2006

## TABLE OF CONTENTS

CLINICAL TRIALS ON MEDICINAL PRODUCTS IN HUMAN SUBJECTS.....	1
TABLE OF CONTENTS.....	2
1. GENERAL.....	3
2. DEFINITIONS AND GLOSSARY .....	4
3. GENERAL PREREQUISITES FOR CLINICAL TRIALS ON MEDICINAL PRODUCTS.....	8
4. MEDICINAL PRODUCTS USED IN CLINICAL TRIALS.....	8
5. NOTIFICATION CONCERNING A CLINICAL TRIAL ON A MEDICINAL PRODUCT.....	9
6. DOCUMENTS TO BE APPENDED TO THE NOTIFICATION .....	10
7. NOTIFICATION FORM .....	11
8. TRIAL PROTOCOL.....	11
9. AMENDMENTS TO THE TRIAL PROTOCOL.....	12
10. REPORTING ADVERSE EVENTS AND REACTIONS .....	13
11. COMMENCEMENT, SUSPENSION AND ENDING OF A TRIAL.....	14
12. REPORT ON THE TRIAL RESULTS.....	15
13. INSPECTIONS AND SUPERVISION.....	15
14. TRIAL DOCUMENTATION AND ITS STORAGE .....	15
15. GRANTING OF WAIVERS.....	15
16. GUIDANCE AND INFORMATION.....	15
DISTRIBUTION.....	17
FOR THE INFORMATION OF .....	17
APPENDIX 1. THE PRINCIPLES OF GOOD CLINICAL PRACTICE.....	19
APPENDIX 2. INVESTIGATIONAL MEDICINAL PRODUCT DOSSIER (IMPD) .....	19
1. Pharmaceutical, chemical and biological data .....	21
2. Toxicological, pharmacological and clinical data.....	21
3. Manufacture, import and distribution.....	21
APPENDIX 3. LINKS .....	24

## **1. GENERAL**

Pursuant to sections 15a and 87 of the Medicines Act (395/1987) and section 10i of the Act on Medical Research (488/1999), the National Agency for Medicines hereby issues the following provisions to be complied with in clinical trials concerning medicinal products on human subjects.

Finnish legislation in force must be observed when conducting the above-mentioned clinical trials.

Regard shall be had to the following in particular:

Act on Medical Research (488/1999) and Decree on Medical Research (986/1999) and the subsidiary regulations issued in pursuance thereof

Medicines Act (395/1987)

Act on Patient Status and Rights (785/1992)

Personal Data Act (523/1999)

Genetic Engineering Act (377/1995) and Decree (821/1995)

Patient Injury Act (585/1986)

This Regulation nationally implements Directive 2001/20/EC of the European Parliament and of the Council on the conduct of clinical trials on medicinal products for human use and, concerning its application, Commission Directives 2003/94/EC on good manufacturing practice and 2005/28/EC laying down principles and detailed guidelines for good clinical practice as regards investigational medicinal products for human use, as well as the requirements for authorisation of the manufacturing or importation of such products. This Regulation does not concern Article 6 of Commission Directive 2005/28/EC.

The EU has issued guidelines on the observance of good clinical trial practice (Good Clinical Practice CPMP/ICH/135/95).

As well as having regard to these provisions, attention should also be paid to the Declaration of Helsinki of the World Medical Assembly and to the Council of Europe convention on human rights protection and biomedical science (ETS 164. Council of Europe. Convention for the protection of human rights and dignity of the human being with regard to the application of biology and medicine. Strasbourg 1997).

Appendix 3 contains a list of internet addresses providing norms, guidelines and recommendations.

## **2. DEFINITIONS AND GLOSSARY**

### **CIOMS**

Council for International Organizations of Medical Sciences

### **EMA**

The European Medicines Agency

### **EudraCT number**

Identification number of a clinical trial in the European EudraCT database obtained by the sponsor

### **EudraVigilance**

An EMA-maintained network and database for processing, evaluation and exchange of information on adverse reactions to medicinal products in the European Economic Area. EudraVigilance CT (Clinical Trial Module) deals with clinical trials on medicinal products.

### **Gene therapy medicinal product**

A gene therapy medicinal product means a product obtained through a set of manufacturing processes aimed at the transfer, to be performed either *in vivo* or *ex vivo*, of a prophylactic, diagnostic or therapeutic gene (i.e. a piece of nucleic acid), to human cells and its subsequent expression *in vivo*. The gene transfer involves an expression system contained in a delivery system known as a vector, which can be of viral, as well as non-viral origin. The vector can also be included in a human or animal cell.

### **Adverse event**

An adverse event is any untoward medical occurrence presenting itself in a trial subject which need not necessarily derive from the said product.

#### **Serious adverse event, SAE**

A serious adverse event is any untoward medical occurrence or effect that results in death, is life-threatening, requires hospitalisation or prolongation of existing inpatients' hospitalisation, results in persistent or significant disability or incapacity or is a congenital anomaly or birth defect.

### **Adverse reaction**

A response to a medicinal product which is noxious and unintended and which occurs at doses normally used in man for the prophylaxis, diagnosis or therapy of disease or for the restoration, correction or modification of physiological function; a noxious and unintended response to a medicinal product regardless of dose when there is a possible causal connection to the medicinal product.

#### **Unexpected adverse reaction**

An adverse reaction, the nature or severity of which is not consistent with the information provided in the summary of product characteristics or investigator's brochure.

#### **Serious adverse reaction, SAR**

An adverse reaction that results in death, is life-threatening, requires hospitalisation or prolongation of existing inpatients' hospitalisation, results in persistent or significant disability or incapacity, or is a congenital anomaly or birth defect.

#### **Unexpected serious adverse reaction, SUSAR**

A serious adverse reaction that is also unexpected.

### **Investigational medicinal product, IMP**

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.

**Investigational medicinal product dossier, IMPD**

Information on an investigational medicinal product which must be appended to the trial notification. The scope of the information depends on whether the medicinal product has marketing authorisation (Appendix 2).

**Interventional clinical trial**

A trial which intervenes with the inviolability of the trial subject for the purpose of the investigation. For example, the administration of an investigational medical product to the trial subject or use of some extra means of intervention (i.e. samples, tests or questionnaires) that would not otherwise be used. See also: non-interventional clinical trial

**Clinical trial**

An interventional clinical trial conducted with human subjects in order to discover the effects of medicinal products in human subjects (effectiveness or safety, i.e. pharmacodynamics) or their pharmacokinetics in the human organism (absorption, distribution, metabolism or excretion), or both.

**Medicinal product**

A product or substance intended to be used internally or externally to cure, alleviate or prevent a disease or its symptoms in a human or animal subject. 'Medicinal product' also means any substance or combination of substances as referred to above that may be used internally or externally to determine the state of health of a person or the cause of a disease or to restore, improve or change his physiological functions through pharmacological, immunological or metabolic means. In the event of uncertainty, in cases where the product, having regard to all its properties, may correspond to the definition of medicinal product and of other preparation appearing in legislation and the instruments of the European Union, the provisions concerning medicinal products shall primarily apply (See also: investigational medicinal product).

**MedDRA (Medical Dictionary for Regulatory Activities)**

MedDRA is a clinically validated international medical terminology used by the European Medicines Agency (EMA) in the classification of adverse events and reactions.

**Multi-centre trial**

A clinical trial conducted according to a single protocol but at more than one trial site.

**Non-interventional clinical trial**

A study where the medicinal product(s) is (are) 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 wholly independent of 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 the data.

**Transgenic micro-organism**

The genetic material of a transgenic micro-organism has been altered in a way that does not occur naturally by mating and/or natural recombination. Micro-organism means any microbiological entity, cellular or non-cellular, capable of replication or of transferring genetic material, including viruses and viroids as well as cultures of animal and plant cells and cultures of human cells and tissue cultures.

**Substantial amendment**

A substantial amendment is one that may affect the safety or physical or mental wellbeing of the subjects, or the scientific value of the trial, or that significantly changes the quality or safety of any IMP used in the trial, or is in some other way significant.

**Independent data-monitoring committee, IDMC**

A group of experts, independent of the sponsor and the investigator, which regularly monitors the progress of the trial. The group monitors the progress, safety data and critical result variables of the trial and may if necessary recommend its continuation, modification or suspension.

**Somatic cell therapy**

Somatic cell therapy is the use in humans of autologous (emanating from the patient himself), allogeneic (coming from another human being) or xenogeneic (coming from animals) somatic living cells, the biological characteristics of which have been substantially altered by manipulation to obtain a therapeutic, diagnostic or

prophylactic effect through metabolic, pharmacological or immunological means. The manipulation methods include the expansion or activation of autologous cell populations ex vivo (adoptive immunotherapy) and the use of allogeneic and xenogeneic cells contained in medical devices ex vivo or in vivo (e.g. micro-capsules and intrinsic matrix scaffolds, biodegradable or not).

### **Informed consent form**

A document given to the trial subject which contains an explanation of the trial subject's rights, the purpose and nature of the trial and procedures to be used therein and any associated risks and disadvantages, and which is signed by the giver and recipient of the consent. The document may be independent or comprise the trial subject information leaflet (or patient information leaflet) and consent form.

### **Inspection**

An official inspection performed by a competent supervisory authority for medicines, such as the National Agency for Medicines, of documents, premises, equipment, quality assurance system and any other circumstances which the authority considers relevant to the clinical trial and the checking of which said authority considers necessary.

### **Sponsor**

An individual, company, institution or organisation that takes responsibility for the initiation, management or financing of a clinical trial. If an outside party participates in the trial only by financing it, the investigator and the sponsor can agree between themselves that the investigator is also the sponsor. The investigator himself is regarded as the sponsor in the case of trials where there is no outside sponsor.

### **Investigator**

An authorised physician or dentist with the appropriate professional and scientific qualification who is responsible for performance of the clinical trial at the trial site. If a trial group is conducting a trial at some trial site, the term 'investigator' refers to the physician or dentist acting as the leader of the group.

#### **Subinvestigator**

A named member of a clinical trial group who carries out measures and makes decisions relating to the trial under the guidance of the investigator or the person responsible for the trial.

#### **Coordinating investigator**

An investigator who is responsible for coordinating the work of the investigators at different trial centres participating in a multi-centre trial.

### **Person responsible for the trial**

An authorised physician or dentist with the appropriate professional and scientific qualifications in Finland who is responsible for the trial. He must ensure that the personnel conducting the trial are competent, the equipment and devices sufficient and the conditions safe. He must also ensure that legally imposed requirements, international obligations affecting the status of the trial subject, and rules and regulations relating to the trial are taken into consideration in its performance. He must suspend the trial as soon as the safety of a trial subject so requires and immediately perform any safety measures needed for protection of the trial subjects.

### **Investigator's Brochure**

A compilation of the preclinical, clinical and non-clinical data on the investigational medicinal product which are relevant to the study of the product in human subjects. The information shall be presented in a concise, simple, objective, balanced and non-promotional form that enables a clinician or potential investigator to understand it and make an unbiased risk-benefit assessment of the appropriateness of the proposed clinical trial.

### **Commencement and end of trial**

A trial is deemed to have commenced when the first trial subject signs a consent document. A trial is deemed to have ended when its entire clinical phase is over in respect of the last trial subject.

### **Trial site**

The location where the trial subjects are studied.

### **Protocol**

A document that describes the objective(s), design, methodology, statistical considerations and organisation of a trial. The term protocol refers to the protocol, successive versions of the protocol and protocol amendments;

**Trial subject**

An individual who participates in a clinical trial as either a recipient of the investigational medicinal product or as a control. A trial subject may be a patient or a healthy volunteer.

### **3. GENERAL PREREQUISITES FOR CLINICAL TRIALS ON MEDICINAL PRODUCTS**

Medical research in Finland is governed by the Act on Medical Research (488/1999). The Act covers all medical research intervening with the inviolability of a human being, human embryo or foetus, including clinical trials on medicinal products in human subjects, which are also covered by the provisions of the Medicines Act (395/1987).

Medical research must respect the inviolability of human dignity. The interests and well-being of trial subjects must always come before the interests of science and society. Every effort must be made to prevent any risks to and adverse effects on the subjects. The trial must be conducted in accordance with the principles of good clinical practice (Appendix 1) and the principles of the Declaration of Helsinki. A trial must be medically justifiable.

Trial subjects must be given sufficient information about the trial and the rights of the subject. An informed written consent must be obtained from prospective subjects prior to their participation in a trial. Even after giving this consent, a trial subject is free to withdraw from the research at any time without providing reasons for so doing or, for example, in the case of people who are sick, without risking their continued care.

Each clinical trial on a medicinal product must have a sponsor and in Finland, a person responsible for the trial, who must be a physician or a dentist with appropriate professional and scientific qualifications. The person responsible for the trial must ensure the availability of competent and appropriately instructed research staff, sufficient equipment and appliances, and otherwise safe circumstances for the conduct of the trial. In addition, the person responsible for the trial must ensure adherence to legal provisions relating to the trial and to the requirements of international obligations or guidelines concerning the status of trial subjects.

An Independent Data-Monitoring Committee (IDMC) must, as necessary, be set up to monitor long-term trials conducted with large numbers of patients and trials relating to new, potentially dangerous, treatments. This Committee monitors trial progress, safety data and critical result variables, and may if necessary recommend continuation, modification or suspension of the trial.

The detailed division of duties between the investigator and the sponsor can be agreed on separately. The investigator himself is regarded as the sponsor in trials where there is no outside sponsor.

In addition to being notified of the commencement of a clinical trial, the National Agency for Medicines must be notified of any substantial amendments to be made to the protocol, serious adverse reactions occurring during a trial, and the termination of a trial, and must also be provided with a summary of the trial results. In addition, the National Agency for Medicines must be provided with an annual account of the safety of persons participating in a clinical trial. The Agency conducts inspections of clinical trials and can order their suspension when necessary.

### **4. MEDICINAL PRODUCTS USED IN CLINICAL TRIALS**

The trial group must have at its disposal sufficient pharmacological, toxicological, pharmaceutical/chemical and biological data on the medicinal products used in clinical trials and this data must be appended to the notification concerning a clinical trial on a medicinal product (Appendix 2).

The responsibility for the adequacy of data relating to medicinal products is primarily borne by the sponsor, who must provide the physician or dentist who will be conducting the trial with all the data on said products and with any other relevant information.

If the sponsor is not a legal person, the person who is responsible for the clinical trial is also responsible for the adequacy and reliability of the data on the medicinal product or the trial substance.

For medicinal products with marketing authorisation as referred to in section 21 of the Medicines Act, it is generally sufficient to refer to the material submitted in connection with the marketing authorisation application (Appendix 2).

The investigator may be supplied with investigational medicinal products for a clinical trial by a pharmaceutical manufacturer, a unit manufacturing medicinal products for clinical trials, a wholesale distributor, a hospital

pharmacy or a pharmacy, operating in Finland. If the trial is conducted at a hospital, the information on investigational medicinal products received must also be provided to the hospital pharmacy/medical centre. If a pharmacy, hospital pharmacy or medical centre is responsible for the storage of investigational medicinal products, the responsible person in the unit concerned may acknowledge receipt of the products.

The sponsor must keep a record stating the delivery, receipt, use, return and destruction of investigational medicinal products.

The investigator is responsible for the record of medicinal products at the trial site stating their delivery, receipt, use, return and destruction.

The trial subject must be provided with investigational medicinal products and any equipment needed for their use without charge, unless there is justifiable reason for acting otherwise.

If necessary, the investigational medicinal products must be labelled in both official languages of Finland. If the patient is not given the package (for example at a hospital), the labelling can be in English only.

Packages which are used for clinical trials, including placebo packages, must be marked 'Kliiniseen tutkimukseen'/'För klinisk prövning' [For clinical trial].

The package label must state the trial code, the batch number or other means of identification, the manufacturer and/or sponsor, the name of the doctor or dentist responsible for the trial and the patient identifier. The label must also indicate the pharmaceutical form, the method and/or route of administration, the number of doses, the instructions for storage (if special storage instructions are necessary), the expiry date and, if necessary, the technical handling instructions. The labelling must also comply with *The rules governing medicinal products in the European Union: Vol IV, 'Good manufacturing practices', Annex 13, 'Manufacture of investigational medicinal products' and Annex 16 'Certification by a qualified person and batch release'*.

## **5. NOTIFICATION CONCERNING A CLINICAL TRIAL ON A MEDICINAL PRODUCT**

The National Agency for Medicines must be notified of clinical trials on medicinal products that intervene with the inviolability of the trial subject in order to investigate the effects or properties of a medicinal product, regardless of whether the investigational medicinal product has marketing authorisation as referred to in section 21 of the Medicines Act. Provisions on the notification requirement and processing times are laid down in section 87 of the Medicines Act.

The National Agency for Medicines must only be notified of interventional trials. No notification is needed for other trials. Such investigations (non-interventional trials) must meet the following criteria:

- they involve normal patient care which does not differ from normal treatment practice;
- there is no intervention of patient inviolability using additional means due to the investigation;
- no additional diagnostic or other monitoring methods are applied to the trial subjects, and the data are collected from information obtained in the course of normal care;
- the medicinal products are prescribed in the normal manner, in accordance with established treatment practice;
- the decision to prescribe the medication is clearly independent of the decision to include the patient in the trial;
- the trial protocol does not define in advance the patient's specific treatment and choice of medication; and
- epidemiological methods are used to analyse the data.

In the event of any uncertainty, the National Agency for Medicines will decide whether a notification for a clinical trial on medicinal products should be submitted.

A multi-centre trial is considered a single trial on which one complete notification must be filed.

## 6. DOCUMENTS TO BE APPENDED TO THE NOTIFICATION

The following documents must be appended to the notification filed with the National Agency for Medicines:

1. Covering letter. The sponsor compiles and signs a covering letter which accompanies the notification. The heading of the covering letter must include the EudraCT number, the sponsor protocol number, the name of the trial protocol and the name of the person responsible for the trial in Finland. The body of the letter must contain a brief description of the trial, focusing on its special features (e.g. specific groups of patients, the first time the medicinal product is administered to human subjects, exceptional features of the medicinal product, exceptional trial arrangement, etc.) In addition, the covering letter shall list the documents accompanying the notification.
2. List of trial sites and investigators. The list must include the address of the trial site, the investigators at each trial site, and their degrees and areas of specialisation, if this information was not provided in the notification form.
3. The curriculum vitae (CV) of the person responsible for the trial in Finland.
4. Notification form. The sponsor shall submit the completed and signed notification form to the National Agency for Medicines on paper and as an electronic file. (See Chapter 7. Notification form.)
5. Payment voucher or request for exemption from payment. The notification must be accompanied by a receipt for payment in accordance with the Ministry for Social Affairs and Health Decision relating to National Agency for Medicines services subject to a charge, or else by a request for exemption from payment. Payment must be made to the National Agency for Medicines account Sampo 800014-21979. Payments must be individualised so as to make it clear which clinical trial on a medicinal product the payment relates to. A single fee is payable in respect of a multi-centre trial. A waiver of processing fee may be requested in respect of a notification relating to a clinical trial on a medicinal product conducted by an individual investigator, a trial team, a university institute, a university hospital clinic, the National Public Health Institute or the National Research and Development Centre for Welfare and Health without outside financing or with financing by a non-profit corporation. In these cases, the notification concerning a trial must be accompanied by an informal statement to the effect that the investigation will not receive any outside financing. Medicinal products received free of charge for the purpose of the investigation are not deemed outside financing.
6. A brief description of any unusual division of duties and responsibilities between the sponsor and the person responsible for the clinical trial, in the event that some of the sponsor's duties have been transferred to the person responsible for the clinical trial.
7. A trial protocol signed by the person responsible for the clinical trial in Finland.
8. A consent document, which may comprise a separate information leaflet and consent form. The informed consent of a trial subject is subject to the provisions of the Act on Medical Research (488/1999) and the content of the consent document to the provisions of the Decree on Medical Research (986/1999). The document must state that a National Agency for Medicines inspector has the right to study the original patient documents and investigational material to the degree necessary to verify the authenticity of the data collected during the clinical trial. A sponsor's monitor or foreign authorities do not have the same statutory right. The written consent of the trial subject must be obtained in order to reserve the same right of inspection to other than National Agency for Medicines inspectors.
9. The investigator's brochure, if one has been compiled. No brochure is required if the investigational medicinal product has marketing authorisation in Finland.
10. Evidence that the manufacture of the investigational medicinal products conforms to good manufacturing practice (GMP).
11. Data on previous trials on human subjects
12. Data on the pharmaceutical, chemical and biological properties of the medicinal product.

13. Data on the pharmacology and pre-clinical toxicology of the medicinal product. In the case of a clinical trial on a medicinal product that has been granted marketing authorisation, or whose application for marketing authorisation is pending at the National Agency for Medicines, reference to the material submitted in connection with the application for marketing authorisation is usually sufficient as regards items 9–12. If trials on an investigational medicinal product have been conducted in Finland earlier, reference may be made to the material accompanying the earlier trial notification, provided that no substantial changes have occurred. (See Appendix 2.)

For communication relating to a clinical trial on medicinal products, a foreign sponsor must have a representative in Finland who is responsible for communication with the National Agency for Medicines.

## **7. NOTIFICATION FORM**

In the case of a clinical trial on a medicinal product, the sponsor or the sponsor's legal representative in the European Community must submit to the National Agency for Medicines a notification on or a request for authorisation of a clinical trial on a medicinal product before the commencement of the trial. If the person submitting the notification is not the sponsor or his legal representative, the notification must be accompanied by a letter in which the sponsor authorises the party submitting the notification to act on his behalf.

Notification of a clinical trial shall be made using the Clinical Trial Application Form available on the EMEA EudraCT database website <http://eudract.emea.europa.eu/>. In the event that a EudraCT number has already been obtained for notification to be made to the competent authority of another State, the same number shall be used. Instructions relating to the database are available in the document "Detailed guidance on the European clinical trials database (EudraCT Database)".

The notification shall be completed in Finnish, Swedish or English using the EudraCT system. The completed notification form is printed out on paper in PDF format and signed. In addition, the notification form is saved in electronic XML format and forwarded to the National Agency for Medicines on disk or CD-ROM (not as an email attachment) along with the signed paper copy. It is recommended that the party submitting the notification also save a copy of the final notification form on its own computer. The National Agency for Medicines verifies the information and transfers it to the European EudraCT database for use by the authorities.

If the investigational medical product has marketing authorisation, the EudraCT application concerning a trial conducted by a non-commercial sponsor may be completed by the simplified procedure described on the National Agency for Medicines website at [http://www.laakelaitos.fi/laaketeollisuus/kliiniset\\_laaketutkimukset/index.html](http://www.laakelaitos.fi/laaketeollisuus/kliiniset_laaketutkimukset/index.html) under the heading "Ohjeita akateemisille tutkijoille" (in Finnish only).

## **8. TRIAL PROTOCOL**

The trial protocol or the documents appended to the notification must include the following information:

1. General administrative information, i.e. the full name of the clinical trial, the abbreviated name of the trial, sponsor's protocol number, the version number and date of the protocol, and the names of the sponsor and the person responsible of the trial in Finland.
2. The purpose of the investigation and the justification for its conduct.
3. A description of the research method (controlled, uncontrolled), structure of the trial (e.g. parallel groups, cross-over), randomisation (the method and procedure), and blinding (e.g. double blind, single blind).
4. A list of the trial sites, investigators and their degrees and specialist qualifications, if not separately listed.
5. A description of the patients. The inclusion and exclusion criteria.
6. The estimated number of patients to be included in the trial, and its justification. Whether the patient material is sufficient from the standpoint of the investigation.

7. The estimated schedule of the trial.
8. The method of administration, dose and dosing schedule of the investigational medicinal product and the comparator, and the treatment period.
9. The control groups and control treatment (placebo, other treatment, etc.).
10. Other concurrent therapy, if any.
11. Assessment of efficacy. Result variables, primary result variable, description and evaluation of measurement methods. Measurement schedule.
12. Assessment of trial safety and related laboratory and other tests.
13. Reporting and assessing of adverse events and reactions. A description of the recording of adverse events and reactions and of any systematic follow-up questionnaire on adverse events.
14. Precautions for emergencies and criteria for opening the trial code and suspending the trial.
15. Any adverse effects in patients' relatives, nursing staff and the surroundings which may be caused by the investigational medicinal product and by the trial, and measures to prevent these.
16. Processing and recording of the data on persons participating in a trial. Compilation of personal data files and processing of related personal information.
17. Information on quality assurance methods.
18. Measures used to ensure the authenticity of the collected data and observance of good clinical trial practice.
19. Analysis of the results. A description of the research methods and statistical methods. Processing of data on subjects who have interrupted the trial.
20. Information on the advance information to be given to trial subjects/patients and on the method for obtaining the informed consent of trial subjects.
21. Ethical aspects relating to the trial.
22. The arrangements for the treatment of patients after the trial (such as gradual discontinuation of the investigational medicinal product, possible replacement by other medication, etc.). An account of the arrangements for the treatment of patients showing good results from the medicinal product investigated.
23. A description of how amendments to the trial protocol are recorded and reported to the National Agency for Medicines and the Ethics Committee.
24. Appendices to the protocol.
25. An account of the manner in which the trial and its results will be published.

The person responsible for the trial in Finland must date and sign the protocol.

Some of the above information may be incorporated in the documents appended to the trial protocol, such as the Investigator's Brochure.

## **9. AMENDMENTS TO THE TRIAL PROTOCOL**

The sponsor must ensure that the National Agency for Medicines is notified in writing of any substantial amendments that may be made to a trial protocol or its appendices submitted earlier under Section 87a of the

Medicines Act. If the National Agency for Medicines does not request any further information on the amendment notification within 35 days of receiving it, the Agency has accepted the amendment. The sponsor must, however, obtain the positive opinion of the Ethics Committee on the amendment(s) before implementation.

Any changes in investigators or trial centres must also be reported to the National Agency for Medicines.

Substantial amendment is notified in writing using the form (Request for authorisation of a substantial amendment) available on the EudraCT home page <http://eudract.emea.europa.eu/>. The form can be completed in Finnish, Swedish or English. The completed form is submitted to the National Agency for Medicines. Notification may not be made by fax or email.

If a new version of the trial protocol or its appendices is later submitted to the National Agency for Medicines, all changes from the earlier version must be clearly itemised.

## 10. REPORTING ADVERSE EVENTS AND REACTIONS

The investigator and sponsor must report the occurrence of any adverse events and reactions occurring in Finland as well as abroad during clinical trials performed in Finland as provided in sections 10e and 10f of the Act on Medical Research (488/1999). The National Agency of Medicines need not be notified of adverse reactions occurring in clinical trials not conducted in Finland.

The sponsor must keep detailed records of all serious adverse events and all adverse events defined as significant in the trial protocol which are reported to him by the investigator. The sponsor must report to the National Agency for Medicines all serious unexpected adverse reactions which are fatal or life-threatening as quickly as possible, however no later than within seven days of the sponsor being informed of such an adverse reaction. Any additional relevant information on such an adverse reaction must be reported within eight days of submission of the first notification.

Serious unexpected adverse reactions which are not life-threatening or fatal must be reported to the National Agency for Medicines and to the competent authorities of the EU Member States concerned as soon as possible and in any case within 15 days of the sponsor first being informed thereof.

Registration with EMEA's EudraVigilance is mandatory for commercial sponsors and recommended for non-commercial sponsors as well. Registration instructions are available at <http://eudravigilance.emea.europa.eu/highres.htm>. Registered sponsors must submit electronic notifications to EudraVigilance. Unexpected serious adverse reactions occurring in Finland must be reported both to the National Agency for Medicines database (recipient identifier FINAM) and the European Medicines Agency (recipient identifier EVCTMPROD). Unexpected serious adverse reactions occurring abroad are reported only to the European Medicines Agency. Specific instructions have been issued by the European Commission in the document "Detailed guidance on the collection, verification and presentation of adverse reaction reports arising from clinical trials on medicinal products for human use".

If the sponsor is not registered with EudraVigilance, a report must be made in writing to the National Agency for Medicines. The report may not be submitted by fax or email. It can be made in the form of a free-form letter or with the CIOMS-I form (available at the Internet address <http://www.cioms.ch/>) or a corresponding form. The report must show at least:

- EudraCT number of the trial or the number provided by the National Agency for Medicines if the trial has been notified prior to June 1, 2004;
- information on whether the event has been reported to the National Agency for Medicines earlier (whether this is a follow-up report);
- name of the investigational medicinal product which is suspected to have caused the reaction. If the pharmacotherapy has been blinded (masked), the code must be broken if no other method has been justified in the trial protocol;
- diagnosis of patients treated or information that healthy volunteers are treated;
- adverse reaction observed, preferably also the MedDRA code of the reaction;
- patient's identification number (the exact date of birth, initials or personal identity code are not given);
- patient's age, in the case of infants under 12 months to an accuracy of one month, and in the case of infants under one-month old to an accuracy of one day;

- patient's gender;
- the name of the person who reported the adverse reaction; and
- the country where the adverse reaction was identified.

If the occurrence of serious adverse events is a result variable of the trial, such as in extensive follow-up trials examining mortality and morbidity, summaries of adverse reactions relating to result variables may be supplied to the National Agency for Medicines at regular intervals, e.g. quarterly or half-yearly. The procedure must in that case be set out in the trial protocol. In such trials there must generally be an Independent Data-Monitoring Committee (IDMC), whose reports must be submitted to the National Agency for Medicines within seven days of their completion.

Once a year, the sponsor must provide the National Agency for Medicines with a list of all suspected serious adverse reactions which have occurred during the period in question. The year is considered to have begun on the date on which commencement of the clinical trial was permitted in the first EU Member State. At the same time, the sponsor must supply a brief report of the safety of persons participating in the clinical trial. The report must be signed by the person responsible for the trial and it shall take into account all facts relating to the trial, not only the safety of the investigational medical product. This requirement remains in force throughout the period of the clinical trial.

The sponsor must without delay inform the investigators and the National Agency for Medicines of any significant new observations relating to the safety of the investigational medicinal product.

## **11. COMMENCEMENT, SUSPENSION AND ENDING OF A TRIAL**

Before commencement, a favourable opinion of the clinical trial must be obtained either from the competent Health District Ethics Committee of the trial site or, in the case of an international multi-centre trial, from the Sub-Committee on Medical Research Ethics (TUKIJA) of the National Advisory Board on Health Care Ethics (ETENE). An opinion relating to Finnish trial centres participating in international multi-centre trials is issued by TUKIJA or, on the instructions thereof, by a Health District Ethics Committee. If the Ethics Committee has proposed changes to the trial, the amended documents such as the trial protocol, its appendices and patient consent must be submitted to the National Agency for Medicines in the form approved by the Ethics Committee prior to commencement of the trial. A trial notification or request for authorisation may be submitted to the National Agency for Medicines regardless of the stage of processing by the Ethics Committee.

The National Agency for Medicines examines the notification or request for authorisation concerning a clinical trial on medicinal products and its appendices. If on preliminary examination the notification is found to be deficient, the Agency requests supplementation of the notification before processing it. The sponsor is sent an announcement of the receipt of a valid notification or request for authorisation; this states the date of commencement of processing and the number assigned to the investigation by the National Agency for Medicines. This number and the EudraCT number must be used as a reference in correspondence regarding the trial.

If the National Agency for Medicines cannot approve the conduct of the trial, the sponsor is asked for further clarification. If such clarification is requested, the request is made in writing within 60 days of the commencement of processing to the party submitting the notification. On the basis of the request for clarification from the National Agency for Medicines, the sponsor may amend its trial protocol to rectify the deficiencies observed. If the amendments are not made or the amendments are not in line with the request for clarification, the trial may not commence. If no clarification is requested, the trial may commence without specific permission from the National Agency for Medicines when 60 days have elapsed from commencement of the processing.

The National Agency for Medicines' processing period is 90 days if the clinical trial involves medicinal products for gene therapy, somatic cell therapy or medicinal products containing genetically modified organisms. Written authorisation from the National Agency for Medicines is required before such clinical trial can commence. The National Agency for Medicines can extend the processing period by a further 90 days if issuance of a statement requires extensive further clarifications. No fixed time limit applies to decisions to authorise trials involving xenogenic cell therapy.

If the trial is not initiated, the National Agency for Medicines must be notified of the decision and the reasons for it in writing within 90 days. If the trial has been interrupted, the National Agency for Medicines must be notified of the interruption and the reasons for within 15 days using the EudraCT form “Notification of amendment”. The same form must be used to notify of re-commencement of the trial.

Clinical trial is deemed to have ended when the last patient has completed the clinical stage of the trial. The National Agency for Medicines must be notified of the end of the trial within 90 days. In the event that an international trial ends in Finland earlier than at the other trial sites, separate notification must be made of its end in Finland and the end of the entire trial. Notification concerning the end or premature suspension of the trial must be made in writing using the EudraCT form “Declaration of the end of a trial”.

All EudraCT forms may be completed in Finnish, Swedish or English. Notifications may not be made by fax or email.

## **12. REPORT ON THE TRIAL RESULTS**

The sponsor or the person responsible for the trial must provide the National Agency for Medicines with a report on the results of the trial not later than one year after it ends. If the trial subjects have included persons under the age of 18 and if the sponsor is the marketing authorisation holder for the investigational medicinal product, the report must be submitted within six months. The report should be submitted in the form of a summary, a synopsis, published article or in some other similar way in writing. An extensive trial report containing complete research data only needs to be supplied at the request of the National Agency for Medicines.

Even if a Final Report on the trial results has been submitted to the National Agency for Medicines as an attachment of an application for marketing authorisation, a summary of the trial results must nonetheless be sent separately to the Clinical Trials Section.

## **13. INSPECTIONS AND SUPERVISION**

The National Agency for Medicines is the supervisory authority for clinical trials on medicinal products. The Agency must, when it so requests, be provided with any clarifications that it requires to perform this supervision. Notwithstanding the rules on confidentiality, the Agency has the right to inspect any aspect necessary, including the trial site, trial documents and the patient documents concerning trial subjects.

If a foreign authority intends to inspect the trial site and the trial documents, the sponsor must report the inspection to the National Agency for Medicines by letter within seven days of the sponsor being informed of the intended inspection.

## **14. TRIAL DOCUMENTATION AND ITS STORAGE**

The original trial documents must be stored for at least 15 years from the end of the trial. The keeping of patient files is governed by the relevant general provisions and regulations. The trial registers are further governed by the provisions of the Personal Data Act (523/1999).

## **15. GRANTING OF WAIVERS**

The National Agency for Medicines may for particular reasons grant waivers from the above provisions.

## **16. GUIDANCE AND INFORMATION**

Guidance and information on the practical application of this Regulation is available upon request from the National Agency for Medicines.

Director General, Professor

Hannes Wahlroos

Senior Medical Officer

Esko Nuotto

## **DISTRIBUTION**

Pharmaceutical manufacturers  
Pharmaceutical wholesalers  
Persons responsible for marketing of a medicinal product  
National Public Health Institute  
Finnish Red Cross Blood Transfusion Service  
Hospital pharmacies and medical centres  
Social and health departments of Provincial State Offices  
Hospital districts  
Central hospitals  
Health centre hospitals and special hospitals  
Psychiatric hospitals  
Health centres  
Finnish Student Health Service  
Family Federation of Finland

## **FOR THE INFORMATION OF**

Parliamentary Ombudsman  
Office of the Chancellor of Justice  
Ministry of Social Affairs and Health  
Ministry of Trade and Industry  
Ministry of Agriculture and Forestry  
National Veterinary and Food Research Institute  
National Food Agency  
National Research and Development Centre for Welfare and Health  
National Authority for Medicolegal Affairs  
National Advisory Board on Health Care Ethics  
Ethics Committees of the hospital districts  
Wholesalers of pharmacy goods  
Central Organisation of Health Food Trade in Finland  
Chemical Industry Federation of Finland  
Pharma Industry Finland  
Finnish Generic Pharmaceutical Industry  
Pharmaceutical Information Centre  
Social Insurance Institution of Finland  
Finnish Consumer Agency  
Consumer Ombudsman  
Defence Staff, Healthcare Department  
Military Pharmacy  
Finnish Academy, State Medical Committee  
State Treasury  
University of Helsinki, Department of Pharmacy  
University of Helsinki, Faculty of Medicine  
University of Kuopio, Faculty of Pharmacy  
University of Kuopio, Faculty of Medicine  
University of Oulu, Faculty of Medicine  
University of Tampere, Faculty of Medicine  
University of Turku, Faculty of Medicine  
Finnish Medical Society Duodecim  
Association of Finnish Pharmacies  
Finnish Veterinary Association  
Finnish Pharmacists' Association  
Finnish Dental Association  
Finnish Union of Practical Nurses  
Finnish Medical Association  
Professional Association of Finnish Pharmacists

Finnish Nurses' Association  
Finnish Union of Public Health Nurses  
Finnish Association of Occupational Health Nurses  
Association of Finnish Local and Regional Authorities Nurse Administrator Association  
Åbo Akademi University, Department of Biochemistry and Pharmacy  
Data Protection Ombudsman's Office

## **APPENDIX 1. THE PRINCIPLES OF GOOD CLINICAL PRACTICE**

According to Directive 2005/28/EC laying down principles and detailed guidelines for good clinical practice as regards investigational medicinal products for human use, as well as the requirements for authorisation of the manufacturing or importation of such products

1. The rights, safety and well being of the trial subjects shall prevail over the interests of science and society.
2. Each individual involved in conducting a trial shall be qualified by education, training, and experience to perform his or her tasks.
3. Clinical trials shall be scientifically sound and guided by ethical principles in all their aspects.
4. The necessary procedures to secure the quality of every aspect of the trials shall be complied with.
5. The available non-clinical and clinical information on an investigational medicinal product shall be adequate to support the proposed clinical trial.
6. Clinical trials shall be conducted in accordance with the Declaration of Helsinki on Ethical Principles for Medical Research Involving Human Subjects, adopted by the General Assembly of the World Medical Association in 1996.
7. The protocol referred to in point (h) of Article 2 of Directive 2001/20/EC shall provide for the definition of inclusion and exclusion of subjects participating in a clinical trial, monitoring and publication policy.
8. The investigator and sponsor shall consider all relevant guidance with respect to commencing and conducting a clinical trial.
9. All clinical trial information shall be recorded, handled, and stored in such a way that it can be accurately reported, interpreted and verified, while the confidentiality of records of the trial subjects remains protected.

## **APPENDIX 2. INVESTIGATIONAL MEDICINAL PRODUCT DOSSIER (IMPD)**

Pharmaceutical, chemical and biological data on the investigational medicinal products, together with toxicological, pharmacological and clinical data on them, must be appended to the notification concerning a clinical trial if the investigational medicinal product does not have marketing authorisation as referred to in Section 21 of the Medicines Act or the investigational medicinal product characteristics have been changed compared with the manufactured/pharmaceutical form that has marketing authorisation.

The information must follow the “Detailed guidance for the request for authorisation of a medicinal product for human use to the competent authorities, notification of substantial amendments and declaration of the end of the trial,” as applicable, published by the European Commission. The guide is available on the Commission web site at <http://eudract.emea.europa.eu/>. The extent of the information depends on the stage of the investigation. When a clinical trial moves from one phase to another, the sponsor may be required to provide more information.

If the data on the investigational medicinal product have been submitted to the National Agency for Medicines as an appendix to a previous trial notification, or if the product has marketing authorisation in Finland, only supplementary information on the trial need be appended to the trial notification (simplified IMPD). Examples of the information which needs to be provided are shown in Table 1.

Table 1.

	Pharmaceutical/ chemical and biological data	Preclinical safety data	Clinical data
The IMP has a MA in any EU Member State and is used in the study	SPC	SPC	SPC
• within the conditions of the SPC			
• outside the conditions of the SPC	SPC	Yes (if appropriate)	Yes (if appropriate)
The drug substance is manufactured in a different process or by a manufacturer other than the MAH of the IMP	S+P+A	SPC* (see below)	SPC
The IMP is blinded	P+A	SPC	SPC
Another pharmaceutical form or strength of an IMP that has an MA in any EU Member State and the sponsor of the trial is the MAH	P+A	Yes	Yes
The IMP has no MA in any EU Member State but the drug substance is authorised in a Member State and the IMP:			
• is supplied by the same manufacturer	P+A	Yes	Yes
• is supplied by another manufacturer	S+P+A	Yes	Yes
Documents concerning the IMP have been submitted to the NAM as an appendix to a previous clinical trial notification** and no new data is available	No	No	No
New data available	New data	New data	New data
Placebo data	P+A	No	No

\* Where the change to drug substance manufacture produces a new potentially toxic substance such as a new impurity or degradation product or introduces a new material in the production of a biological product, the results of preclinical toxicology tests may be required as an appendix to the trial notification.

\*\*If the sponsor wishes to refer to data submitted by another applicant, the sponsor shall when so required present the consent thereto of the previous sponsor or marketing authorisation holder.

(IMP = investigational medicinal product, SPC = summary of product characteristics, S = drug substance data, P = drug product data, A = data referred to in section 2.1 .A of the European Commission guidance concerning facilities and equipment, adventitious agents' safety evaluation, novel excipients and solvents for reconstitution and diluents, MA= marketing authorisation, MAH = marketing authorisation holder, NAM = National Agency for Medicines)

## **1. Pharmaceutical, chemical and biological data**

The data must be compiled in accordance with the guidelines of the European Union Commission, CPMP and ICH. The best way to present the data is to follow the Commission's instructions *Detailed guidance for the request for authorization of a medicinal product for human use to the competent authorities, notification of substantial amendments and declaration of the end of the trial*, 'Attachment 2. The instructions of the CHMP appearing in "CHMP/QWP/185401/2004 guideline on the requirements to the chemical and pharmaceutical quality documentation concerning investigational medicinal products in clinical trials" shall be taken into consideration when presenting pharmaceutical, chemical and biological data.

The quality requirements for the active ingredient and final product must always be provided. In addition, analysis results from one or several batches must be included. Investigations into the shelf-life of the active ingredient and the final product must also be provided.

In case of products containing substances of biological origin, the starting materials should also be specified. In the information relating to substances of biological origin, special attention should be paid to the manufacturing process for the active ingredient and to ensuring its virus and prion safety.

If a placebo or some other reference product is used in the trial, an adequate account must be provided of its manufacture, composition, appearance and taste. Table 1 contains more detailed instructions. Attention must also be paid to other relevant guidelines provided by the European Commission, CPMP and ICH.

Changes in a medicinal product being used for a trial already in progress which substantially affect the kinetics, manufacture or shelf-life of the medicinal product must be reported without delay.

If the pharmaceutical, chemical and/or biological characteristics of the medicinal product have changed compared with the characteristics of the medicinal product used in animal tests or in earlier clinical trials, the nature of this change must be explained and the reason for the change stated.

## **2. Toxicological, pharmacological and clinical data**

Before Phase I clinical trials, the National Agency for Medicines must be provided with the toxicological data referred to in ICH M3 (CPMP/ICH/286/95) and ICH S7A (CPMP/ICH 53 9/00). In addition, note should be taken of other relevant guidelines issued by the European Commission, CPMP and ICH.

Relevant data from earlier clinical trials in human subjects must be submitted to the National Agency for Medicines before Phase II, III and IV trials. Specifically, the instructions given in "ICH Topic E 8. General Considerations for Clinical Trials CPMP/ICH/291/95" must be noted.

## **3. Manufacture, import and distribution**

### **Manufacture and import**

The manufacture and release of medicinal products used in a clinical trial on medicinal products (investigational medicinal products) in the EU/EEA is subject to a manufacturing authorisation granted by a competent supervisory authority for medicines. A corresponding authorisation is also required of the importer of investigational medicinal products manufactured outside the EU/EEA.

Investigational medicinal products must be manufactured in accordance with the principles on Good Manufacturing Practices (GMP) in respect of medicinal products implemented in the EU and observing rules issued separately concerning investigational medicinal products (*EUDRALEX Volume 4 – Medicinal Products for Human and Veterinary Use: Good Manufacturing Practice*, <http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/homev4.htm>)

Moreover, it must be noted that pharmacies, hospital pharmacies and pharmaceutical wholesalers may only import into Finland investigational medicinal products that have already been released on the market in the EEA/EU. Private individuals may not import investigational medicinal products into Finland. All aspects of the importation, storage and delivery of medicinal products used in clinical trials shall comply with relevant legislation.

### **Manufacturer in Finland**

In Finland, investigational medicinal products must be manufactured by a manufacturing authorisation holder or a unit authorised to manufacture medicinal products for clinical trials. The operating licence of the manufacturing authorisation holder or unit authorised to manufacture medicinal products for clinical trials must cover the pharmaceutical form used in the trial. A corresponding licence is also required when investigational medicinal products are imported directly into Finland from outside the EEA/EU.

A pharmacy or auxiliary pharmacy, a hospital pharmacy or a dispensary may only manufacture investigational medicinal products for its own use. Under section 15a of the Medicines Act, such manufacturers must submit a notification to the National Agency for Medicines on the manufacture of a medicinal product for a clinical trial before commencing such manufacture. The notification shall provide data on the medicinal product, its pharmaceutical form, the trial code, an estimate of production volumes and a brief account of the quality control and release procedures.

No licence or GMP certificate needs to be submitted to the National Agency for Medicines in the case of above-mentioned manufacturers that conform to the provisions of the Finnish Medicines Act.

### **Manufacturer abroad**

The manufacturer of and/or importer and party releasing the investigational medicinal products in the EEA/EU must be a manufacturing authorisation holder located in the EEA/EU, for which a copy of the current pharmaceutical factory operating licence or GMP certificate issued by the EU authority supervising the activity must be submitted. The licence or certificate must cover the manufacture/importation/release in the EEA/EU of the pharmaceutical form to be used in the trial. In addition, a notification must be provided concerning the qualified person, as referred to in Directive 2001/83/EC, responsible for the release and certification of the medicinal products for the trial. The said qualified person shall sign an affirmation that the said investigational medicinal products have been manufactured in accordance with GMP as required in the EU.

In respect of those manufacturers of the investigational medicinal product located outside the EEA/EU, the qualified person shall issue an affirmation containing the information necessary to the National Agency for Medicines to assess the manufacturer's GMP compliance and the need for a GMP inspection by the authorities. GMP compliance and the need for inspection is assessed by the National Agency for Medicines on a case by case basis on the basis of the information provided on the manufacturer and a risk assessment based on the characteristics of the trial. The principles of the Commission instructions *Compilation of Community Procedures on Inspection and Exchange of Information* published on the EMEA website (<http://www.emea.europa.eu/Inspections/GMPCompproc.html>) shall be observed in the risk assessment. Factors taken into consideration in the risk assessment include:

- pharmaceutical form and type of investigational medicinal product,
- number of trial subjects and duration of treatment,
- the number of trials conducted using the same manufacturer's medicinal products,
- GMP inspections and/or supervision of licensed operations performed by the competent supervisory authority for medicines of the relevant country
- the system of licensing of quality control tests performed outside the EEA/EU, if any

## **4. Vaccines**

The Vaccine Safety Unit of the National Public Health Institute releases the batches of vaccines for use in clinical trials on medicinal products in Finland. For this purpose, it shall be provided with the manufacturer's own analysis certificates and the relevant batch release certificates for the vaccine.

If a vaccine that has marketing authorisation is used as a reference or to supplement to vaccination programme and an EU Official Control Authority Batch Release Certificate is available for the said batch, no other batch documentation is required.

### APPENDIX 3. LINKS

#### Legislation

National Code of Statutes <http://www.finlex.fi/>  
Medicines Act  
Act on Patient Status and Rights  
Act and Decree on Medical Research  
Personal Data Act  
Genetic Engineering Act and Decree

#### Ethical guidelines

Finnish Medical Association <http://www.laakariliitto.fi/etiikka/>  
WMA Declaration of Helsinki  
Other WMA declarations  
Other ethical guidelines

Council of Europe <http://www.coe.int/defaultEN.asp>  
Convention on Human Rights and Biomedicine

National Advisory Board on Health Care Ethics (ETENE) <http://www.etene.org/>  
and its Medical Research Ethics section (TUKIJA)  
ethical evaluation  
investigations involving children  
requests for Ethics Committee opinions  
DNA investigations  
withdrawal periods prior to pregnancy

CIOMS <http://www.cioms.ch/>  
ethical guidelines  
adverse reaction report form CIOMS-I

Guidance for clinical trials on medicinal products  
EMA and ICH guidelines <http://www.emea.europa.eu/index/indexh1.htm>  
Good Clinical Practice (GCP)  
quality of medicinal products (quality)  
clinical trials (efficacy)  
preclinical trials (safety)  
adverse reactions (pharmacovigilance)  
biotechnology

European Clinical Trials Database EudraCT <http://eudract.emea.europa.eu/>  
acquisition of EudraCT number  
notification form for clinical trials on medicinal products  
forms for substantial amendments and end of trial notifications

EudraVigilance <http://eudravigilance.emea.europa.eu/highres.htm>

Detailed instructions on clinical trials, Eudralex Volume 10 <http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/homev10.htm>

European Commission guidelines and Directives [http://ec.europa.eu/enterprise/pharmaceuticals/index\\_en.htm](http://ec.europa.eu/enterprise/pharmaceuticals/index_en.htm)

Good Manufacturing Practice (GMP)  
Good Clinical Practice (GCP)  
detailed instructions for clinical trials on medicinal products

Office of the Data Protection Ombudsman  
Guidance material relating to the Personal Data Act

<http://www.tietosuoja.fi>

MedDRA

<http://www.meddrasso.com/>