

Good Clinical Principles (GCP) Standards in Conduct of Clinical Trials in Georgia

Nikoloz Gongadze, Levan Shalamberidze, Zaza Chapichadze

Pharmacological Committee, Ministry of Health of Georgia

Abstract

Background: This article presents the principles for carrying out clinical trials of drugs in Georgia in compliance with the international standards and the Declaration of Helsinki of the World Medical Association and WHO Good Clinical Practice standards. Methods: The review of 7 international multi-center clinical trials in Georgia and the new legislation of Georgia and European guidelines in this field are presented in the article. The ways of adaptation and implementation of this rules in Georgian practice are discussed. Ethical, regulatory, and other aspects required by international law are considered from the point of view of Georgian Drug and Pharmacy Law. Results: all international multi-center clinical trials conducted in Georgia confirms to the international standards and the Declaration of Helsinki of the World Medical Association and WHO Good Clinical Practice standards.

Keywords: *GCP, Good Clinical Practice, Ethical Committee, informed consent, clinical trials*

Introduction

This article presents the principles for carrying out clinical trials of drugs in Georgia^{1,2} as well as the requirements that must be considered to assure that the trials are carried out in compliance with the international standards and the Declaration of Helsinki of the World Medical Association. Accordance with WHO Good Clinical Practice standards and legislation of other European countries the GCP standards of conduct of clinical trials has started to be effective since 1997^{3,4}.

The purpose of GCP is to protect the interests of patients, investigators and the society by ensuring that only adequately planned and conducted clinical trials are carried out^{5,6,7}. Providing a competent supervision over the whole procedure of the clinical trial minimizes the hazards and risks that can create serious ethical problems.

GCP should be apply to all studies concerning clinical evaluation of medicinal products with the aim of systematically providing or verifying knowledge on the clinical effect and/or side effects of medicinal products (pharmacodynamics) and to studies of the fate of medicinal products in the human organism (pharmacokinetics).

The coordinator of clinical trial (manufacturer of the drug or responsible investigator) must use GCP in studies when a drug under investigation has not been registered and permitted for general use in Georgia; new effects, doses, administration methods or duration of administration, a new combination of drugs is use that have been not investigated before or groups of patients are studied to whom the drug has not been previously administrated (children, elderly etc.); the research lasts for long time and/or involves a large number of patients.

According to the new regulations GCP should apply also to studies in which a medicinal product is used solely to induce a known and well documented effect of the medicinal product and where no data are compiled concerning the medicinal product (the medicinal product is used as a tool).

Clinical trials of drugs can be conducted after the purpose of the research has been medically and scientifically justified and on a sufficient pharmacological, toxicological, pharmaceutical and chemical knowledge about the investigated drug.

The investigator, who performs clinical trials, guarantees the competence, safety and conformity of the trials to approved plans. The responsibility for clinical trials of drugs must always rest with a physician. If these conditions are not available, clinical trial of drugs should not be allowed to begin.

Qualification of the Trialists

The doctor, conducting the clinical trial of the drug must have sufficient experience and knowledge in the clinical field and about the disease in the treatment of which the drug will be administered. The responsibility for performing the trial on a competent level during its course rests with doctor who signs the application for beginning the trial.

The whole personnel, involved in the clinical trial must be fully informed about the properties, effects and side effects of the investigated drug. The research team must include experts in the field of pharmacology and statistical data processing. The less the investigated drug has been experimented on people, the more it is necessary to involve experts in clinical pharmacology and adverse drug reaction monitoring in carrying out the trial.

Clinical trials are as a rule carried out in hospitals. The clinical trials of the first and second phase are carried out in big hospitals and normally in co-operation with the clinical faculty of the corresponding university. If the purpose of the trial is to evaluate the effect of the new drug in conditions of a dispensary, the research of the third and fourth stage can also be carried out in an outpatients and doctor's office.

Qualification of the Center

The venue of clinical trial or the medical institution should provide accessible scientific and ethical level of clinical trial. The staff with scientific degree and experience, diagnostic and laboratory equipment, medical practice license documents, conclusion of supervised regulatory body about the possibility to

conduct clinical trial in accordance with GCP (requirements of patients written informed consent, archiving of documentation, keeping the records, etc) should be presented at site. The responsible doctor (preferably clinical pharmacologist) experienced in conduction of clinical trials, familiar with computing and fluent in one of foreign languages should be appointed as a principle investigator.

Requirements Concerning the Protocol

The Protocol must be enclosed concerning the chemical, pharmaceutical, animal pharmacological, toxicological and human pharmacological properties of the product as well as information on the existing clinical experience. The documentation could be submitted as a summary - e.g. as an "Investigator's Brochure". It is necessary, that the sponsor establish written standard operating procedures to comply Good Clinical Practice.

Changes of or amendments to the protocol (changes in dosage, treatment period, number of patients/volunteers, trial design, inclusion and exclusion criteria, effect parameters and sampling procedures, etc.) must be submitted to the local Ethical Committees in the same version before the changes or additions are implemented. Furthermore, considerations on the possible influence of the changes on the final result of the trial must be submitted if patients have been entered into the trial before the changes are implemented.

Ethical Committees

All medical scientific research projects can be carried out only with the consent of the ethical committee, proceeding from the Declaration of Helsinki.

An ethical committee is an independent body that consists of representatives of different spheres of life who must be sufficiently competent to assess the possibility of carrying out biomedical research and its safety under current conditions (see Georgian Drug Law, chapter II, article 8, Protection of the Clinical Trial Subject's Rights).

The activity of an ethical committee has been determined by its statute and its purpose is the protection of interests and rights of human subjects (both healthy and sick) in clinical trials and complementation on new methods and means of treatment.

Procedures for Obtaining Informed Consent

The written and oral informed consent shall be obtained from patients/volunteers participating in clinical trials. Healthy or sick human subjects can be used in clinical

trials only with their free-willing consent. Patients can be involved in the trial only after they have been informed comprehensibly and in detail about the essence of the trial. If it has been impossible to obtain informed consent, it must be preceded on the basis of the recommendations of the Declaration of Helsinki of the World Medical Association.

Human subjects are free to withdraw their consent at any time. The doctor, performing the clinical trial guarantees that refusal from participation in the trial will never interfere further treatment of the patient.

In obtaining the informed consent it is recommended that the human subjects are informed both verbally and in writing and that sufficient time is left for deciding. The informing of human subjects should include:

- characterization of the trial, methods of scientific research
- type, purpose and methods of trial study
- possible hazards or inconveniences
- possible alternative treatment
- conditions under which the participation of the human subjects will be discontinued
- a written statement that the participation is voluntary and that withdrawal from the participation at any moment is possible
- a written statement that participation in the trial is confidential
- a requirement that a human subject reports of all changes in his or her health that appear during the trial
- an agreement to give up using simultaneously other medicaments (and alcohol)
- a written statement that the human subject has read through and understands the information above

All the personnel, engaged in a clinical trial of a drug (pharmacy, laboratories, departments, consultants, etc.) must be informed in due manner by the doctor who conducts the clinical trial about the ethical aspects of the trial.

Both the medical doctor, responsible for the clinical trial, and the personnel, engaged in carrying out the trial, must ensure that it is carried out in conformity with the all ethical requirements, enunciated in GCP.

Notification of Adverse Reactions

Adverse drug reaction is a reaction which is noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis or therapy of disease or for the modification of physiological function. In the cases of clinical trials injuries by overdosing, abuse/dependence and interactions with other medicinal products should be considered as adverse drug reactions.

Serious adverse drug reaction is an adverse drug reaction which is fatal, life-threatening, disabling, or which results in in-patient hospitalization or prolongation of hospitalization. Also congenital malformations and occurrence of malignancies are considered as serious adverse events. Serious adverse drug reactions shall immediately be reported to the drug regulatory authority and study coordinator.

Serious adverse drug reactions occurred abroad should be reported if they are supposed to have consequences for the trial in progress.

Confidentiality and Source Document Checks

All documentation with patient information and information on clinical trial should be treated as confidential. There are special regulations concerning access to source documents for monitors, auditors or/and inspectors and all these issues should be solved according the WHO GCP procedures.

The investigator must be prepared to receive and be available for periodic visits by the monitor(s), audit(s) and clinical inspectorate, submit all necessary documents and accept the implications of such visits for quality assurance.

According the WHO GCP standards and instruction of the Ministry of Health all documents on clinical trial should be archiving during 5 years after termination of trial.

Conclusion

All international multi-center clinical trials conducted in Georgia confirms to the international standards and the Declaration of Helsinki of the World Medical Association and WHO Good Clinical Practice standards.

References

1. N. Gongadze, Z. Chapichadze. Georgian chapter in: "International Clinical Trials- A Guidebook and Compendium of National Drug Laws". edited by Dominique Brunier and Gerhard Nahler, Interpharm Press, Denver, Colorado, USA, 1999, pp. 309-333.
2. Z. Chapichadze. Georgian Drug Policy and Pharmacy. Newsletter of the European Society of Clinical Pharmacy, N 78, June 1997, p. 9-10.
3. Meyboom RHB, Royer RR. Causality assessment in the European Community. Pharmacoepidemiology and Drug Safety 1999; 1:87-97.
4. Hansson L, et al. Principal results of the Hypertension Optimal Treatment (HOT) randomised trial. Lancet 2000; 351: 1755-62.
5. Good Clinical Practice for Trials on Medicinal Products in the European Community. CPMP Working Party on Efficacy of Medicinal Products, Commission of European Communities; Brussels 1991: Document 111/3976/88-EN (Final).
6. Official Journal of the European Communities. Clinical Documentation. Document L270/48, Brussels 1991: Part 4
7. Hutchinson D.R., Organising your practice for clinical trials. Medical Monitor 1989; 16 June: 33-34.

Внедрение стандартов правильной клинической практики (GCP) в Грузии

Николоз Гонгадзе, Леван Шаланберидзе, Заза Чапичадзе

Комитет фармакологии Минздрава Грузии

Р Е З Ю М Е

Основой этой статьи является оценка клинических исследований проводившихся в Грузии в соответствии с Хельсинской декларацией медицинской ассоциации мира и стандартами правильной клинической практикой декларируемой ВОЗ. Было рассмотрено 7 интернациональных мульти-центровых клинических исследований проводившихся в Грузии и новое законодательство Грузии и европейское руководство отражавшее в этой статье. В этой статье обсуждаются пути адаптации и внедрения новых правил. Этические, регуляторные, и другие аспекты требующиеся по международным законам рассматриваются с точки зрения локальных лекарств и законов. Результаты: Все интернациональные мультицентровые исследования проводившиеся в Грузии соответствуют международным стандартам и с хельсинской декларацией медицинской ассоциации мира и стандартами правильной клинической практикой декларируемых ВОЗ.

Ключевые слова: *правила правильной клинической практики, этические комитеты, информированное согласие, клинические исследования*