Local Knowledge
for Global Business

www.gratanet.com

Common market of medicines in the Eurasian Economic Union: clinical trials

On 17 July 2018, the Board of the Eurasian Economic Commission (EEC) adopted the following acts aimed at regulation of the general market of medicines in the Eurasian Economic Union (EAEU):

- Recommendation by the EEC Board No. 11 'On the Guidance for General Clinical Trials Issues';

- Decision of the EEC Board No. 113 'On Approval of the Guidance for the Validation of Analytical Methods for Testing of Medicines'.

1. The Guidance for General Clinical Trials Issues

The Guidance for General Clinical Trials Issues is recommended for use by the EAEU member states after 6 months from the date of its publication:

- when conducting clinical trials of medicinal products for their registration in accordance with the Rules for Registration and Examination of Medicines for Medical Use approved by the Decision of the EEC Board No. 78, dated 3 November 2016;

- when bringing the registration files of medicines in compliance with these Guidance.

1.1 Clinical Trials Classification

Clinical trials are classified according to the order of their conduct during the clinical development of a medicine, or in accordance with their objectives.

The Guidance distinguishes the following types of clinical trials depending on their objectives:

1) Study of the pharmacological properties of a medicine;

2) Pilot therapeutic study;

3) Confirmatory therapeutic study;

4) Study of therapeutic use.

According to the Guidance, the fundamental principle of consistently conducted clinical trials of medicines is the effect of the previous trials results on the subsequent trials.

1.2 Phases of the Clinical Development of a Medicine

Clinical development of a medicine is meant a process consisting of four phases (I-IV development phases).

Under the Guidance, the concept of 'phase' shall be considered as a characteristic of the process of developing a medicine rather than a set of requirements therefor. Besides, the phases do not imply a strict order of trials because the development plan represented by a strict order of trials is unsuitable or optional for some medicines. The Guidance recommends using the

classification based on the objectives of the trial.

The development of medicines shall be a logical step-by-step process where previous results with a small number of participating humans are used to substantiate and plan for larger well-designed trials. It is required to establish characteristics of a new medicine at an early stage and based on the established profile to develop a further study plan.

Within the development phase I, the most typical type of trials is the study of the pharmacological properties of a medicine with human participation.

For development phase II, the most typical type of trials is a pilot therapeutic study, which is mainly aimed at revealing the therapeutic effectiveness of a medicine for patients.

Within the development phase III, the most typical type of trials is the confirmatory therapeutic study to confirm the therapeutic benefit of the medicine.

The development phase IV may include any trials (in addition to the standard monitoring) conducted after registration and affecting approved indications. Such trials are required to optimize the use of the medicine and must have sound scientific objectives. Such trials generally involve the study of additional drug interactions, dose-effect studies, and safety studies aimed at confirming the use according to the approved indication.

1.3 Protection of Trial Subjects

The safety of human subjects shall be provided, in particular, by:

1) submission of the results of preclinical or previous clinical trials confirming the safety of the planned clinical trial to the competent authority of the EAEU member state prior to the clinical trial;

2) consideration in the course of the medicine development of the results of clinical trials and safety assessment thereof again with respect to the subjects of toxicological and clinical trials;

3) timely and proper change of the planned and (if necessary) ongoing clinical trials based on the results of clinical trials.

Some groups of patients (in particular, those with renal and hepatic insufficiency, elderly patients, patients of different ethnic groups) may require additional studies due to special circumstances that need to be taken into account during the medicine development, or due to the expected need for modification of the dose or dosage regimen compared with the same for the general population in determining the benefit-risk ratio.

If the medicine is planned for paediatric use, examination thereof in the relevant age groups is required.

1.4 Principles of Clinical Trials in the Development of Medicines

Before any clinical trial, each part thereof must be described in the protocol, as indicated in the Rules for Good Clinical Practice.

When making changes (amendments) to the protocol, such changes (amendments) shall be clearly justified.

When conducting clinical trials, it is necessary to report and document in a timely manner the undesirable reactions that arise during the trial.

The Guidance establishes the principles that shall be observed when planning objectives, design of a clinical trial and preparing

a report thereon, in particular, the ones provided below.

a) Design

The trial's design shall be selected to obtain the required information (e.g., parallel, cross, factor, dose-escalation or dose-effect ratio), in accordance with the Guidance for selection of the medicine dose, Guidance on the principles of biostatistics use in clinical trials, guidance on the principles of selection of the control group in clinical trials approved by the EEC Council, and the Rules for Good Clinical Practice.

To achieve this goal, the appropriate methods of comparison shall be used and a sufficient number of subjects shall be engaged.

b) Selection of Trial Subjects

When selecting the trial subjects for the early development phase, the development stage and the tested indication, as well as the results of preclinical and previous clinical trials shall be taken into account.

As a rule, the participation of subjects in more than one clinical trial at the same time is unacceptable, but there can be justified exceptions.

The number of trial subjects depends on the investigated disease, the trial objective, and its endpoints. The statistical estimate of the sample size shall be based on the expected therapeutic effect, data variability, (low) probability of error (Guidance for the principles of biostatistics used in clinical trials), as well as the required information, patient groups or secondary endpoints.

c) Selection of the Control Group

The proper control groups shall be engaged in the trials. Comparisons are performed with placebo, lack of treatment, active control or other doses of the medicine under trial. The choice of comparison method also depends on the trial objective.

The Guidance contains as an annex Recommendations on the Amount of Exposure in Population Required to Assess the Clinical Safety of Medicines intended for long-term treatment of non-life-threatening conditions.

2. The Guidance for the Validation of Analytical Methods for Testing of Medicines

The Guidance defines the rules for validation of analytical methods for testing medicines, as well as a list of characteristics to be assessed when validating such methods and including them in registration files submitted to the competent authority of the EAEU member states.

The analytical procedure is defined as a method for conducting testing of medicines, which includes a detailed description of the order of actions required for analytical testing.

The validation of the analytical method for testing of medicines is to document the confirmation of its suitability for the intended purpose.

The Guidance overviews validation approaches for the four most common types of analytical methods:

1) identification tests (authenticity);

2) quantitative tests for impurities content;

3) limit tests for the control impurities;

4) quantitative tests of the active moiety to determine the active part of the molecule of the active substance in the test sample.

The Guidance provides for the characteristics to be taken into account in the validation of analytical methods, and some approaches and recommendations to establish various validation characteristics of each analytical method.

In addition, the Guidance establishes cases when re-validation can be required: when changing the synthesis scheme of the pharmaceutical substance or the composition of a medicine.

The Guidance shall enter into force in 6 days after its official publication.

****

Both Guidances relate to the third level acts aimed at harmonisation in the application of the requirements for medicines circulation within the EAEU. In total it was planned to adopt 67 third level acts in 2016-2018. The other guidance and recommendations to be adopted in 2018 specify specific issues of the development and study of medicines, production thereof, as well as detail and formalise inspection procedures, provide instructions for medicines manufacturers on the formation of medicines dossier, and regulate a number of issues related to the production of medicines from medicinal plant material [1].

---

[1] https://pharmvestnik.ru/publs/lenta/v-rossii/kollegija-eek-utverdila-rjad-23-7-18.html

Download

Contacts:
Yana Dianova
Director of the Corporate and Commercial Law Department, GRATA International (Moscow)
Tel: +7 (495) 660 11 84
E-mail: ydianova@gratanet.com

Industries

PHARMACEUTICALS & HEALTHCARE

Locations

RUSSIA

Key contacts

Yana Dianova

Counsel

Moscow, Russia

+7 495 660 1184

+7 906 734 6817

ydianova@gratanet.com