T.C. SAĞLIK BAKANLIĞI
TÜRKİYE İLAÇ VE
TIBBİ CİHAZ KURUMU

GUIDELINE ON RISK-BASED GOOD CLINICAL PRACTICE INSPECTIONS

Department of Medicines Inspection

2022

1. Purpose:

The purpose of this guide is to define and standardize processes related to risk-based good clinical practice inspections.

2. Scope:

This guide covers the clinical trials submitted in the marketing authorization application, including the BA/BE studies, the ongoing clinical trials and the institutions, organizations and individuals related to these trials.

3. Basis:

This guide has been prepared on the basis of paragraph 1 of article 22 of the Regulation on Clinical Trials of Pharmaceuticals and Biological Products (Amendment: RG-13/09/2015-29474), published in the Official Gazette dated 13.04.2013 and numbered 28617.

4. Abbreviations:

The meanings of abbreviations included in this guideline are as follows:

Agency	Turkish Medicines and Medical Devices Agency,
BA/BE	Bioavailability/Bioequivalence,
CRO	Contract Research Organization,
ESY	Electronic Process Management,
GCP	Good Clinical Practice
IMP	Investigational Medicinal Product
Phase 1	Phase 1 clinical trials

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5. Genel Hususlar:

GCP inspections can be carried out in any of the situations listed below::

- Before, during or after the clinical trial is conducted,
- In order to verify the marketing authorisation application,
- For follow-up purposes after marketing authorisation.

Any clinical trial included in the marketing authorisation application file may be subject to inspection. In this way, a GCP inspection can be carried out for a "For Cause" or within the scope of a routine inspection. The GCP inspection request to be made by the Agency's Department of Medicines Marketing Authorization and/or Department of Herbal and Support Products is determined depending on the risk assessment to be made by the relevant departments.

Purpose of aforementioned GCP inspections:

- To determine whether the clinical trial is carried out in accordance with the relevant legislation and GCP Guidelines,
- To provide answers in cases where it is determined that the answers to the questions that arise during the evaluation process can best be provided through inspection,
- To determine whether the data presented in the file is reliable and accurate.

GCP inspections can be triggered for various reasons:

- To verify the GCP compliance statement,,
- For a more detailed examination of the clinical trials in terms of the following issues::
    - The importance of the clinical trials in the application and the risk situation,
    - Inclusion of vulnerable subjects or other ethical concerns,
    - Concerns about the investigational medicinal product,
    - Concerns about the reliability and accuracy of data (e.g. if the volunteer recruitment program is out of the ordinary, when efficacy or safety results are inconsistent with the results of other studies, when the results of one center differ significantly from the others, serious findings in previous GCP inspections of the center and/or institution and/or when GCP non-compliance is reported continuously).

However, guidelines ("Guidelines for Identifying Triggers and Scope of Inspections for Routine and/or Cause-Related Inspections" and ""Guideline on Triggers for Inspections of Bioavailability/Bioequivalence Studies") should be considered to provide an overview of potential triggers that can be identified at different stages of the assessment process.

6. Routine Inspections:

Routine GCP inspections are inspections carried out for the purpose of routine control of GCP compliance without any specific trigger or concern. In routine GCP inspections, marketing authorisation application, clinical trial and clinical trial centers can be selected for inspection as a result of the risk assessment to be made by taking into account the issues specified in the relevant guidelines ("Guidelines for Identifying Triggers and Scope of Inspections for Routine and/or Cause-Related Inspections" and ""Guideline on Triggers for Inspections of Bioavailability/Bioequivalence Studies").

The inspections after the opening inspections of phase 1 and BY/BE centers which operating in domestically are carried out within the scope of routine inspection, taking into account the issues specified in the relevant guides ("Guidelines for Identifying Triggers and Scope of Inspections for Routine and/or Cause-Related Inspections" and ""Guideline on Triggers for Inspections of Bioavailability/Bioequivalence Studies").

Within the scope of routine inspection, the selection of the generic and original medicinal product registration application file is made on a risk-based basis by the Department of Medicines Marketing Authorization and/or Department of Herbal and Support Products. While determining the centers to be inspected and the scope of the inspection can be contacted with Department of Medicines Inspection. In order to ensure that the current inspection resource is used in the best way, the points specified in the aforementioned guidelines are taken into account. In line with the inspection request made by the aforementioned Departments, it is decided by the Vice Presidency of Inspectorate whether an inspection is required or not.

The inspection request is sent to the Vice Presidency of Inspectorate via the ESY system by the Department of Medicines Marketing Authorization and/or Department of Herbal and Support Products. The inspection request should clearly include the reasons and scope of the inspection, the site(s) to be inspected and, if any, a list of specific questions to be addressed during the inspection and other inspection-related issues. In line with the inspection request made by the aforementioned Departments, whether an inspection is required or not is decided by the Vice

Presidency of Inspectorate, taking into account the inspection resources. After the inspection decision, inspection planning is made by the Department of Medicines Inspection.

In order to include ongoing clinical trials in the routine inspection program, the inspection request is sent to the Vice Presidency of Inspectorate via the ESY system by the Department of Clinical Trials, taking into account the provisions of the relevant guideline. In line with the inspection request made by the aforementioned Departments, whether an inspection is required or not is decided by the Vice Presidency of Inspectorate, taking into account the inspection resources. After the inspection decision, inspection planning is made by the Department of Medicines Inspection.

7. For Cause Inspection:

Such inspections are triggered inspections requested by assessors due to a concern about deviation from GCP in the marketing authorisation application evaluation process, in all clinical trials conducted in relation to an IMP, or in a study conducted at a particular centre. In addition, for ongoing studies, an inspection request is made by the Department of Clinical Trials due to a concern about deviation from the GCP.

The inspection request with triggers defined for clinical trial and clinical trial center that clearly includes the reasons and scope of the inspection, the center(s) to be inspected and, if any, a list of specific questions to be addressed during the inspection, and other inspection -related issues is sent to the Vice Presidency of Inspectorate via the ESY system by the Department of Medicines Marketing Authorization, Department of Herbal and Support Product or Department of Clinical Trials. In line with the inspection request made by the aforementioned Departments, whether an inspection is required or not is decided by the Vice Presidency of Inspectorate, taking into account the inspection resources. After the inspection decision, inspection planning is made by the Department of Medicines Inspection.

8. Announcement of Inspection:

In GCP inspections carried out within the scope of routine inspection, the sponsor, CRO, investigator and/or other relevant parties within the scope of the trial may inform before the planned inspection date. “For Cause” inspections can be made either with prior notice or without notice.

9. Miscellaneous and Final Provisions

9.1. Enforcement:

This guideline goes into effect on the day of approval.

9.2. Execution:

The provisions of this Guide are executed by the President.