REPUBLIC OF TÜRKİYE
MINISTRY of HEALTH

TÜRKİYE MEDICINES AND
MEDİCAL DEVICES AGENCY

Guidelines on Application for Good Clinical Practice Inspections

Version : 1

Date : 25.11.2021

1. **Purpose:**
   The purpose of this guideline is to point out issues concerning the applications that must be submitted to the Department of Medicine Inspection for good clinical practice inspections and associated processes.

2. **Scope:**
   This guideline outlines the procedures for submitting applications to the Department of Medicine Inspection for good clinical practice inspections and associated processes.

3. **Basis:**
   Articles 11 (2) and 22 (1) of the Regulation on Clinical Trials of Medicinal And Biological Products served as the foundation for the establishment of this guide.

4. **Definitions/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,
Department	Department of Medicines Inspection
EAS	Electronic Application System,
EPM	Electronic Process Management,
GCP	Good Clinical Practices,
Ministerial	Ministry of Health,
Phase 1	Clinical trial phase in which the investigational product is used on humans for the first time
Unit	GCP Unit

5. **General Considerations:**

Phase 1 clinical trials and BA/BE studies are conducted in research and development centers affiliated with the Ministerial or universities that have been approved by the Agency, have emergency response facilities, and meet uniquely established standards according to the relevant legislation. The inspections of the centers in question shall be performed within the scope of a routine inspection.

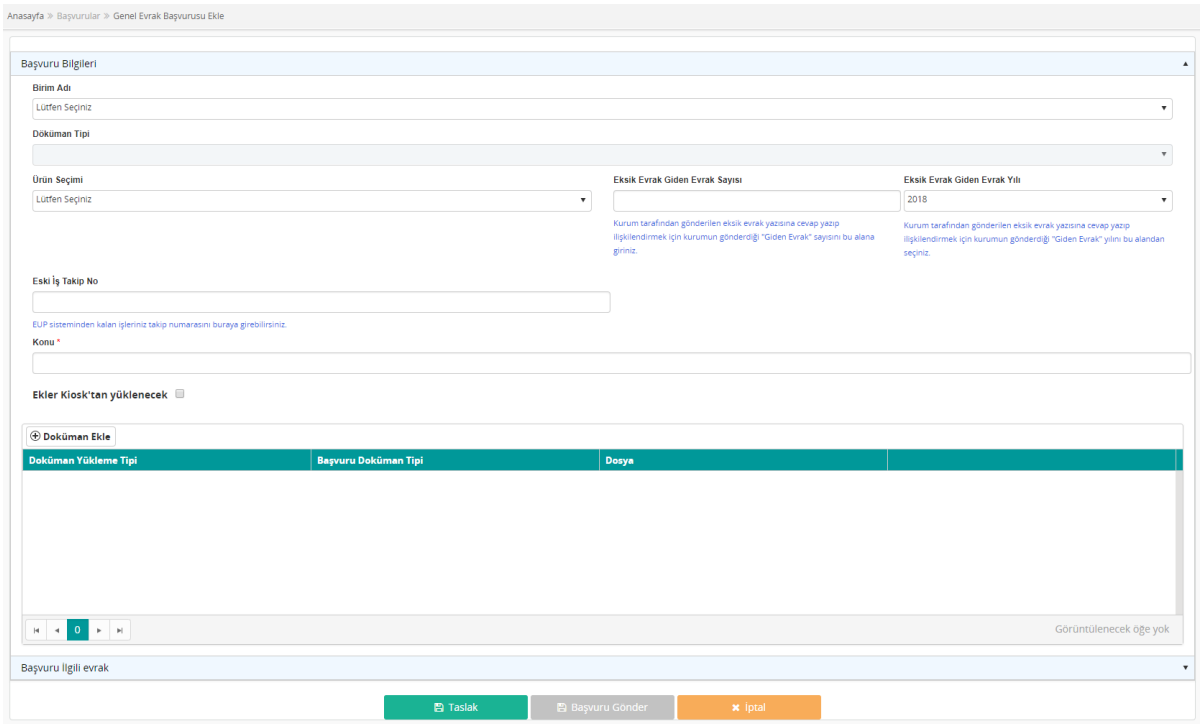
Inspections of BA/BE facilities that are located abroad, as well as sponsor and/or CRO inspections are carried out in line with their requests.

6. **Application for Inspections:**

Applications regarding inspection of centers established for the purpose of conducting Phase 1 clinical trials and BA/BE studies, as well as foreign voluntary BA/BE center and SAK inspections, are submitted electronically through EAS. Institution/organization and company registration to EBS is done via http://ebs.titck.gov.tr.

Applications regarding good clinical practices inspections and subsequent notifications are made through the electronic application system of our Agency. Applications and notifications are created in the EAS system by clicking "Applications -> Add General Document Application".

EAS General Document Application screen:



Fields	
Unit Name (required)	Good Clinical Practices (GCP/GLP) Inspection Unit
Document type (required)	After the unit name is selected, the document type concerning the general document application is selected from the drop-down menu of the active list. (e.g. Corrective and Preventive Action Notification)
Number of Missing Documents:	This is the field in which the number of missing documents are entered.
Year of the Missing Document	This is the field in which the year of missing documents is entered.
Subject (Required)	e.g. CAPA submission
Add Document	This shall be used to add documents and cover letters. The application-related documents shall be uploaded here. A minimum of one uploaded document with the "Cover Letter" "Document Upload Type" is required for the application to be properly saved. Additional application documents are uploaded here. This is how documents shall be uploaded: • Click the Add Document button, • The default selection for the document upload type is ""Cover Letter". (A maximum of one document with the type "Cover Letter" can be uploaded), • Click the Select button, • The file to upload is chosen in the newly opened window, • In order to attach a file to the cover letter click the Add Document button.

	• Document Upload Type is automatically selected as "Attachment". (Multiple documents with the type "Attachment" can be uploaded.) • Click the Select button, • The file to upload is chosen in the newly opened window, • The document upload process is completed.
Functions	
Draft	The general application is saved into the system in a way so it can be updated later.
Update	Updates the application which was saved as a draft.
Submit Application	The application is registered into the system. The date and number of the application is displayed.

Applications for inspections of domestically running centers may be submitted either directly via the centers themselves (Phase 1 BA/BE (domestic)) or by natural or legal entities authorized by such centers. Inspection applications of BA/BE centers operating abroad shall be submitted by natural or legal entities residing in Türkiye.

Applicants;

- If natural entities should hold a degree in pharmacy, medicine or chemistry, be qualified to practice their profession in Türkiye, and also have training and expertise in clinical trials.
- If legal entities should employ someone who has the qualifications listed in the preceding article and has knowledge and experience in clinical trials, as an "authorized person"

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6.1. Phase 1 Center Establishment Inspection Application

Inspection applications concerning the opening of Phase 1 centers operating domestically are submitted by filling out the "Phase 1 Clinical Trial Center Opening / Control Inspection Application Form" (Annex-1) and by selecting the document type "Establishment Inspection/ Control Inspection Application of the Centers where Phase I Studies are to be Conducted" and by uploading the application form together with a suitable cover letter and necessary documents listed in the form into the EAS.

6.2. BA/BE Center Opening Inspection Application

Inspection applications concerning the opening of a BA/BE center operating domestically are submitted by filling out the BA/BE Center (Clinical and/or Bioanalytical) Establishment/Control Inspection Application Form" (Annex-2) and by selecting the document type "Good Clinical Practices (GCP) for BA/BE Studies (Clinical and/or Bioanalytical Laboratory) Establishment Inspection/Control Inspection Application (Domestic)" in the EAS system and by uploading the application form with a suitable cover letter and necessary documents listed in the form into the EAS.

6.3. CRO/Supporting Control Inspection Application

Inspection applications concerning voluntary CRO inspection are submitted by filling out the Contract Research Organization Inspection Application Form" (Annex-3) annex to this guideline and by selecting the document type "Contract Research Organization Control

Inspection Application" in the EAS system and by uploading the application form with a suitable cover letter and necessary documents listed in the form into the EAS.

6.4. Compliance Certificate Application:

6.4.1. General Considerations:

In case BA/BE and/or phase 1 clinical research centers and CRO are found appropriate after the inspection in which their compliance with the relevant legislation is evaluated a Certificate of Conformity is issued by our institution.

6.4.2. Application:

The EAS system notifies the applicant that an application should be submitted to the Agency with a request for an accrual reference number so that a document may be sent to the proper center after the center's inspection has been completed.

An application for an accrual reference number request is made to the Institution by selecting the appropriate application document type (for phase 1 centers: Compliance Certificate for Centers where Phase I Studies are to be Conducted, for BA/BE centers: Good Clinical Practices (GCP) (Clinical and/or Bioanalytical Laboratory) Compliance Certificate for BA/BE Studies)) by the applicant.

If the proper application document type is chosen, the Department of Medicine Inspection will generate an accrual reference number in the EAS system and send it to the applicant's EAS system-registered email address.

Payment should be made using the reference number to the bank and account number specified in the current price list accessed from the "Price Tariff" tab under the "Important Lists" heading on the website of our Agency.

6.5. Other Applications:

Applications made after the inspection application to get information about the processes related to the application are made by selecting the "Application Tracking" document type in the EBS system.

7. Notifications:

7.1. Notifications on Changes:

Following the inspection, the Agency should be notified of the changes in the physical area, key personnel, and important contractual (3rd Stage intensive care service for Phase 1 centers), such as center relocation, the inclusion of a new physical area in the center, and/or closing/moving of an existing area, as soon as possible together with their justifications, and such period for notification should not exceed five (10) business days The aforementioned notification is created by using the "Notifications on Changes Form" (Annex-4) and by selecting the document type "Central Activity Notification." Whether or not the relevant change necessitates a new inspection is conveyed to the center within 15 days of the application being received by the Agency.

If the center relocates to a new address or a different area within the same building/campus, a re-establishment inspection shall be performed and a new compliance certificate shall be issued. In this case, depending on the type of center, an application is submitted in accordance with Articles 6.1 and/or 6.2.

7.2. Corrective and Preventive Action Notification:

Supporting documents for the center's corrective and preventive actions taken in response to deficiencies discovered during the inspection are created using the "Corrective and Preventive Action Notification Form" (Annex-5) together with cover letter, as well as the "Corrective and Preventive Action Notification" document type in the EAS system.

8. Examination of information and documents

The Good Clinical Practices Inspection Unit evaluates applications submitted electronically to the Department of Medicine Inspection via the EAS in terms of the type of application document and the suitability/completeness of the submitted documents. The Good Clinical Practices Inspection Unit will evaluate applications for a maximum of fifteen (15) working days after receiving them. The applicant is notified in writing about unsuitable/incomplete applications via the EPM system, and the missing aspects are expected to be eliminated. If any missing aspects of the applications have been eliminated, the evaluation process restarts. Eligible applications are included in the inspection program if they are inspection applications.

9. Miscellaneous and Final Provisions

Effective Date: This guideline goes into effect on the day of approval.

Execution: The provisions of this Guide are executed by the President .

GUIDELINE ANNEXES

ANNEX - 1	Inspection Application Form for Phase 1 Clinical Research Centers
ANNEX - 2	Inspection Application Form for Centers (Clinical and/or Bioanalytical) Where Bioavailability/Bioequivalence Studies are Conducted
ANNEX - 3	Inspection Application Form for Contract Research Organizations
ANNEX - 4	Notifications on Changes Form
ANNEX - 5	Corrective and Preventive Action Notification Form