EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

18 May 2020
EMA/INS/GCP/162006/2020

# Guidance on remote GCP inspections during the COVID-19 pandemic

This document is intended to provide guidance on the steps to be followed during remote good clinical practice (GCP) inspections.

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| Adopted by GCP IWG | 18 May 2020 |

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| **Keywords** | ***COVID-19, pandemic, GCP inspection, remote, virtual, distant, good clinical practice*** |

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# 1. Introduction

Verification of compliance with ICH GCP and applicable legislation is crucial in ensuring that the rights, safety, and wellbeing of trial subjects are protected, and that the clinical study data used to support marketing authorisations of medicinal products in the EU / EEA are accurate and reliable. Therefore, it is indispensable to continue conducting GCP inspections in the context of assessment of marketing authorisation applications (MAA) submitted to the European Medicines Agency (EMA), during crises like the COVID-19 pandemic.

ICH GCP E6 defines a GCP inspection as the act by regulatory authority(ies) of conducting an official review of documents, facilities, records, and any other resources that are deemed by the authority(ies) to be related to the clinical trial, and that may be located at the investigator site of the trial, at the sponsor's and / or contract research organisation's (CRO's) facilities, or at other establishments deemed appropriate by the regulatory authority(ies).

During the COVID-19 pandemic, on-site inspections may not be possible due to multiple factors such as difficulties and restrictions related to travelling between and within the borders of countries (including travel warnings / restrictions, border controls, transportation difficulties), restrictions to accessing facilities justified by health hazards and local authorities' recommendations / orders, as well as additional health risks for inspectors and inspectees.

To enable the continuity of GCP inspections requested by the Committee for Medicinal Products for Human Use (CHMP), this document provides guidance on conducting GCP inspections remotely during the COVID-19 pandemic.

The inspection team, in agreement with the CHMP requesting the inspection, should make a case-by-case decision on whether a remote inspection is considered appropriate and feasible. Remote inspections should follow the applicable procedures that already exist for coordinating, preparing and conducting GCP inspections requested by the CHMP, but should also take into consideration the limitations imposed by using a remote process and recognise that such a remote process cannot completely replace on-site GCP inspections.

The purpose of this document is to outline the requirements and specificities of remote GCP inspections identifying the points to be considered during the preparation, conduct, and reporting phase in this context.

# 2. Scope

In the context of this guidance, a remote / distant GCP inspection is defined as "the process of conducting inspections at a distance / virtually, supported by technology for communicating, sharing, reviewing, and developing documents and accessing systems, without the inspectors being physically present at the sites where the activities subject to an inspection have taken place / where the inspection would routinely be hosted".

Sponsors, CROs and service providers (e.g. medical imaging, central laboratories) in general, often have at their disposal advanced technologies, electronic systems and virtual working environments which facilitate remote staff or company locations worldwide to communicate systematically. These technologies may allow the necessary access for inspectors to the relevant systems (e.g. electronic trial master file (eTMF)) remotely and enable appropriate communication settings during inspection.

Remote inspections at investigator sites are not considered to be feasible, because a) it is crucial to avoid any additional burden (e.g. to provide access to appropriate paper-based documentation) on investigator site staff at this time, b) inspection of source documents may not be possible due to local legal requirements concerning accessibility and data protection and c) potential limited access to relevant electronic systems by investigational site staff and / or by inspectors.

# 3. Inspection initiation - impact analysis and feasibility assessment

For this phase the standard procedure for preparing GCP inspections requested by the EMA (INS-GCP-2) is applicable, but due to the nature of remote inspections, the preparation of the inspection will be significantly more demanding compared to on-site inspections. This necessitates an early contact with the trial sponsor / the applicant in order to explore the possibility to conduct this type of inspection.

Nevertheless, there may be many challenges on an organisation to support remote inspections. It is fundamental to assess whether the inspectee meets the technical requirements to provide remote access to electronic systems and maintain communication with and support to inspectors. The technical nuances of these systems as well as the IT policies (of the inspectee and regulatory authority(ies) performing the inspection) are likely to cause additional challenges and need to be duly taken into consideration.

When an inspection is requested by the CHMP, the rapporteur and co-rapporteur, together with the inspection team, taking into account the type of site, the scope and nature (routine or for cause) of the inspection, the activities delegated to CROs and service providers and inspection history of the inspectee, may decide that the requested inspection could be conducted remotely instead. Following the announcement of the CHMP inspection request the remote inspection feasibility will need to be assessed by the inspection team.

During the remote inspection initiation phase, the inspectee should provide detailed information as requested by the inspectors to allow a feasibility assessment by the inspection team, taking into account the computerised systems used for the clinical trial.

It is crucial to bear in mind that some electronic systems owned and managed by service providers, CROs and sponsors, may not be accessible remotely due to business confidentiality rules as these systems contain other organisations' (sponsors, vendors, third parties) information not related to the trial(s) subject or data to be inspected. Subsequently, contacting the organisation to be inspected is vital, in order to explore the availability of technology and established procedures that permits a remote inspection with appropriate mitigation strategies in place (e.g. for poor communication, interferences, non-optimal system performances and interruptions).

For feasibility assessment, the inspectee should also ensure the provision of remote technical support for inspectors for all computerised systems (e.g. eCRF[1], eTMF) during inspection preparation, conduct and reporting phase and build a functional reaction capacity to questions raised by inspectors. If the remote inspection is considered feasible, the remote inspection will be conducted and EMA should formally communicate this decision to the applicant.

If it is not deemed feasible to carry out a remote inspection, the inspection team shall communicate this fact to EMA, rapporteur and co-rapporteur without delay, and a proposal should be made by EMA,

[1] electronic case report form

rapporteur and co-rapporteur to the CHMP to determine in each case the most suitable course of action (e.g. adjust procedure timelines to facilitate an on-site inspection when restrictions are lifted).

# 4. Inspection preparation

After a positive feasibility assessment, and the decision to announce / prepare / conduct a remote inspection, inspectors should evaluate an approach to be followed during the preparation phase.

According to the standard procedure for preparing GCP inspections requested by the EMA (INS-GCP-2) this includes obtaining and reviewing documentation, and presentations (if required / applicable), and planning how to conduct interviews, and a tour of the facilities ("facility tour"), if applicable. The inspection plan, including the duration of the inspection and daily schedule should also be determined. Remote inspections require a more customised preparation by the inspectee and the inspection team as compared to on-site inspections. The functionality of critical communication pathways (direct access to critical / key computerised systems) should be tested prior to the start of the remote inspection. The inspectors should have read-only access, but not otherwise be limited. The expectations and requirements should be discussed and agreed on between the inspectee and the inspection team during the preparation phase. Please refer to the EMA GCP IWG Q&A #12[2].

## *4.1. Inspection setting*

Remote inspections could be longer in duration than on-site inspections given the particularities of this type of inspection and the fact that inspectors may need to control several systems simultaneously when conducting the inspection. Duration of daily sessions should be agreed between inspectors and inspectee and adherence to procedures in place by both sides. A host should be assigned by the inspectee to coordinate and manage further requests and queries during the inspection.

## *4.2. Team location*

A crisis situation may impede team members of inspectors / inspectee to be at the same location during the inspection. Notwithstanding regulatory authority guidance on remote working during the COVID-19 pandemic and the general principles to reduce the spread of COVID-19, the inspectors and experts (if applicable) should be in the same location, if possible. Additional considerations should be made, if the members of the inspection team are in different locations.

The latter may represent an additional challenge for both parties as the quality of the network, the different capacities of the internet bandwidth, in addition to e.g. the potential time zone difference, amongst other factors, can impair the inspection conduct and reduce the effectiveness of this method. Furthermore, the immediate feedback and reactions from inspectors may be impossible, if they are in different locations. Therefore, consideration should be given that inspectors can communicate via a secondary independent communication channel.

## *4.3. Technical requirements*

As mentioned above, inspectors should explore the technical capabilities of the situation / setting at the inspectee as well as the capabilities at their own location / agency. Usually, there are certain restrictions imposed by the regulatory agencies' IT departments on the use of additional software,

[2] https://www.ema.europa.eu/en/human-regulatory/research-development/compliance/good-clinical-practice/qa-good-clinical-practice-gcp

devices, applications and access to cloud computing services as well as file transfer protocols for downloading documents that could affect the planned inspection.

There are several software applications (apps), video conferencing systems, interactive tools for document sharing, instant messaging apps, whiteboarding apps and meeting platforms providing the users with more real time interactive communication tools that could enhance remote working.

Ideally, a video streaming system, embedded video conferencing or interactive tool for managing questions, queries and decisions, document sharing, or intuitive inspectors viewing tool, would facilitate all involved parties' work and avoid disruptions, overlapping of activities and optimise resources and time invested. A chat / instant-messaging platform should also be considered, in case of sound interferences.

Any recording (audio / video / screenshots) during the inspection process should be notified and agreed upfront between all involved parties.

### *4.4. Inspection agenda*

A detailed inspection agenda should be submitted in advance by the lead inspector to the inspectee in accordance with SOPs in place at his / her inspectorate. The agenda should list all (planned) sessions and anticipated time slots. Sessions that require subject matter experts to be present for interviews or to deliver presentations should be marked in the agenda.

## 5. Conduct of the inspection

The procedure for conducting GCP inspections requested by the EMA (INS-GCP-3) is applicable for this phase.

### *5.1. Opening meeting*

Many processes may need to be adopted to a remote inspection. Thus, the opening meeting should point out the particularities of a remote meeting setting. It is fundamental that the scope and logistics are understood by all parties involved. Delays and modifications should be taken into consideration. However, these should be kept to a minimum and should be under the control of the inspection team in order to cause the least disruption to the remote inspection process.

The inspectee should provide a list of attendees for the opening meeting. This process should be followed for any subsequent meeting / session.

### *5.2. Inspection*

Essential components of the inspection include interviews, presentations (by the inspectee) relating to the topics requested by inspectors in the agenda, documentation review and facility tours (if applicable).

As mentioned above, inspectees usually grant direct remote access to eTMF and eCRF systems in advance of the inspection, if requested. During on-site inspections clarifications, explanations and queries from inspectors are resolved at the facilities where the inspection takes place. During the conduct of a remote inspection, it is necessary to have remote access to the crucial electronic systems, especially to the eTMF and the eCRF as they are usually the most relevant repositories to inspect.

Thus, there are some important aspects to be considered. It is the inspectors' expectation to be able to review the eTMF (related) audit trails, activity logs and metadata in order to reconstruct its management since its deployment. Completeness, quality and timeliness of the retrieval of documents from the eTMF are therefore important during a remote inspection. Moreover, inspectors should be enabled to use export / save functions to retrieve documents from the eTMF. This could be provided through a sharing document platform or other media like email or a secure system after the applicable Quality Assurance (QA) checks by the document owner / subject matter experts have been performed.

It is recommended to use an electronic document request form that can be shared among the inspectee and the inspection team. The inspection team may request the inspectee to keep track of all requests and provide a regular update of the electronic document created.

It is important that sponsors / CROs provide remote technical support for inspectors, that the eTMF is robust and capable to support a remote inspection even if the eTMF is decentralised and managed from different locations and its content spread across different systems. It is important that inspectors can still gain access to (or via) a centralised system with one or several connected systems.

### *5.3. Closing meeting*

In accordance with the standard procedure for conducting GCP inspections requested by the EMA (INS-GCP-3), a closing meeting with the inspectee(s) should be held at the end of the inspection.

The inspection attendees list should be shared by the inspectee before the closing meeting or immediately afterwards.

## 6. Inspection reporting process

Inspection-derived records should be maintained, and the reporting of remote inspections will be followed as per the standard procedure for reporting of GCP inspections requested by CHMP (INS-GCP-4).

## References


- CPMP/ICH/135/95 Guideline for good clinical practice E6 (R2)
- Directive 2001/20/EC on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use
- Directive 2005/28/EC on 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
- Guideline on the content, management and archiving of the clinical trial master file (paper and/or electronic)
- Procedure for preparing GCP inspections requested by the EMA (INS-GCP-2): https://www.ema.europa.eu/documents/regulatory-procedural-guideline/ins-gcp-2-procedure-preparing-gcp-inspections-requested-emea_en.pdf

- Procedure for conducting GCP inspections requested by the EMA (INS-GCP-3): https://www.ema.europa.eu/documents/regulatory-procedural-guideline/ins-gcp-3-procedure-conducting-gcp-inspections-requested-emea_en.pdf
- Procedure for reporting of GCP inspections requested by CHMP (INS-GCP-4): https://www.ema.europa.eu/documents/regulatory-procedural-guideline/ins-gcp-4-procedure-reporting-good-clinical-practice-inspections-requested-chmp_en.pdf