

Points to Consider for Virtual Inspections – An Industry perspective

Executive Summary

The R&D-based biopharmaceutical industry has demonstrated that maintaining high-quality reliable supply is possible in the context of a pandemic through close coordination with national regulatory authorities (NRAs) and other stakeholders in the supply chain to prevent and mitigate shortages. Delays in approval of innovative medicines were however noted with some NRAs pushing back on scheduled pre-approval inspections.

The pandemic has also demonstrated that digital alternatives can support standard regulatory practices. They have demonstrated effectiveness and have now established their role as additional tools and can be an integral part of the regulatory frameworks that ensure the quality and efficacy of medicines and vaccines. Inspections normally carried out on-site by an inspector at manufacturing facilities by NRAs were successfully held using virtual tools. Virtual inspections can:

- Provide additional flexibility to NRAs, as virtual inspections can be carried out on non-consecutive days. NRAs can also review the relevant documentation ahead of a virtual inspection, at their own pace and prepare for targeted dialogue.
- Create more opportunities for both parties to exchange information, with industry experts from different locations e.g., a site and headquarters, to participate in real-time.
- Decrease environmental pollution by reducing travel while enabling business continuity.

We also acknowledge that, as with every tool, a virtual setting has limitations such as lack of direct interaction, body language or context, the need for additional preparation while having the increased possibility of technical issues impeding/delaying inspections, and potentially need for working between different time zones.

As technology advances, and experience is gained, the use of digital tools will become more and more prevalent in all fields of regulatory processes, and time will allow further evidence to be collected regarding safety and efficacy of such processes.

Introduction

The COVID-19 pandemic has resulted in governments imposing measures such as confinement, quarantine orders and travel restrictions that have impacted NRAs in their capacities to perform on-site GxP inspections. Consequently, a number of NRAs have adopted alternative tools including virtual (or remote) inspections elements to sustain the supply of high-quality medicines to patients. These innovative tools are likely to continue being used post-pandemic.

This paper is based on the biopharmaceutical research-based industry's experience to date with inspections conducted since the pandemic. It consolidates industry lessons learned from working with these inspection tools. It is meant to complement efforts ongoing in other industry organizations such as EFPIA^[1] and PhRMA^[2]. These recommendations can assist in carrying out an efficient and effective virtual inspection and can be developed further as more experience is gained and more data is collected.

Different options exist to allow a NRA to verify compliance of site operations in accordance with applicable laws and regulations. During conventional **on-site inspections**, inspectors are physically present at the manufacturing facility to assess the site's conformity with regulatory expectations and related GxP requirements.

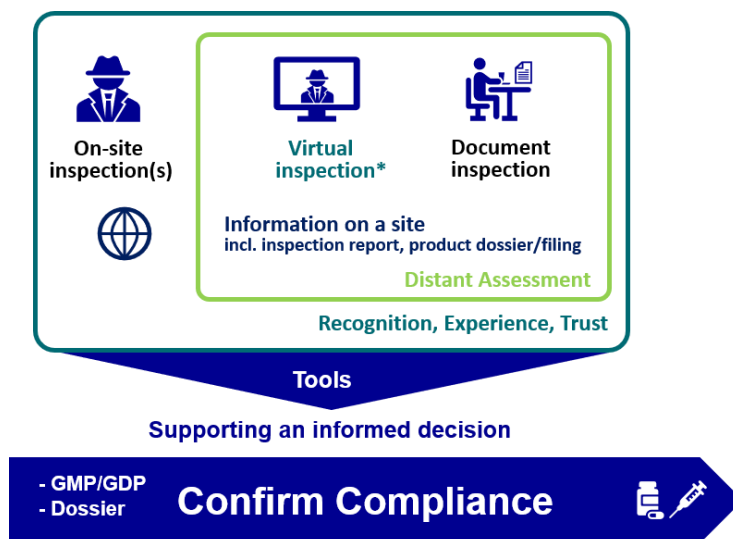


Fig 1. Inspection tools applied to confirm compliance.

Inspections can also be carried out on the basis of a **distant assessment** ^{[1],[3],[4]}. It can consist of the evaluation of information obtained from several sources, including documentary evidence provided by companies and can include a “**document inspection**”, and/or a “**virtual inspection**”, as outlined in Figure 1 (ref: EFPIA^[5], PIC/S^[3], WHO^[6]). Whatever tools are used, an on-site inspection cannot be precluded if the outcome of the assessment does not confirm compliance with the expected practices.

In this paper, the term ‘**virtual inspection**’ applies to inspections that are performed with the inspector being off-site and communicating with the site through the use of enhanced communication and information technologies; these serve to inform inspectorates with regard to deciding on the GxP compliance of a site.

Considerations for preparing and conducting efficient virtual inspections

Virtual inspections can contribute to more efficient time management, with experience to date showing that inspectors allocate about 4-5h per day per site, without needing to set aside additional time for travel and the associated necessary logistics. Virtual inspections also give inspectorates and manufactures additional flexibility, as the “offline” part of this process (document preparation and review) can be performed at any time. Below are additional considerations to enhance the virtual setting.

Documentation

Time spent preparing for virtual inspections can still be significant though, with manufacturers having to allocate significant time to respond to an increasing amount of different document requests, including after the inspection has formally ended.

In order to make the process more efficient, the “document inspection” component of any review should always be the primary focus of the inspectorate. The site being inspected can be open and on stand-by to support virtual interactions as required, and this should be targeted to clarify specific questions after the supporting documentation has been reviewed.

Expectations linked to documentation to be sent in advance by the manufacturer and how it will be used to support the regulatory decision should be clearly defined, thus avoiding misinterpretation due to the language style used or translation being requested. International organizations such as PIC/S and WHO have a key role to play in this regard, by developing harmonized standards to guide NRAs in setting the necessary documents.

Timelines

As early as possible in the process of a virtual inspection, clear timelines and milestones should be defined and agreed between both parties for the preparation, conduction and close out of a virtual inspection.

Use of local language

Arranging and ensuring adequate simultaneous translation has been flagged as an issue which can add to the difficulty of ensuring clear communication in a virtual setup. In some cases, when agreed upfront by both parties, companies may be available to support the local NRA conducting the virtual inspections by providing office space and IT support at the company country affiliate. This may allow additional benefit as of access to company staff speaking the local language.

Technology considerations

Inspections performed remotely heavily rely on supporting Informational Technology (IT). It is therefore critical to carefully select, manage and agree among the parties on the technology aspects to allow for a smooth virtual inspection; pre-testing of IT and connection is recommended e.g., one week before an inspection. Other key elements to consider, besides technical feasibility, are privacy, security and confidentiality of remote connections. Legal concerns and understanding of requests to perform recordings need to be addressed upfront. Secure pathways for sharing documents, transferring files and information should be identified, agreed upon and installed. These are not different and follow the same rules as those established for sharing documents in advance or in lieu of an onsite inspection (ref: FDA^[7]).

Final considerations for defining approaches to inspection and tools to be used

Industry recommends for on-site inspection to remain the norm for domestic inspections, while virtual inspections can provide a valuable alternative particularly for 3rd country inspections, where business continuity may be more at risk.

Where an inspection is deemed necessary in a 3rd country, virtual inspection can serve to increase reliance on an inspection report from a recognised NRA e.g., PIC/S member inspectorate.

Inspection history is also an important consideration when deciding on the type of inspection and the time when it is most appropriate to carry out.

References:

[¹] EFPIA position paper, 28 May 2020: Alternative GMP/GDP Inspection Practices in a Pandemic Situation (COVID-19) and Beyond. ([link](#))

[²] See Comment from Pharmaceutical Research and Manufacturers of America (PhRMA) to Docket No. FDA-2020-D-1136: Manufacturing, Supply Chain, and Drug and Biological Product Inspections During COVID-19 Public Health Emergency Questions and Answers; Guidance for Industry, Dec. 8, 2020.

[³] GMP-Inspection reliance, PIC/S guideline PI 048-1, 1 June 2018 ([link](#))

[⁴] PIC/S guideline PI 037-1; Risk-based inspection planning; 1 January 2012.

[⁵] EFPIA position paper, 26 June 2019: Request for Optimising the GMP paper-based Inspection Process by Regulatory Authorities ([link](#)) and Considered as primary documents to be asked in paper-based inspections (see Enhanced Good Manufacturing and Good Distribution Practices (GMP/GDP) Inspection Efficiency, EFPIA, *Position Paper*, 19. May 2014.

[⁶] WHO TRS 1010, Annex 9: Guidance on good practices for desk assessment of compliance with good manufacturing practices, good laboratory practices and good clinical practices for medical products regulatory decisions, 2018 ([link](#))

[⁷] FDA staff manual: POLICY AND PROCEDURES FOR REQUESTING RECORDS IN ADVANCE OF OR IN LIEU OF A DRUG INSPECTION, 31 August 2017 ([link](#))