EU Regulatory Q&A Updates on Pharmacovigilance Activities for MAH's during COVID-19 Pandemic

Sanjay Bajaj, *Ph.D.*
CEO & Managing Director, Glostem Private Limited, Chandigarh, India
Email: s.bajaj@glostem.com

COVID-19 pandemic has been specifically tough for the pharmaceutical industry across the globe. Providing safe and sufficient quality medicine for the sick as well as for the prevention of diseases has been a great challenge in the times of lockdown while struggling with a lack of workforce and pandemic situations. This has also affected the regulatory inspections and made it difficult for marketing authorization holders of medicinal products for human use (MAHs) to follow the standard operating procedures for pharmacovigilance reporting. Although most of the activities have now been resumed still travel restrictions are expected to stay longer, which means that the on-site audits will not be possible for quite some time, or at least for the next couple of months.

In light of the above, the European Medicine Agency (EMA) had issued a document containing "*Questions and Answers on Regulatory Expectations for Medicinal Products for Human Use During the Covid-19 Pandemic" on 10 April 2020.* The purpose of this document was to provide guidance to MAHs on regulatory expectations and flexibility during the COVID-19 pandemic. This document has recently been updated on July 1, 2020, and three new questions and answers related to Pharmacovigilance activities have been added. This article covers the updated Q & A's recently added in the above document.

This previously published document provides answers to several questions which the MAH's might like to be addressed by the EMA. These questions are related to medicinal products intended for use in COVID-19, renewal applications, application of the 'sunset clause' during a pandemic, implementation of changes in the manufacturing/supply chain, manufacture/import in light of difficulties to conduct on-site GMP inspections, quality requirements for COVID-19 medicines, flexibility in the labeling and packaging requirements to facilitate the movement of medicinal products within the EU, GMP Flexibilities, new lines or re-purposed facilities to ensure continuous availability of crucial medicines, temporary flexibilities to address the imminent market shortage of imported medicines, adaptations to the work of the Responsible Person (RP), as well as related to use of new equipment or newly authorized premises for storage and distribution of medicinal products with limited prospective qualification and so on.

In relation to the Pharmacovigilance activities, the original document states that "During the current pandemic, the exceptional circumstances may force companies to activate business continuity plans and prioritise activities. Therefore, in case MAHs are for justified reasons relating to the pandemic unable to continue standard reporting operations (SOP), they should temporarily – until the pandemic is resolved – prioritise the reporting obligations". The list of Individual Case Study Reports (ICSRs) has also been provided for the same. This document clarifies the intention of the EMA to support the MAHs and allows them to include some reasonable temporary deviations in the SOPs. The new questions included in the July 1, 2020 update are an extension to the above and further clarifies some points related to reporting and audits.

In the recent update, the first new question is that "*Is there any impact on corrective and preventive actions management under the pharmacovigilance provisions?*". In answer to this question the document states that "in case MAHs are unable to continue standard management of corrective and preventive actions, for justified reasons relating to the pandemic, they should temporarily prioritise the deviations by applying risk-based approach taking into account relative criticality of the deviation to risks impacting the pharmacovigilance system, processes and parts of processes".

According to the above statement, if a MAH finds it difficult to follow the SOP and needs some reasonable deviation in the SOP, for the time being, the same should be followed by applying a risk-based approach and should be properly recorded. Further that as soon as the circumstances permit, these deviations in SOP should be addressed and closed. These deviations must be regarded as purely temporary and shall continue up to a reasonable time period only. Because at this point of time it is not possible to define any specific time frame for the pandemic, therefore it is left on the MAH's to decide on the continuity of the deviation and their closure.

The other question in the updated document relates to the audits and goes as *"Is there any flexibility in the planning and conduct of pharmacovigilance system audits?"*. In response to this question, the updated document supports the MAHs and agrees that MAH may need to activate the implementation of business continuity plans which may have an impact on planned audits. It states that "Any adaptation in the planning and conduct of audits should be based on a risk-based approach with all decisions clearly justified and duly documented as part of a prioritisation strategy. For cause audits should be prioritised and planned audits should be conducted as soon as possible and without undue delay".

The above points clarify the EMA's stand that the audits must go on, with prioritization. Option for conducting audits through remote means or video conferencing should also be looked into. In this regard, the document states that "Before considering to delay a planned audit, alternative approaches, such as remote audits may need to be considered in the short-term. Where a decision has been made to conduct remote audits, the MAH should consider how these audits will ensure the independent and objective evaluation of the fulfilment of pharmacovigilance requirements by the auditee".

There is also a recommendation on how the audits can be done using the remote means. According to it "This would typically involve a mixture of interview sessions (e.g. via telephone or video conferencing) and document review. Utilising questionnaires alone, without supporting evidence, would not be accepted as audits. Partners should be kept informed on the overall risk-based strategy. In case of uncertain results, a follow up audit shall be performed as soon as possible". The above statement undoubtedly means that in such cases after the remote audit, the on-site audit will follow once the situation is favorable for a visit.

The third question in the update is *"Which measures will be taken in light of difficulties to conduct on-site pharmacovigilance inspections during the COVID-19 pandemic?"* The document allows the inspectors and assessors to propratise and reschedule inspections as well as look for the possibility of conducting remote inspections. However, the "Decision on "for cause" inspections should be considered on a case-by-case basis by inspectors and concerned assessors, as applicable, to determine whether a remote inspection is feasible and it could fulfil the purpose of the requested inspection".

For conducting the remote inspections, the inspectors have been suggested to consider and check the pre-conditions or provisions available with the MAH to conduct a remote inspection. It states that "Remote inspections should follow, where applicable, the guidelines that already exist for the conduct of pharmacovigilance inspections but should also take into consideration the limitations imposed by using a remote process. It is fundamental to ensure that the inspectee meets the technical requirements to provide remote access to electronic systems, as well as maintains communication with and provides support to inspectors".

The above answer is also guidance and recommendation for the MAH's to arrange for the remote access systems like video conferencing systems, CCTV cameras with speaker and mic, the internet connection of sufficient bandwidth, telephones, etc. before they plan to get their site inspected by remote means since the inspectors have to ensure that these systems are in place before they decide to go ahead for remote inspection. The MAH or the inspectee has to provide details regarding the availability of such facilities to the inspectors because it requires that "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".

These three updations guide the MAHs, as well as the auditors on the expectations by the EMA and, expects that there might be some deviations in the Pharmacovigilance SOP's. The update clarifies the EU stand on the deviations and also explains the availability of provision for remote inspections during the pandemic. These updates seem to be very timely and will relieve the MAHs from the dilemma of the fate of regulatory audits and deviation in following SOPs.

References

https://ec.europa.eu/health/sites/health/files/humanuse/docs/guidance_regulatory_covid19_en.pdf