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Survey of qualified persons on remote certification

by Ulrich Kissel, PhD, and David Cockburn

Social distancing posed an interesting question for the Qualified Person (QP) in the early days of the COVID-19 pandemic: Is it permissible, or practically possible, to certify batches for release while working from home? The European Qualified Persons Association (EQPA) asked its members to share their knowledge and this article details what it found out.

Introduction

In March 2020, the EQPA surveyed its members on the topic of batch certification performed by a QP whilst not physically present at the site of the manufacturer, or "Remote QP Certification". The topic was perceived as an area of non-harmonised national interpretations and the EQPA sought to better understand the differences across the European Union (EU)/European Economic Area and on how QPs positioned themselves in such a procedure.

The survey was launched shortly after the UK's Medicines and Healthcare Products Regulatory Agency (MHRA) published views on the topic by way of its inspectorate blog in February 2020. At that time, the COVID-19 pandemic was rapidly spreading across Europe and public health bodies were promoting remote working where possible, in order to avoid unnecessary contact.

Survey and results

The survey, responded to by more than 300 QPs, revealed an interesting pattern of approaches. As would be expected, the responses reflected the perceived expectations of their respective national authorities and/or their understanding of national law. QPs acting in a generally acceptive environment for remote QP certification were much better equipped to answer the questions posed in the survey than those who believed that their national law would not allow it.

The EQPA believes that neither the EU Guidelines for Good Manufacturing Practice (GMP) nor Directives 2001/8(2)3/EC require the physical presence of the QP at the manufacturing site during certification. However, in several member states such physical presence is enforced, either clearly through national law, or less clearly, by the interpretation of law by national authorities. An argument for the QP's physical presence on site is that the responsibilities of the QP can be met in full only through a high level of continuous interaction with manufacturing operations. Another known argument is that QP

certification, being an integral part of GMP regulation, can only be executed at the listed premises of the Manufacturing/Import Authorisation Holder.

The EQPA was interested in whether rules might change in the face of a pandemic. It did not know how many QPs already had the freedom to exercise remote QP certification in their local environment. In this respect, the survey revealed an even split with almost 50% of QPs aware, at the start of the COVID-19 pandemic, that remote QP certification would not be an option on their territory.

QPs were asked whether they were aware of any communication about remote QP certification from their national authorities under certain circumstances. It was clear that the recently published MHRA blog article was widely known to QPs based in the UK. On the other hand, almost no other QP had knowledge of any similar local communication bearing in mind that they would be expected to actively keep themselves up-to-date on developments impacting their role. In some countries, the law may be clear on remote QP certification. However, taking Germany as an example, it was widely understood there that remote certification is not permitted but no German QP was able to cite a public reference to this.

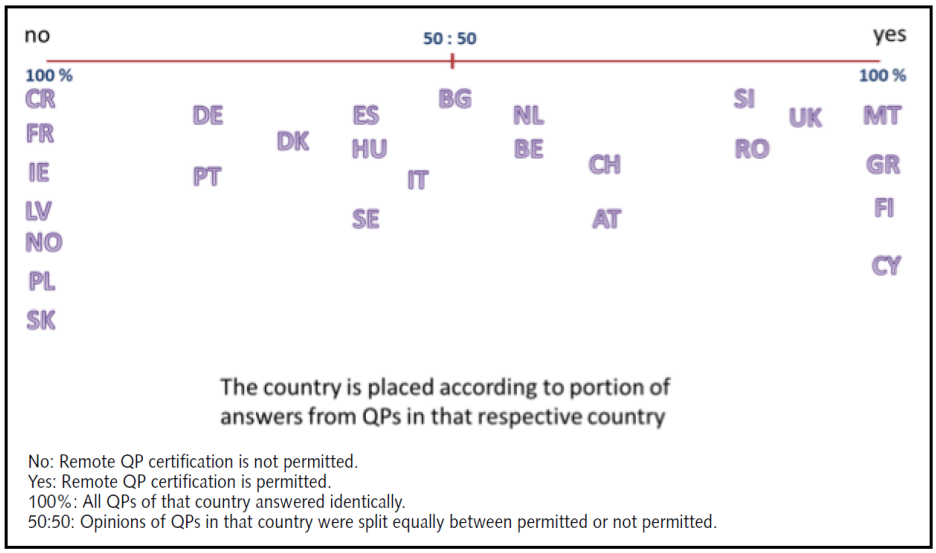

Figure 1 QPs' awareness of the acceptance of, or limitations to, remote QP certification in their country

Figure 1 shows QPs' awareness of the acceptance of, or limitations to, remote QP certification in their country. In the chart, QPs in the countries listed on the extreme left and right all answered identically demonstrating that, in those countries, all QPs understood local expectations. For countries positioned between the extreme left and right, QPs did not respond in the same way. Lack of knowledge of the applicable rules by QPs illustrates inadequate clarification and communication by the national authorities concerned and that needs to improve.

About 30% of the QPs who responded to the survey had experience with remote QP certification; but before looking into the wider details, we first examine two key questions.

1. What safeguards are in place with respect to transmission of information to

ensure that no batch can be transferred to saleable stock prior to QP certification?
2. How is certification documented in the register?

With regard to the first question, a few QPs transfer paper documents between the site and the QP's location. Approximately two-thirds of QPs have access to core company systems via the internet allowing them to directly document certification and transfer batches into saleable stock. One third of QPs use email with attachments or scans for communicating batch certification allowing others to transfer the batch to saleable stock. The use of email for GMP-relevant communication raises questions about security, data integrity and compliance with EU Guidelines for GMP Annex 11. On that specific point, the survey surprisingly reveals that only 75% of participants expressed concern about secure communication of QP certification.

With respect to the batch register, only 35% of those performing remote QP certification require clarification of its location. This may reflect a common misinterpretation that "QP certification" is "the transfer to saleable stock" or "the issuance of a batch certificate". However, according to the Guidelines for GMP Annex 16, the definition of certification is the signature of the QP in the batch register. It is therefore difficult to understand how certification can be executed without clarity of the location and ownership of the batch register. Another question however, specifically about completion of the batch register, revealed that 75% of QPs agreed that clarification is needed.

QPs were asked whether they considered the impact of the COVID-19 crisis as sufficient justification to argue a case for remote QP certification with their national authorities. The responses were collected prior to the joint European Medicines Agency/European Commission/Heads of EU Medicines Agencies communication on 10 April 2020 urging all member states to allow remote QP certification during the COVID-19 crisis and confirming that EU law does not rule it out. Interestingly, at the time of the survey, many QPs did not expect remote QP certification to be a legally defensible position. A point that the EQPA takes from the survey is that this may reflect unwillingness to perform remote QP certification for various reasons. Considering that half of the QPs in the survey considered remote QP certification to be supported in their countries, 40% of them would be unwilling to do so, even under the impact of the COVID-19 pandemic.

The survey sought to understand whether deviation management or change control would be used to handle the introduction of remote QP certification. Around 60% of the answers indicated that deviation management and/or change control would be used. Sadly, the survey design did not allow the EQPA to conclude whether only one or both systems are used. Usually, deviations would document unexpected situations and change control would be used for planned changes. Without prejudice, the authors favour the latter in this case.

Interestingly, only 72% of QPs expect updates of Pharmaceutical Quality System elements and standard operating procedures (SOPs) as a prerequisite for remote QP certification. This may have been influenced by the fact that in many cases a system had already been established prior to the COVID-19 pandemic. Based on the authors' experience, a change from on-site certification to remote certification is a significant and complex change needing thorough analysis and description in SOPs. Performing this change without appropriate process analysis bears significant risks and is not recommended.

The aforementioned MHRA blog identified a minimum of 15 types of data that the QP should have access to, illustrating the complexity of an adequate remote QP certification system. One of the survey questions specifically asked QPs which of those 15 elements they considered essential. Only the following four out of the 15 elements were actually considered essential by more than 90% of QPs.

- Batch records.
- Quality control test results.
- Relevant deviations.
- Out-of-specification reports.

Access to relevant parts of marketing authorisations and related changes were considered necessary by less than 80% of QPs. In other words, up to 20% of QPs considered themselves to be in a position to certify batches without having at least one of these data elements to hand or accessible via the internet. Access to the remaining nine data elements were not considered essential for certification by up to 50% of QPs. There may be good reasons for this finding, but it may highlight room for harmonisation and improvement. All QPs are expected to continuously assess their certification procedures for gaps and areas in need of improvement. It is difficult to argue that remote QP certification should not be based on the same depth of information as certification carried out on-site.

At the time of the survey, the COVID-19 crisis was still in an early phase. Nevertheless, most QPs had experienced some impact on their operations. Some 75% were involved in applying additional hygiene precautions and personnel monitoring measures and more than 50% had already experienced the implementation of additional disinfection steps, enforced changes to manufacturing shifts, social distancing and remote working. As the crisis continued after the survey, these figures would likely have increased.

At the time of the survey, about 40% of QPs noted some COVID-19-induced supply chain problems and 60% experienced changes to operations that needed to be implemented rapidly. Some drug shortages may have been driven by unexpected demand, but it appears that pharmaceutical supply chains had, at the time of the survey, predominantly proven to be robust in the reported experience of QPs.

Summary and conclusion

The survey revealed that remote QP certification, despite being possible according to the EU Guidelines for GMP, is often not supported by national laws or by the interpretation of some inspectorates. QPs in many member states do not know where answers to their questions on the topic can be found. Consequently, responses to the survey were mixed. We see that national authorities often failed to make their views on this subject public. QPs without practical experience of remote certification are not always convinced that it is, or could be, possible within their national environment.

The circumstances arising from the COVID-19 crisis had, at the time of the survey, not convinced all QPs to consider remote QP certification. This needs further examination in view of the aforementioned publication by EU authorities in April 2020 supporting the use of remote QP certification during the COVID-19 crisis. The EQPA is very supportive in enabling QPs to perform remote certification provided appropriate conditions are met. When examining the conditions that need to be met, as discussed in the MHRA inspectorate blog, the EQPA concludes that remote QP certification is complex and difficult to implement without considerable preparation. It would be particularly

challenging for a QP new to an organisation or not familiar with a particular product.

QPs need to have experience at the site and should know their products and respective manufacturing processes. They could then more easily move to remote certification with the support of highly integrated information technology systems ensuring free access to all relevant data. In some cases, the need for paper-based documentation exchange may still be required. Specific care should be taken to ensure compliant communication of the certification decision, the location of the batch register, and safeguards to ensure that only certified batches can be transferred into saleable stock. For QPs just recently nominated to their role or faced with a new product, remote QP certification may not be appropriate.

The reliability or quality of QP certification should not be impacted by the way it is executed, i.e. remotely or on-site. The elements of data that need to be available for remote certification should be very much aligned. The MHRA blog and Guidelines for GMP Annex 16 list 15 and 21 areas, respectively. In practice, the survey reveals that QPs do not consider the entire list of these elements mandatory for every batch certification. The spread of responses in this regard seems to be significant, so in addition to further experience, training is needed as well as discussion both within the QP community and with authorities to better align approaches. From the survey responses it appears that some QPs are taking too much of a compliance risk and may want to examine their procedures with a view to improvement.

Finally, there did not appear to be any pattern in the survey responses in relation to the size of the organisation that the QP operates in.

This article was first published in the GMP Journal of the ECA Foundation of which the EQPA is part. It is based on a survey of EQPA members. A more comprehensive summary of the survey results has also been shared with EQPA members via the membership's GMP Newsletter.

Authors:

Ulrich Kissel, PhD
Founder and owner of Kissel Pharma Consulting GmbH
Chairman of the EQPA

David Cockburn
Formerly head of the Manufacturing and Quality Compliance Service at the European Medicines Agency (EMA)
Member of the board of the EQPA

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