



The Changing Role of the QP

Abstract

With Article 13 of the impending EU Clinical Trials Directive stating that the manufacturing and importation of all clinical trial samples must be subject to an authorization by the competent authority, the spotlight now, more than ever before, is on the role of the Qualified Person (QP). **Dr Ken Caldicott**, Chief Scientific Officer and one of three QPs at Penn Pharmaceutical Services, talks about the Directive and what it will mean to the role of the QP.

Qualified Person is a term that is well used in the UK and the rest of Europe but many people working in the pharmaceutical sector in the US and Asia are still unfamiliar with it. For those exporting clinical trials samples into Europe however, it is a term that will fast become part of everyday language as the impact of the new EU Clinical Trials Directive (2001/20/EC of the European Parliament and the Council) is seen across the continent from its deadline of 1 May 2004.

A QP must be qualified in chemistry, pharmacy or biology and be experienced within the pharmaceutical industry. Within the UK, the QP must be named in an indicative register and, in order to act, must be named on a manufacturers or wholesale dealers import license. This final requirement ensures that the competent authority has the final approval of the individual QP.

Even before the Directive, the QP was a role that carried with it a great deal of responsibility in the industry as the person responsible for the final decision on the use, or otherwise, of medical products. For commercial products he or she must ensure that a particular product has been produced in accordance with its manufacturing authorization - a series of documents that provide all of the data necessary for the Regulatory Authorities to decide if a product is both safe and effective.

For Investigational Medicinal Products (IMP), the role of the QP will be somewhat different. It will still be required that the QP should ensure that the product has been manufactured and released in accordance with its authorization (in this case the CTA) but there should also be certification by the QP that EU standards of GMP have been observed and that support processes are up and running - for example ensuring that the Product Specification File is kept up to date and available for inspection. A major area is that, historically, changes made to processes during the development cycle are recorded but not necessarily communicated very well. This must improve and any changes must be checked by the regulatory affairs department and assessed as to their impact on the active regulatory approval document.

The EU Directive effectively means that all companies wishing to manufacture or import materials for clinical trials into EU countries will need to have a Qualified Person (QP) continuously available, who is charged with ensuring that all of the requirements of GMP will be met. This may seem fairly straightforward but, in the UK for example, more people are retiring from the register than are being replaced by newly qualified experts and this could easily cause problems in the future.

As mentioned above, under the new Directive, the QP will be responsible for releasing batches of clinical materials before use in a clinical trial and the revised Annex 13 indicates that the QP must satisfy him or herself that equivalent standards (to those of the EU) of GMP apply at the site of the manufacturer. The Directive states that this is usually confirmed by way of an audit of the manufacturing and testing facilities and may be completed by a single visit unless processes change significantly and, in comparison with full batch-to-batch quantitative analysis, can be a very cost-effective means of releasing product.

There are many differences in the application of GMP between Europe and by our colleagues in other parts of the world and an interesting part of the QP's role is to explain these differences and help the non-EU facility to comply with our requirements, whilst maintaining their own local needs. This often requires a considerable amount of tact and diplomacy as most Member States (but not all) will not require repeat analytical testing of IMPs on import. However, the QP must be able to confirm that the original analysis was carried out under GMP conditions and, again, the application of laboratory GMP can vary between countries. It is also critical that the QP releasing clinical supplies understands and appreciates the differences between commercial products and IMPs, particularly in areas such as process validation. Although sterilization processes must be validated for any stage of development, typical non-sterile processes for IMPs are rarely validated so extra support systems must be in place to verify that the product is satisfactory.

For IMPs, the Directive will lead to increased QP responsibility in a training capacity - it is not really helpful to visit a facility, "tick boxes" and write a list of problems. During the early transition stage of the Directive, the QP should be pro-actively helping the manufacturing and testing groups who may not have been subjected to the audit ordeal previously.

The role of the QP has certainly grown from covering solely commercial products to also embrace 'Investigational Medicinal Products'. QPs are now getting more requests to review the suppliers of 'Active Pharmaceutical Ingredients' even though there is no legal requirement, as yet, for QP involvement. For clinical supplies, the sponsor is responsible for API quality so it appears that they are making sure that quality is satisfactory by using an independent assessor. As for drug product, the approach for the manufacture of API for an investigational product is different from that of an established, commercial drug.

It is interesting to see how many companies try to meet the GMP requirements by applying a tight specification for APIs used for early stage trials, both pre-clinical and early clinical. Unfortunately, tight specifications do not guarantee GMP compliance and can also lead to complications if impurities increase during the typical scale-up process. This could mean that toxicology studies would have to be repeated in order to qualify these impurities.

The three main attributes of a good QP are flexibility, a willingness to learn and a global view of what the role was designed for. There is often more than one way to comply with a GMP requirement, so a QP needs to weigh up all factors during an audit of any premises or process. Another key element of the job is to keep pace with changes in the industry and its various regulatory requirements. The EU Directive is a prime example of this change which can have a huge impact on companies wanting to run clinical trials, specifically in terms of two of the most important factors in any trials process: money and time.

Changes seem to happen on almost a daily basis and a mix of formal Continuous Professional Development allied to an informal exchange of information at all levels is often required to maintain the necessary knowledge base. A final piece of advice would be to always remember that you are there to protect the patient by making sure that the drug prescribed by the physician and dispensed by the pharmacist has been made safely and is exactly what is expected.

About This Article

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About The Author :: Ken Caldicott

Ken started his career in the Pharmaceutical Industry in the Parke-Davis production division as Head of Raw Material Testing. In 1975 he transferred to the Research Division as Manager of Analytical Chemistry and in 1982 also assumed responsibility for Quality Assurance. He has been involved with international teams addressing analytical and quality issues and has delivered several lectures on these and also regulatory issues.

Ken joined Penn in 1993 and has been associated with successful licence applications in Europe and the United States. He has also been involved with numerous CTX and IND submissions.

He has a PhD in Analytical Chemistry, is a Fellow of the Royal Society of Chemistry, and is also registered as a European Qualified Person.

Ken Caldicott, CSO, Penn Pharmaceutical Services, Tredegar, Gwent, NP22 3AA
kcaldicott@pennpharm.co.uk | www.pennpharm.co.uk