

**ROYAL
PHARMACEUTICAL
SOCIETY**



**Qualified Person involved in the manufacture of
pharmaceuticals**

QP Code of Practice

November 2018

QUALIFIED PERSON Code of Practice

1. INTRODUCTION

- 1.1. The concept of the Qualified Person (QP), first established in 1975, is a unique regulatory requirement that applies only within the European Union (EU). The only comparable situation exists within Member States of the European Economic Area with whom the EU has reciprocal agreements.
- 1.2. Each holder of an Authorisation to manufacture products for use in a Clinical Trial or products subject to Marketing Authorisations, within Member States of the EU, must name a person or persons who are eligible to act in the capacity of QP.
- 1.3. The requirement for QP covers both Human and Veterinary Medicinal Products including any product only intended for export.
- 1.4. Particular conditions for formal qualifications and practical experience for eligibility to act as a QP are specified in the relevant EU Council Directives (see section 2 below). Ensuring compliance with these conditions is the responsibility of the Competent Authorities of the Member States.
- 1.5. The primary legal responsibility of the QP is to certify batches of Medicinal Product prior to use in a Clinical Trial (Human Medicinal Products only) or prior to release for sale and placing on the market (Human and Veterinary Medicinal Products). However, the wider technical, ethical and professional obligations in terms of patient safety, quality and efficacy must also be considered. Hence this professional Code of Practice is designed to take account of these issues

2. REGULATORY BASIS FOR THE QUALIFIED PERSON

For ease of reference the key regulatory documents concerning the QP are as follows:

- i) Directive 2003/94/EC - Principles and Guidelines of Good Manufacturing Practice for Medicinal Products for Human Use – **Article 7**.
- ii) Directive 91/412/EEC – Principles and Guidelines of Good Manufacturing Practice for Veterinary Medicinal Products – **Article 7**.
- iii) Directive 2001/20/EC – Good Clinical Practice in the Conduct of Clinical Trials on Medicinal Products for Human Use – **Article 13**.
- iv) Directive 2001/82/EC – Community Code Relating to Veterinary Medicinal Products – **Title IV – Manufacture and Imports – Articles 44-57** (NB Articles 44, 50, 51, 53, 54 and 55 have been amended by Directive 2004/28/EC)
- v) Directive 2001/83/EC – Community Code Relating to Medicinal Products for Human Use – **Title IV – Manufacture and Importation – Articles 40-53** (NB Articles 46, 47, 49, 50 and 51 have been amended by Directives 2004/27/EC and 2011/62/EC) .
- vi) Directive 2011/62/EC – Falsified Medicines Directive

- vii) Eudralex Volume 4 – Good Manufacturing Practices – in particular
- Annex 13 – Manufacture of Investigational Medicinal Products
 - Annex 16 – Certification by a Qualified Person and Batch Release

3. PURPOSE OF THE CODE

- 3.1.** It is a requirement that all QPs are subject to a professional code of conduct.
- 3.2.** The purpose of this UK Code of Practice is to provide guidance to QPs on how to comply with the professional code of conduct requirements.
- 3.3.** It aims to provide guidance on how an individual QP can safeguard him or herself, aspects a QP needs to be aware of when working with other QPs named on the same authorisation, and where a QP can obtain support in difficult situations.
- 3.4.** This Code applies to all QPs involved in the manufacture of pharmaceuticals where the QP is:
- employed or providing contract QP services;
 - involved in human or veterinary medicines; and
 - qualified under the permanent or transitional provisions.
- 3.5.** It should be noted that the Licensing Authority may refer to this Code of Practice in connection with disciplinary proceedings against a QP under Article 52 of Directive 2001/83/EC or Article 56 of Directive 2001/82/EC.

4. TERMINOLOGY

- 4.1.** The terminology used in this Code of Practice corresponds with that used in the current versions of the EC Directives on Good Manufacturing Practice (GMP) and the Guide to Good Manufacturing Practice.
- 4.2.** Within the EU, the terms Marketing Authorisation, Manufacturer's Authorisation and Clinical Trial Authorisation are generally used and shall henceforth be referred to throughout this Code.

5. GENERAL PRINCIPLES

- 5.1.** Pharmaceutical Manufacturers and the Regulatory Authorities of each Member State must ensure that patients are protected and that all medicinal products, whether for sale or supply, meet the appropriate requirements for safety, quality and efficacy.
- 5.2.** The QP performs a unique role on behalf of the patient and the Regulatory Authority when certifying that a batch complies with its pre-determined requirements and can be released for sale or supply.

- 5.3. The QP is responsible for ensuring that each individual batch has been manufactured and checked in compliance with laws in force in the Member State where certification takes place.
- 5.4. The QP's legal roles and responsibilities apply regardless of where the final product will be sold and/or supplied.
- 5.5. The QP must understand the requirements of each Authorisation (Manufacturer's, Marketing or Clinical Trial) and ensure that the Pharmaceutical Quality System (PQS) in place is fit for purpose for the activities being performed and types of products involved.
- 5.6. The QP must use risk-based principles and apply sound knowledge and understanding of the relevant steps of manufacture before certifying any batch for release.
- 5.7. The QP needs to refer to all applicable guidance and ensure he/she is fully conversant with the requirements detailed in Annex 16 of the EU GMP Guide.
- 5.8. All QPs should ensure adequate professional indemnity insurance arrangements are in place.
- 5.9. QPs have a professional duty to decline to certify any batches of product types for which they do not possess the relevant experience and/or knowledge.
- 5.10. QPs should ensure that this Code of Practice is brought to the attention of senior management and, where practical, the Chief Executive Officer/Site Head so they are aware of the requirements and expectations detailed within.

6. PRACTICAL DUTIES OF A QUALIFIED PERSON

- 6.1. QPs have duties, some of which may be delegated in line with the above general principles. Before certifying a batch prior to release, the QP should always ensure that all requirements have been met.

Annex 16, Volume 4 EU Guidelines for Good Manufacturing Practice for Medicinal Products for Human and Veterinary Use provides the current guidance on these duties and should be consulted for the details.

- 6.2. The QP should also recognise the need to consult other experts to reinforce knowledge where required (for example but not limited to: stability, unusual analytical results, process or equipment changes, potential environmental or microbiological risks, re-labelling, abnormal yields, cross contamination risks, new technologies).
- 6.3. The QP should also take account of the nature and size of the operations being performed. For example, in a very small company with a limited range of products, it may be possible for the QP to take direct responsibility for some or all of the duties as detailed in Annex 16. In larger organisations, the QP will typically be dependent upon the knowledge and expertise of colleagues. It is of paramount importance that the QP

is assured that the tasks allocated are being performed satisfactorily. Hence the duties of a QP depend upon a team effort.

7. PERFORMANCE OF DUTIES AND REGULATORY COMPLIANCE

- 7.1.** Each QP has a personal and professional responsibility for being certain that the various checks and tests have been carried out, however, the detail of this work can be the responsibility of others.

Ultimately, the QP must be satisfied either directly or, more usually, by the proper operation of the PQS, that manufacturing, packaging and quality control testing comply with the relevant requirements and that any deviations are controlled and managed effectively. These requirements apply whether the work is carried out on site or at a different site.

Batch certification without such adequate steps may be regarded as professional misconduct.

- 7.2.** The QP depends upon many colleagues for the achievement of quality and regulatory compliance in the manufacture of medicinal products. It is therefore of paramount importance that the QP achieves good working relationships with others.
- 7.3.** The QP should take the necessary steps to inform other functional groups of the legal role and responsibilities of a QP and help them to understand how they can provide effective support.
- 7.4.** Manufacturer's Authorisations include the names of the persons responsible for Production, Quality Control and the name(s) of the QP(s). The duties of these members of staff must be clear in their respective job descriptions and they must have the authority required under the relevant EC Directives.

8. NUMBER AND LOCATION OF QUALIFIED PERSONS

- 8.1.** Safety of patients is of paramount importance therefore it is vital that at each relevant site there are sufficient QPs available to cover all activities involved, including appropriate measures in place for any shift patterns. This may require a single QP, a team of QPs, a QP providing contract services or a combination thereof.
- 8.2.** The QP should be present at the manufacturing site for a sufficient proportion of the working time to discharge their legal and professional duties. The time spent on site should also allow the QP to fulfil their other duties with respect to the PQS.
- 8.3.** Where there is more than one QP working on the same site, it is an expectation that each QP is sufficiently aware of the activities of the other QP(s). Where any significant discrepancies regarding decision-making are observed, these should be discussed between the QPs. Where significant differences cannot be resolved, these should be brought to the attention of senior management. It may also be advisable for a concerned QP to contact their Professional Body for advice.

- 8.4.** It is expected that QPs will inform senior management if they believe there are insufficient QPs to perform all the required duties.
- 8.5.** QPs are typically part of the Quality organisation at site. Ideally, the QP or “lead” QP would also be a member of the senior management team.

9. CONTRACTED QUALIFIED PERSONS

- 9.1.** In a number of cases, especially with smaller companies, a ‘Contracted’ QP provides the service. In such cases, the duties and responsibilities of a ‘Contracted QP’ are the same as those for QPs who are permanently employed by their company.

The term ‘Contracted QP’ is not a formal title and is used only to describe a QP providing an independent service under contract to a company.

- 9.2.** In addition to compliance with the provisions applicable to all QPs including all the practical duties detailed in Annex 16, Contracted QPs should observe the following:
- Have a clear written contract, which delineates the duties and responsibilities of the QP – as agreed between the company and the ‘Contracted QP’. Both should sign and retain a copy of the contract;
 - Be on site for sufficient time to fulfil all legal and professional requirements;
 - Be readily available to the staff of the company for advice and discussion, be present during regulatory inspections and involved in communications with the inspectors;
 - Ensure that the company to whom the services are provided will allow free access to any people, information, documentation, premises, systems, etc. which are relevant to the decision-making processes when certifying batches; and
 - The QP must be informed and aware of any issues arising relating to the PQS that are relevant to a QP, in particular, any events that occur when the QP is not on site.
- 9.3.** Particularly for smaller companies, a Contracted QP may agree with the company to personally provide some additional services for example, staff training, internal audits and maintenance of authorisations, in addition to performing strictly batch related QP duties.
- 9.4.** If any doubt exists between the QP and the company concerning the duties and responsibilities of the QP, it is recommended that the QP contact their Professional Body or UK Medicines and Healthcare products Regulatory Agency (MHRA) Inspector for advice.

10. OUTSOURCED ACTIVITIES

- 10.1** Where products are manufactured and/or packed under contract there should be a clearly written Quality/Technical Agreement between the contract giver and the contract acceptor; such an agreement should be reviewed by a QP.

- 10.2** It may be necessary to consider a direct QP/QP agreement in addition to any Quality/Technical Agreement(s) where there is a requirement for clarity on division of responsibilities for QPs, or where there are a number of QPs in the supply chain.
- 10.3** The provisions in 10.1 apply equally to QC testing of samples under contract. Refer to MHRA current guidance on the use of UK standalone contract laboratories for details

11. CONTINUING PROFESSIONAL DEVELOPMENT

- 11.1** QPs have a personal and professional duty to ensure they keep their knowledge and experience up to date.
- 11.2** This should include all relevant Regulatory aspects, changes to GMP guidelines, regional and international standards and guidelines.
- 11.3** In addition, it must also include any advances in manufacturing techniques or control technologies relevant to the dosage forms / types of products they work with.
- 11.4** Each QP must also ensure he/she keeps up to date with all changes relating to the PQS, current expectations, recent issues and best working practices.
- 11.5** Adequate records must be maintained to demonstrate that sufficient CPD is being performed, which also complies with any Professional Body requirements.
- 11.6** Where appropriate, these records need to be submitted to the relevant Professional Body and to be available for review during any Regulatory inspection.
- 11.7** In the event of a QP undergoing a significant change in job responsibilities in the same company, eg introduction of new dosage forms, it is a requirement that the QP undergoes formal training. There should be a plan prepared and approved by senior management that details the gaps and training required with timelines. Training must be satisfactorily completed and the QP must be named on the relevant company Authorisation prior to performing batch certification.
- 11.8** In the event that a QP moves company, it is expected that the same approach is taken as 11.7 above and that the QP does not certify any batches until he/she is familiar with the new PQS and product range.
- 11.9** If a QP has a break from work and/or temporarily moves away from the QP role, the QP must ensure he/she is fully up to date before returning to a QP role and certifying any batch.

12. PROFESSIONAL CONDUCT

- 12.1** QPs are subject to the overall jurisdiction of the By-laws, Charters and Regulations, Codes of Conduct, Disciplinary Regulations and any general guidelines of their own Professional Body, and should have access to them.

- 12.2** QPs have duties not only to their employer but also to the MHRA, in particular its Inspection, Enforcement and Standards group. They must ensure that appropriate senior company executives are made fully aware of any manufacturing and/or testing issues that may cast doubt on the certification of batches or may necessitate a product recall.
- 12.3** If there is any aspect of the PQS that is not in accordance with the Directives and Guidelines for GMP then the QP has a duty to bring this to the attention of senior management and ensure that appropriate corrective and preventative measures are taken.
- 12.4** QPs should establish a good working relationship with Regulatory Inspectors and, as far as possible, provide information on request during site inspections.
- NB. There may be situations outside of site inspections where the QP may wish to consult with the local Regulatory Inspector for advice.
- 12.5** QPs may consult their Professional Body for confidential advice in cases where undue pressures to depart from professional obligations cannot be counterbalanced by reference to this and other relevant guidance, preferably having informed their employer first.
- Management has a duty to provide appropriate resources, training and expertise within its organisation to ensure that QPs can operate effectively in discharging their responsibilities and to ensure that the PQS and communications are not compromised. Those resources may not necessarily reside in a Quality function.

13. PROFESSIONAL BODIES

Each Professional Body in the UK has an “Officer” who is a point of contact for QPs. Each Professional Body has made arrangements so that any QP contacting their Professional Body can be directed to an experienced QP to discuss any difficult situations and obtain advice on possible courses of action.

14. DISCIPLINARY PROCEDURES

- 14.1** Article 56 of EU Directive 2001/82/EC and Article 52 of EU Directive 2001/83/EC require that Member States ensure that the duties of QPs are fulfilled, either by means of appropriate administrative measures or by making such persons subject to a Professional Code of Conduct.

Member States may provide for the temporary suspension of such a person upon the commencement of administrative or disciplinary procedures against him/her for failure to fulfil their obligations.

If it was found that a QP had certified a batch as fit for sale or supply without ensuring that the relevant tests and checks had been performed, this would be a matter for

consideration by both the appropriate Professional Body and the MHRA as a matter of professional misconduct.

- 14.2** The Professional Bodies each have established disciplinary procedures to deal with cases of possible misconduct. One of the powers is to remove the name of an individual (or individuals) from the appropriate register or registers. Where required, the Professional Bodies will work together (eg if a person is a member of more than one). In all cases, the Professional Bodies will inform the MHRA of these situations.
- 14.3** The MHRA has the power to delete the QP's name from any Manufacturer's Authorisation.