



# **Code of Practice**

for QUALIFIED PERSONS

EUROPEAN INDUSTRIAL PHARMACISTS GROUP



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## Code of Practice for Qualified Persons

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The European Industrial Pharmacists Group (GPIE/EIPG) is the European Association representing the national professional organisations of pharmacists employed in the pharmaceutical and allied industries of the member states of the European Union.

Further information can be found on their website <http://www.eipg.eu>

# EUROPEAN INDUSTRIAL PHARMACISTS GROUP

## Code of Practice for Qualified Persons

### 1. INTRODUCTION

- The concept of the Qualified Person (QP), first established in 1975, is a unique regulatory requirement which applies within the European Union (EU). The only comparable situation exists within Member States of the European Economic Area (EEA) with whom the EU has reciprocal agreements.
- Each holder of an Authorisation to Manufacture products for use in a Clinical Trial or products subject to a Marketing Authorisation, within Member States of the EU, must name a person or persons who are eligible to act in the capacity of QP.
- The requirement for QP covers both Human and Veterinary Medicinal Products but not those intended for export outside the EU.
- Particular conditions for formal qualifications and practical experience for eligibility to act as a QP are specified in the relevant EU Council Directives. Ensuring compliance with these conditions is the responsibility of the Competent Authorities of the EU Member States.
- 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 in some EU states the legal responsibility is that of the supervisory pharmacist and not the delegated QP who may have certified release of a particular batch.
- This Code does not detail the responsibilities for QP responsible for distribution or for those additional duties as required in the EU states where the titles of Pharmaciens Responsable or Technical Director include responsibilities for medical information, regulatory affairs, advertising copy and pharmacovigilance
- The first EIPG Code of Practice for QP's was published in June 1996 and this revised version takes account of the most recent regulatory requirements.

## 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
  - (ii) Directive 91/412/EEC – Principles and Guidelines of Good Manufacturing Practice for Veterinary Medicinal Products.
  - (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.**
  - (v) Directive 2001/83/EC – Community Code Relating to Medicinal Products for Human Use – **Title IV – Manufacture and Importation – Articles 40- 53**
  - (vi) Eudralex Volume 4 – Good Manufacturing Practices 2002

**Annex 13 – Manufacture of Investigational Medicinal Products**

**Annex 16 – Certification by a Qualified Person and Batch Release**

## 3. PURPOSE OF THE CODE

- The aims and objectives of the Code of Practice are to provide operational guidelines for carrying out the functions of the QP within a professional Code of Conduct.
- The legal functions of the Qualified Person are stated in article 51 of directive 2001/83/ EC or Article 55 of directive 2001/82/ EC.
- To make available to the Competent Authorities of the EU Member States a professional Code of Conduct in accordance with Article 56 of Council Directive 2001/82/EC and/or Article 52 of Council Directive 2001/83/EC.
- The Code is in the interests of QP's, their Employers, Patients and the Competent Authorities of the EU Member States.

#### **4. APPLICATION OF THE CODE**

- The Code is equally applicable to QP's who have achieved that status under the transitional arrangements or under the permanent provisions of the relevant Council Directives, and who are named on Authorisations as the "Qualified Person"; Industrial Pharmacist, Technical Director or Responsible Pharmacist, hereafter referred to as the QP.
- The Code applies equally to QP's involved in human and/or veterinary medicines, except Veterinary Medicinal Products for use in an animal trial.
- QP's have a professional duty to decline to act as QP's in the release of product types for which they do not possess the relevant experience and knowledge.
- Licensing Authorities may refer to this Code in connection with disciplinary proceedings against a Qualified Person under Article 52 of Directive 2001/83/EC or Article 56 of Directive 2001/82/EC.

#### **5. TERMINOLOGY**

- The terminology used in this Code of Practice corresponds with that used in the relevant, up to date, EU Council Directives and corresponding guidelines on GMP.

#### **6. GENERAL PRINCIPLES**

- Pharmaceutical Manufacturers and the Competent Authorities of the Member States have a duty to ensure that patients are properly protected and that Medicinal Products meet appropriate requirements for Safety, Quality and Efficacy.
- The legal framework is provided by the European Directives and the Rules Governing Medicinal Products in the European Union, and implemented by national legislation in individual Member States.
- An operational framework is provided in the current Volume 4 of the Rules Governing Medical Products in the European Union 'Good Manufacturing Practices'. In Chapter 1 of the Guidelines, Quality Management, it states that:-

*"The holder of a Manufacturing Authorisation must manufacture medicinal products so as to ensure that they are fit for their intended use, comply with the requirements of the Marketing Authorisation and do not place patients at risk due to inadequate safety, quality or efficacy. The attainment of this quality objective is the responsibility of senior management and requires the participation and commitment by staff in many different departments and at all levels within the company, the company's suppliers and the distributors.*

*To achieve the quality objective reliably there must be a comprehensively designed and correctly implemented system of Quality Assurance incorporating Good Manufacturing Practice and thus Quality Control. It should be fully documented and its effectiveness monitored. All parts of the Quality Assurance system should be adequately resourced with competent personnel, and suitable and sufficient premises, equipment and facilities. There are additional legal responsibilities for the holder of the Manufacturing Authorisation and for QP's.*

*The basic concepts of Quality Assurance, Good Manufacturing Practice and Quality Control are inter-related. They are described here in order to emphasise their relationships and their fundamental importance to the production and control of medicinal products".*

- QP's should be aware that whilst Quality Management applies to full-scale manufacture, it also extends to original product design, development, formulation and preparation of medicinal products for use in clinical trials. This includes the establishment of well-defined manufacturing processes, sampling programmes and analytical tests methods and appropriate specifications for ingredients, printed and unprinted packaging components and finished dosage forms.

## **7. ROUTINE DUTIES OF A QUALIFIED PERSON**

- QP's have routine duties, some of which may be delegated (see later), in line with the above general principles. Before certifying a batch prior to release the QP doing so should always **ensure** that the following requirements have been met as specified below.

*NB. The meaning of the word **ensure** in this context is that the Qualified Person must be confident that various actions, which may not be under his/her direct control, have in fact been taken. See also Section 8.*

- The Marketing Authorisation and Manufacturing Authorisation requirements for the Medicinal Products have been met for the batch concerned and that the appropriate legal requirements for that particular Member State have been complied with.
- The principles and guidelines of GMP as stated in Directive 2003/94/EC (Human Medicinal Products) or Directive 91/412/EC (Veterinary Medicinal Products) and as interpreted in the EU Guide to GMP have been followed.
- The principal manufacturing and testing processes have been validated.
- All the necessary quality control checks and tests have been performed, and account taken of the manufacturing and packaging conditions including a review of batch records.

*NB. The EU Guide to GMP suggests that the Head of Production and the Head of Quality Control assume line management responsibilities for these activities.*

- Any changes or deviations in manufacturing, packaging or quality control have been notified in accordance with a well-defined reporting system before any product batch is certified by the QP and released. Such changes may need notification to and approval by the Competent Authority of the Member State.
- Any additional sampling, inspection, tests and checks have been carried out as appropriate, to cover changes or deviations.
- All necessary manufacturing, packaging and associated documentation has been completed and endorsed by suitably authorised staff trained in the concept of Quality Assurance and in the appropriate GMP's.
- Regular audits, self-inspections and spot checks are being carried out by experienced staff and correctly documented according to an agreed system.
- All relevant factors have been considered including any not specifically associated with the output batch directly under review (eg. calibration and maintenance records, environmental monitoring).
- To maintain a register (or equivalent document) as a record of product batches certified by the QP prior to batch release.
- To retain reference samples of each product batch at the site of manufacture for a period of time in compliance with EU regulations and/or Member State requirements.
- The legal requirements regarding imported products have been fully met.

*NB. For products imported from outside the EU or EEA, the Qualified Person should ensure testing within the EU/EEA to the requirements of the Marketing Authorisation and any other tests to assure quality of the products, unless a mutual recognition agreement between the EU and the third country concerned allows the acceptance of manufacturer's batch certification in lieu.*

**The QP should also be satisfied that the medicinal products have been manufactured in accordance with GMP standards which are equivalent to those of the EU or EEA.**

- The QP should also recognise the need to consult other company experts in certain technical or regulatory areas to reinforce his/her knowledge on appropriate points when a doubtful situation arises (*eg. stability, unusual analytical results, process or equipment changes, potential environmental or microbiological risks, re-labelling, abnormal yields, cross contamination risks etc.*).
- In considering how to perform the above duties, the QP will have to 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 that the QP can take direct responsibility for some or all of the tasks outlined above. In larger organisations, the QP will be dependent upon the knowledge and expertise of his/her colleagues in undertaking some or all of the tasks.



However, it is of paramount importance that the QP takes steps, within a well-planned Quality Management System, to assure himself or herself that the tasks allocated are in fact being performed satisfactorily. Hence the routine duties of the QP depend very much upon a team effort wherein the individuals concerned realise the position and responsibility of the QP and provide every support.

**What cannot be over emphasised in this context is the QP's commitment to meet regularly with professional colleagues in all functional groups and to understand their contribution and impact upon quality.**

- The certification of a batch prior to release must be performed by a Qualified Person named on the appropriate Manufacturing Authorisation.

## 8. PERFORMANCE OF DUTIES AND REGULATORY COMPLIANCE

- Management, as a requirement of Quality Assurance, should clearly define the areas of work and the method of operating in the absence of the regular QP.

*NB. In the absence of one QP, the task of certifying batches can only be delegated to another QP nominated on the Manufacturing Authorisation and who is knowledgeable and experienced with regard to the medical products under review.*

- Whilst each QP has a personal and professional responsibility for being certain that the various checks and tests have been carried out, the detail of this work is described in the EU Guide to GMP as normally the responsibility of the Head of Production and the Head of Quality Control who must ensure that appropriately trained and experienced staff are available.

*Ultimately the QP must be satisfied either directly or, more usually, by the proper operation of quality systems which include appropriate approvals, audits, self-inspections and spot checks that manufacturing, packaging and quality control testing have complied with relevant requirements. **Batch certification without such adequate steps may be regarded as professional misconduct.***

- It must be recognised that the QP depends upon many of his/her working colleagues for the achievement of quality and regulatory compliance in the manufacture of Medicinal Products. It is therefore of paramount importance that he or she achieves a good working relationships with other persons in positions of responsibility. These are likely to include those responsible for:-
  - *processing and packing operations*
  - *quality control laboratories*
  - *validation*
  - *application and maintenance of Manufacturing and Marketing Authorisations*
  - *provision of engineering services*

- *procurement of starting and packaging materials*
  - *storage, transport and distribution*
  - *contract services*
- It is recommended that the company and the QP take the necessary steps to appraise other functional groups, and the responsible people who belong to them, of the role of the QP within the company and how they should give proper support.
  - Ensuring compliance with the conditions of the Marketing Authorisation is a primary duty of the QP. It is, therefore, essential that the Qualified Person has access at all times to the dossiers upon which Marketing Authorisations have been granted, including any variations affecting such approval. The control of change needs to be rigorously monitored by the QP especially where there are implications for compliance, quality and patient safety. Particular attention needs to be paid to this when the manufacturer is making products for a Marketing Authorisation holder in a different company.
  - The QP should be present at the manufacturing site for a sufficient proportion of the working time in order to discharge the legal and professional obligations outlined in this Code and to ensure the proper operation of a Quality Management System including the control of any delegated duties.
  - Manufacturing Authorisations contain the names of the persons responsible for Production, Quality Control, and the name(s) of the Qualified Person(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 EU Directives.

## **9. NUMBER AND LOCATION OF QUALIFIED PERSONS**

- The provisions in Article 52 of directive 2001/82/ EC and/or Article 48 of directive 2001/83/EC only require a company or organisation to nominate one person on a Manufacturing Authorisation to carry out the duties of the QP provided that person is at the disposal of the company at all times and can carry out the required functions.
- Some organisations may have a complex structure, or operate at several locations, or both, which would make it necessary, where justified, to nominate several QP's on its Manufacturing Authorisation.
- In France the Pharmacien Responsable (Responsible Pharmacist) has overall legal responsibility for all products produced by the company, he may delegate this responsibility to an Interim Responsible Person in his absence who assumes legal responsibility. Delegate pharmacists at site level may have a number of QP's working for him, but they have no legal responsibility but must act at the direction of the Responsible Pharmacist or his nominated interim.

## 10. CONTRACTED QUALIFIED PERSONS

- Smaller companies in some EU countries are permitted to employ a 'Contracted QP' who provides a part time service. In such cases the duties and responsibilities of a 'Contracted QP' are the same as those QP's who are permanently employed; the QP is not an employee of the company but provides his services under contract.

*NB. The term 'Contracted Qualified Person' is not a formal title and is used only in the sense of a QP providing an independent service under contract to a company.*

- In addition to compliance with the provisions applicable to all QP's including all the routine duties outlined in this Code of Practice, Contracted QP's are recommended to 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 readily available to the staff of the company for advice and discussion, and also 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, procedures etc. which are relevant to the decision-making processes when certifying batches for sale. In addition the company should inform the QP of any deviations which need to be considered in relation to batch certification. Such deviations should be provided to the QP promptly and in writing.*
  - *ensure that sufficient spot checks, inspections, and audits of the company are carried out. In particular the 'Contracted QP' should satisfy himself/herself that an Effective Pharmaceutical Quality Management System is being operated.*
- Particularly for smaller companies, the person acting as Contracted QP may agree with the company to provide some of the necessary services such as, for example, staff training, internal audits and maintenance of Authorisations, personally in addition to performing strictly QP duties.
- If any doubt exists concerning the duties and responsibilities between the QP and the company who requires his/her services, it is suggested that he or she should contact their Member State Inspection Service.
- **This Code of Practice should be brought to the attention of the Chief Executive Officer of the company who wishes to have the services of a 'Contracted QP'.**

## 11. CONTRACT MANUFACTURE AND/OR TESTING

- Where products are manufactured and/or packed under contract there should be a clearly written technical agreement between the contract giver and the contract acceptor. Such an agreement should be reviewed and approved by the QP engaged by the contract giver and acceptor. The agreement should clearly delineate the areas and responsibilities of both QP's.
- The contract acceptor, who normally will be required to hold a Manufacturing Authorisation, may accept full responsibility for batch certification provided that the QP has all the appropriate information (including access to relevant details in the Marketing Authorisation(s)) and authority to fulfil these duties. Nevertheless the decision concerning responsibility for batch certification remains a matter between contract giver and acceptor depending on the circumstances.
- The provisions above apply equally to the testing of samples under contract. The contract testing laboratory may not hold its own Manufacturing Authorisation but in this case must be authorised on the contract giver's authorisation and may be subject to inspection by the Inspection Service of the Member State.
- **Reference to Chapter 7 (Contract Manufacture and Analysis) and Annex 16 (Certification by a QP and Batch Release) of the EU Guide to GMP is especially important.**

## 12. CONTINUING PROFESSIONAL DEVELOPMENT- Continuing education

- QP's have a personal and professional duty to keep their knowledge and experience up to date ( Annex 16 8.3 EU Guide to GMP, and volume 4 of the rules Governing Medical Products in the European Union). It is expected that this would cover the current state of pharmaceutical quality management, regulatory aspects and GMP guideline standards, product manufacturing and control technology, and general work practices.
- It is suggested that records of Continuing Professional Development (CPD) should be kept to reflect this important longer-term aspect of the QP's continued performance of professional duties.
- In the event of a QP making a major change in job responsibilities, for example from a company making only sterile dosage forms to one with a wider range of products including solid dose forms, the QP and the senior management of the company involved should recognise the need for additional education and training and take adequate steps to demonstrate that proper provision is made for this. Such extra training should be undertaken before the QP acts in a new situation.

### 13. PROFESSIONAL CONDUCT

- QP's have duties not only to their employer but also to the Competent Authority and its Inspection Service. They must ensure that appropriate senior company executives are made fully aware of any manufacturing and/or testing difficulties which do not comply with the registered specifications or post facto might require a product recall.
- If there is any aspect of the Quality Assurance system which is not in accordance with the Directives and Guidelines for Good Manufacturing Practice then the QP has a duty to bring this to the attention of Senior Management and ensure that appropriate corrective measures are taken.
- QP's are encouraged to establish a good working relationship with the Inspection Service of the Member State 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 Inspection Service of the Member State for advice or clarification in particular circumstances with which the QP is faced.*

- In cases where undue pressures to depart from professional and technical standards cannot be counterbalanced by reference to this and other relevant Codes of Practice, QP's should contact the appropriate Authority of the Member State, preferably having informed their employer first.
- Management has a duty to provide QP's with appropriate resources and to ensure that Quality Management Systems and communications are working effectively. Therefore, QP's also have a duty to make representation to management, if necessary in writing, whenever standards appear to be falling short of Good Manufacturing Practice(s). This duty should be reflected by appropriate wording in the QP's job description.

## 14. DISCIPLINARY PROCEDURES

- Article 56 of directives 2001/82/EC and Article 52 of directive 2001/83/EC require that Competent Authorities of Member States put in place administrative measures as follows:-

*"Member States shall ensure that the duties of QP's ... 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 for failure to fulfil his obligations".*

- The QP has a personal and professional responsibility for ensuring that the various tests and checks have been carried out. This does not necessarily mean that he/she must have carried out those tests or have directly supervised them, but in certifying in the register or equivalent document he/she is in effect indicating that they have satisfied themselves that the appropriate tests have been carried out and that the batch complies with all the relevant requirements.

**If it were found that a person had certified a batch without taking adequate steps to assure compliance, this failure might be a matter for consideration by the appropriate Competent Authority of that Member State.**

- Professional Orders and Associations in most EU countries have established disciplinary procedures for withdrawing the right to practice from individuals who have not complied with the duties and responsibilities of the QP.
- In cases involving disciplinary procedures the Competent Authority of the Member State is the body with the ultimate power to remove the QP's name from the Manufacturing Authorisation.

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