

The roles and responsibilities of the Qualified Person in the pharmaceutical industry

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Introduction

Malta's accession into the European Union in May 2004 brought with it a number of changes within the local pharmaceutical industry. Foremost amongst these was the requirement for the holder of a manufacturing or import authorisation to have permanently and continuously at his disposal the services of one or more Qualified Persons (QPs).¹

QP certification and batch release were originally defined approximately a quarter of a century ago in Council Directives 75/319/EEC (Human) and 81/851/EEC (Veterinary), which have now been incorporated in Directive 2001/83/EC (Human) and 2001/82/EC (Veterinary), respectively, as amended by subsequent Directives. Currently, no

batch of medicinal product may be released to the market within the European Union (EU), unless a nominated QP has certified that it has been manufactured and checked in compliance with national and European law, and the requirements of the marketing authorisation.

However, the logistics existing in today's pharmaceutical industry are in stark contrast to the situation that existed in the seventies, where single-site manufacture was the norm. Today's complexity implies that QP overview and batch certification has become a much more laborious task, due to mergers and acquisitions leading to 'split-site' or 'multiple-site' manufacture.

The Legal Duties of the Qualified Person

The legal duties of the qualified person are

to ensure that:

- Medicinal products manufactured within the European Union have been manufactured and checked within the boundaries of national law and the requirements of the Marketing Authorisation (MA).
- Any pharmaceutical imported from a third country must have undergone, within the EU, a full qualitative analysis, a quantitative analysis of at least all the active ingredients and all other tests necessary to confirm compliance with the MA.
- Finally, the QP is bound by law to certify in a register or equivalent document, that the above-mentioned provisions are satisfied before the batch is placed on the market.

The Routine Duties of the Qualified Person

Placing a medicinal product on the market involves various stages from development at laboratory scale up to commercial manufacture.

A well planned, organised and maintained Quality Management System (QMS), as referred to in Article 6 of 2003/94/EC, is key to ensuring that a medicinal product of the required quality, safety and efficacy reaches the patient.

For a product to meet the required standards various elements of current Good Manufacturing Practices (cGMP) need to be in place, including training, documentation control, validation, change control, maintenance, control of purchasing, and self inspection to name but a few.

Given this plethora of responsibilities, in all except small scale operations the QP has no alternative but to delegate some or all of these routine duties to colleagues. Delegation of these duties should be clearly defined within the QMS.

Having said this, it should be specified that the legal duties mentioned previously may only be delegated to another QP. Conversely, sufficiently qualified and trained personnel should be designated to perform any day-to-day tasks related to ensuring adherence to the quality systems in place.

Thus, the critical requirements that a QP must take into account when certifying batches of medicinal product for release include, but are not limited to, the following:

- Batch compliance to the provisions of the MA.

- Adherence to the fundamentals of cGMP as stipulated in Directive 2003/94/EC and other relevant regulations.
- Validation of manufacturing and analytical procedures.
- Documentation and evaluation of any deviations or planned changes during manufacture.
- Adequate batch documentation endorsed by authorised staff.
- Assurance of a suitable internal/external audit schedule and respective corrective and preventive actions.
- Consideration of factors that may directly or indirectly affect the quality of the batch in question, such as environmental monitoring, calibration and preventative maintenance records.

The aforementioned list is not exhaustive and readers are referred to the various Codes of Practice listed in the Bibliography for further details.

The Qualified Person: A professional

Directive 2001/83/EC, as amended, requires Member States to ensure that the duties of QPs are fulfilled by appropriate administrative measures or by making them subject to a professional code of conduct. The latter provision is a clear indication of the professional role of the QP, and the necessary legislative framework to support this status of the QP has recently been enacted in Malta, establishing QPs as professionals within the Health Care Professions Act, under the auspices of the Pharmacy Council.

In considering the complexity of the roles of QPs discussed previously within the sphere of the QMS, team effort is of paramount importance. The individuals concerned must realise the position and

responsibility of the QP and provide every support.

Furthermore the QP must be committed to interact with professional colleagues and comprehend their contribution and impact upon product quality. Having said this, the QP must possess various key attributes which facilitate his/her role within the QMS. Of special mention are a sound knowledge of the laws, authorisations, products and processes coupled with experience of manufacture and its business requirements. On a personal level problem solving skills, teambuilding and professionalism play a crucial part in executing one's role successfully. Furthermore, active collaboration with the company's senior management is imperative, with the latter aiding in the implementation, maintenance and development of the quality system.

In conjunction, the QP's relationship with Regulatory Authorities is of utmost importance in the understanding of all the legal and regulatory obligations which his/her company must fulfill. This must be based upon the principles of mutual trust and respect for each other's role in relation to patient safety. It is also very important that the QP understands the organisational structure of the Regulatory Body and its operation, together with its key personnel.

Finally, as outlined in Annex 16 to the EU GMP guidelines, 'Certification by a Qualified Person and Batch Release', continuous training is essential in maintaining knowledge and experience current in the light of technical and scientific progress. Although there are no specific requirements regarding the content of the continuous training defined in EU legislation, various guidelines and Codes of Practice are available to give direction to the QP in the execution of his/her duties.

Conclusion: a look to the future

The professional aspect of the responsibilities of the QP, as outlined above, has led to a discussion at European level as to whether amendments to Annex 16 should grant QP's greater discretion in dealing with one-off minor deviations from the details set out in the MA, provided that such deviations do not influence the safety or efficacy of the product, and the decision whether to release the medicinal product notwithstanding such deviation is based on principles of quality risk management, as outlined in the recent Annex 20 to the EU GMP guidelines. However it is generally accepted that the implementation of quality risk management principles will require a cultural change in the pharmaceutical industry, and in the light of the reticence of the competent authorities in certain Member States to accept the EMEA proposal, further discussion at the highest level is required before this principle can be implemented.

More recently, greater emphasis has emerged on the role of QPs in the prevention of the penetration of counterfeit medicinal products in the EU. The latest proposal for amendments to Directive 2001/83/EC introduces a requirement for features on the outer packaging making it possible to ascertain the identification, authenticity and traceability of medicinal products subject to medicinal prescription. The role of the QP in this field is being considered so important that ensuring the presence of these features is being proposed as a new legal duty, one which will certainly call upon the professional responsibility of Qualified Persons to update their knowledge in this field, as befits health professionals responsible for ensuring the quality, safety and efficacy of medicinal products.

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