The roles and responsibilities of the EU qualified person for pharmacovigilance under Volume IXa March 2007

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Abstract

The role of drug safety both in drug development and post-marketing surveillance has increased enormously over recent years. For the EU, this has culminated in a designated individual, the qualified person for pharmacovigilance (PV), who has responsibility for the overall procedures that exist in a company for safety management. This role has evolved since it was first introduced in the late 1990s to a critical role in the company both in terms of managing risks with products while either still in the clinical phase or the post-marketing phase. Such a role demands that the person who takes on the mantle has to be knowledgeable in PV legislation. The new Eudralex Volume IXa issued in both January and then revised in March 2007 has again emphasised and clarified this role. All licence holders in the EU must have this person in place, and the scope of this role is discussed below.

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INTRODUCTION

In recent years, there has been a growing trend within Europe to appoint either at an EU level or at a national level, a person responsible for the safety of all marketed products. With the advent of Volume IX and now the new Volume IXa [1] and similar legislation, this evolved into a person called the EU qualified person (QP) for pharmacovigilance (PV). A deputy EU QP is also required in case the EU QP is not contactable (holidays, sickness, etc).

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Additional national legislation around the EU has also required local QPs for PV to be in place who may also serve as the EU QP as well as the national QP.

This paper explains both the qualifications of the EU QP and the role and responsibility of this person as outlined in the now issued Volume IXa January/March 2007.[1]

THE EU QP FOR PV

Qualification of the EU QP

There is a very vague reference in Volume IXa of being trained in all aspects of PV. This term conjures up the image of a guru of PV knowledge and does little to help both Companies and regulators ensure a consistent

standard is applied to this position across various companies.

Of clearer definition is the fact that the EU QP PV should be supported by a safety physician (note the word safety – implying knowledge of regulatory definitions of medicines safety) if the EU QP PV is not medically qualified. This allows medical interpretation of safety information on the company products.

The deputy EU QP PV is equally expected to be suitably qualified as the EU QP PV since the deputy may need to take over safety issues if the EU QP PV is not around, and so must be equally conversant with safety legislation, the safety set up of the company and any pending product specific safety issues.

Both the EU QP PV and deputy must reside within the EU and so delegation outside of the EU is not allowed.

Regarding the PV knowledge of the EU QP PV and deputy, this does not have to be exhaustive because providing the EU QP PV understands the concepts of safety being applied, then the actual tasks can be delegated (such delegation being documented), the EU QP PV does not therefore have to physically perform some of the tasks. This should, however, not be construed as an excuse for not knowing the legislation or being appointed in the position so that such knowledge can be gained 'on the job' or delegated to someone who is aware of the legislation.

The curriculum vitae (CV) of the EU QP PV must be registered with the EMEA and competent authorities. Additionally, for any new licence submission in the EU, the CV of the EU QP PV must be supplied when applying for a product licence. The competent authorities may question, from the CV, the competency of the EU QP PV if it is viewed that such a person has not demonstrated enough safety experience from their CV to date. The regulatory agency may also ask (in addition to the EU QP PV) for the details of the local (national) QP, if this is required, and that individual is not fulfilling both roles.

If such experience is limited in a company then it is possible to contract out such a position (including deputy) to consultants who have the necessary experience – as evidenced in their CV and previous safety roles in various companies.

It is not acceptable to appoint a person within the company with little experience because 'there was no one else' as the role is far too critical for this.

The larger the company the more important it is to have a permanent member of staff take on this role, but use of such a person in an interim situation, however, would be acceptable.

What must the EU QP PV be in charge of?

Volume IXa is quite explicit in the level of oversight required for the EU QP PV. Succinctly, the EU QP PV must ensure the following are in place:

- Individual case safety reports (ICSRs).
- Periodic safety update reports (PSURs).
- Reports on company-sponsored post-authorisation safety studies.
- Quality control and assurance procedures.
- Standard operating procedures.
- Safety database operations (including validation, administration and support).
- Contractual arrangements (licensee–licensor interactions).
- Compliance data (eg in relation to the quality, completeness and timeliness for expedited reporting and submission of periodic safety update reports).
- Audit reports (for affiliate compliance).
- Training of personnel in relation to PV.
- The conduct of continuous overall PV evaluation during the post-authorisation period.
- Ensuring that any request from the competent authorities for the provision of additional information necessary for the evaluation of the benefits and the risks afforded by a medicinal product is answered fully and promptly, including the provision of information about the volume of sales or prescriptions of the medicinal product concerned.
- The provision to the competent authorities of any other information relevant to the evaluation of the benefits and risks afforded by a medicinal product,

including appropriate information on post-authorisation studies.
- Ensuring that the safety labelling for the product is maintained and promptly updated to ensure both patients and healthcare professionals are aware of the risks associated with the product (as determined by signal detection/safety reviews looking for new potential events).

Naturally, the EU QP PV does not need to perform all of these actions him/herself but must be knowledgeable of what is required to get all of the above performed to an acceptable and compliant standard according to the various legislation that supports the production of all of the above requirements. This will also require personnel, appropriately trained to perform the duties described.

If the EU QP signs, as agreed, any of the above outputs above, then this is an endorsement both of the accuracy of the documentation and the format required to be seen by the regulatory authorities in terms of the compliance of the company in its PV activities and responsibilities.

The EU QP PV will then be required to justify such actions, outputs and documentation to the regulatory authorities in any PV Inspection.

The qualities and experience of the EU QP PV are expected to be the same irrespective of the company's product portfolio, be they over the counter (OTC) medicines, innovative products, biotechnology products or generics.

Availability of the EU QP PV

The expectation is that the EU QP PV will be available 24 h a day and seven days a week in order to answer any urgent safety issues with any product, even older generic products. No distinction is made concerning the knowledge, experience and availability of the EU QP PV simply because the company has old generic products, OTC medicines, herbal products or a single biotechnology product.

This raises the issue of holidays, sickness and lack of availability when on long distance flights and so on, if there was an urgent safety issue that required his/her attention.

Therefore, the deputy EU QP PV has to be ready to step into the role whenever the EU QP PV is indisposed. This requires that the deputy EU QP PV has to be knowledgeable of all issues and status of PV within the company at any time so that they can assume the responsibility for monitoring the safety of the company products, have to be conversant with the company role of the EU QP, again reflected in their job description and training, and ensure that holidays are not taken at the same time as the EU QP PV.

THE EU QP PV AND THE PRODUCT LIFECYCLE

At what stage does the EU QP PV take responsibility for products within the company? Traditionally, the EU QP PV was responsible for marketed products only. With the advent of risk management plans (RMPs), this has, however, altered.

A PV RMP may be developed during the clinical development programme. Since the EU QP PV is expected to approve this while the product is on the market, then it is logical that this also involves approval of any RMP during product development too which means that the EU QP PV should approve such programmes while the product is being developed.

Also, as a company launching its first product, the EU QP PV must be mentioned on any licence submission and so before a company has even launched a product it must have the services of an EU QP PV.

REGULATORY INSPECTIONS FOR PV

The EU QP PV is expected to be the primary contact point for all regulatory PV Inspections. The aim is that all licence holders in the EU will be seen within four years of placing a product on the market. This time-span may be early depending on the type of product approved (patient risk), the extent of marketing and whether the regulatory agency has previous experience with the company.

The EU QP PV must be able to demonstrate their knowledge of the EU legislation and the systems in place for PV

including any audits for compliance and any quality management systems in place to improve on compliance.

If systems are inadequate and this is because the EU QP PV is not understanding of the role and responsibilities then action and penalties can be made against the EU QP PV.

CHALLENGES FOR THE EU QP PV AND COMPANY

Key challenges still exist for the implementation of such a role within the company. The EU QP PV is almost exclusively an EU role (notable exceptions being Turkey and Croatia who require national QPs for PV) and therefore multinational organisations, where the Headquarters may not be located in Europe, may have difficulty understanding the requirement for the level of oversight and involvement in safety issues for the QP.

Additionally, the EU QP PV, according to Volume IXa must be supported by the company in their efforts to establish such PV activities, which could mean that the EU QP PV requires more resources (both temporary or permanent) and systems hardware (safety databases) in order to provide a compliant safety system.

The regulations are clear on this point, that empowerment of the EU QP PV to perform such duties is the responsibility of Senior Management within the company, and if this is not provided it is they and not the EU QP PV that will attract attention in circumstances of noncompliance from regulatory authorities.

This is undoubtedly a challenging and vital role within the company and needs to be reflected as such both in terms of their place within the company, who they report to and their knowledge.

For companies that have a single product or old OTC medicines, their challenge is to either train up an individual in the company to perform such activities and be knowledgeable of the company's PV obligations or to obtain the services of a suitably trained contract QP to provide the necessary oversight. Such contract personnel do exist but again the company has the responsibility to select suitably qualified people to perform such activities and must ensure that the CVs of such individuals reflects their safety training and therefore suitability.

Reference

1. European Commission (2007) EudraLex. The Rules Governing Medicinal Products in the European Union. Enterprise and Industry Directorate General, European Commission. Available at http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/index.htm, accessed 16th July, 2007.

