REGULATORY REQUIREMENTS AND RESPONSIBILITIES OF A QUALIFIED PERSON IN THE PHARMACEUTICAL INDUSTRY

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Abstract: A Qualified Person (QP) is a person who is responsible for ensuring the safety, quality and efficacy of medicinal products throughout their entire life cycle.
Directive 2001/83/EC on medicinal products for human use represents a regulatory requirement for EU countries for delegating a role for Qualified Persons. In the EU Guidelines for Good Manufacturing Practice for Medicinal Products for Human and Veterinary Use in Chapter 2: Personnel there is a designated part of the document for the Key Personnel, where the Qualified Person belongs. Its duties and obligations are clearly stated as they are stated in the Article 51 in the Directive 2001/83/EC. In the Article 49 of the Directive 2001/83/EC is stated the qualification level as well as the necessary experience of a Qualified Person. A qualified person must hold a diploma, certificate, or other official document attesting to their formal qualifications, which must be the result of at least four years of theoretical and practical study in one of the scientific fields of pharmacy, medicine, veterinary medicine, chemistry, pharmaceutical chemistry and technology, or biology. These fields must be recognized as equivalent by the Member State in question.
In the Republic of North Macedonia, there is also a legal obligation for the Manufacturing license holder who puts a drug on the market, to have a Qualified Person appointed. According to the Law on Medicinal Products and Medical Devices of the Republic of North Macedonia, Part III Production of Medicinal products, Article 68, every manufacturer of medicinal products should employ responsible persons for production, quality control and a qualified person for batch release with specific education requirements. This law has a requirement that the qualified person for batch release should be highly educated in the field of pharmacy and have additional knowledge in the field of production and quality control of the medicinal products. Also this person should be fully available in any part of the day and guarantee for every produced and controlled batch of the medicinal product produced by the manufacturer.
This person should have special continuous training and specific skills that help him/her in his/hers daily work. The qualified person should possess specific skills that include: Ability to make effective decisions, ability to solve problems, communication skills, ability to manage priorities and many others. The personnel professional development, especially that of qualified persons, is considered the most important element of the pharmaceutical industry and is one of the conditions for the success of their activities.
The aim of this article is to present current regulatory requirements and roles and responsibilities of a qualified persons in EU and North Macedonia.
Keywords: qualified, person, QP, pharmaceutical, industry

1. INTRODUCTION

A Qualified Person (QP) is a person responsible for ensuring the safety, quality and efficacy of the medicinal products throughout their entire life cycle.
The EU GMP regulation has a strict requirement that each drug manufacturer has designated the key persons in the authorization for production: Head of Production, Head of Quality Control and Qualified Person.
When delegating the role of Qualified Persons, the EU member states are guided by Directive 2001/83 EC, for medicinal products for human use. However, each country has its own national requirements for qualifications that the Qualified Person should possess. (Directive 2001/83/EC, 2001)
In the Republic of North Macedonia, the legal obligation of the holder of the authorization to put a drug on the market is to have a qualified person appointed. This person is a full-time person employed by the manufacturer of the drug and makes a decision and approves the release of a batch of a drug into the market or rejects it. (Official Gazette of R.N.Macedonia, 2007)
The aim of this article is to present current regulatory requirements for a qualified persons in EU and North Macedonia. Also, this article presents the role and responsibilities of a qualified person in the pharmaceutical industry.

2. MATERIALS AND METHODS

The paper presents literary data, gathered from several regulatory and professional sources which are compiled, analyzed, and presented as a preview of regulatory requirements and responsibilities of a qualified person in the pharmaceutical industry.

3. DISCUSSIONS

Regulatory requirements

Directive 2001/83/EC on medicinal products for human use represents a regulatory requirement for EU countries when delegating a role for Qualified Persons. However, since it is a Directive of the European Union, each member state has introduced its own national requirements for qualifications that a qualified person should possess.

In the Article 49 of the Directive 2001/83/EC there is a statement for the qualification level as well as the necessary experience of a Qualified Person. Qualified persons must hold a diploma, certificate, or other official document attesting to their formal qualifications, in any of the scientific fields of pharmacy, medicine, veterinary medicine, chemistry, or medicinal chemistry. It should be the result of at least four years of theoretical and practical research. technology or biology. These fields must be recognized as equivalent by the Member States concerned. However, the minimum length of an undergraduate course can be three and a half years when the course is followed by a period of theoretical and practical training lasting at least one year and including a little internship. six months at a pharmacy open to the public, supported by a college-level exam. Where two university courses or two courses recognized as equivalent by the State co-exist in a Member State and one lasts four years and the other three years, the three-year course will result in a diploma, certificate or other training title granted at the conclusion of an undergraduate course of study or recognized equivalent to be deemed to have met the deadline condition set out in the second paragraph to the extent that the diplomas, certificates or other training titles granted after completion of two courses recognized by the relevant State as equivalent. The course will include theoretical and practical studies covering at least the following fundamental topics: Applied physics, General and inorganic chemistry, Organic chemistry, Analytical chemistry, Pharmaceutical chemistry including analysis of medicinal products, General and applied biochemistry (medical), Physiology, Microbiology, Pharmacology, Pharmaceutical technology, Toxicology and Pharmacognosy (studies on the composition and effects of natural active ingredients derived from animals and plants). (Directive 2001/83/EC, 2001)

In the Republic of North Macedonia, there is also a legal obligation for the Holder of the authorization to put a drug on the market, to have an appointed Qualified Person. This person is a full-time person employed by the manufacturer of the medicinal products and decides and approves the release of a batch of a drug into the market or rejects it. According to the Law on Medicinal Products and Medical Devices of the Republic of North Macedonia, Part III Production of Medicinal products, Article 68, every manufacturer of medicinal products should employ responsible persons for production, quality control and a qualified person for batch release with specific education requirements. This law has a requirement that the qualified person for batch release should be highly educated in the field of pharmacy and have additional knowledge in the field of production and quality control of the medicinal products. (Official Gazette of R.N.Macedonia, 2007)

Specific skills of a qualified person

The qualified person should possess specific skills that include:

Ability to make an efficient decision: Making a decision on releasing or rejecting a batch of medicinal product should be: timely, reasoned and fast.

Skills that the Qualified Person should possess when making a decision on a batch of medicinal product are:

- Ability to make a decision based on the available information,
- Ability to make own decision without other people's influences,
- Ability to make unpopular decisions,
- Ability to make decisions under pressure,
- Ability to make reasoned decisions.

Problem Solving Ability: In the context of making a decision to certify a drug batch, this skill includes recognizing the real problem, analyzing the situation, and being able to draw a conclusion. It is necessary to emphasize the importance of recognizing the real problem, which prevents the repetition of the same situation, which increases the efficiency of work and makes it easier and faster to make the right decision. During all this time the Qualified Person must maintain focus and be stable, regardless of whether he is solving one or more problems at the same time.

Communication skills: The qualified person should possess good communication skills which are a very important tool, especially when announcing an unpopular decision, e.g. to the Management or the Sales Department.

Ability to manage priorities: The qualified person should understand the broad context of responsibility and responsibilities, as well as the work environment and interactions and expectations in that environment.
A qualified person should successfully define priorities, thus managing his time well. (European Industrial Pharmacists Group, 2004)

Activities and responsibilities of a qualified person

The qualified person has the obligation to ensure that each batch of the drug is manufactured and analyzed in accordance with the applicable laws in the respective country and in accordance with the marketing authorization. It also supervises the entire pharmaceutical quality system in the company and contract manufacturers in accordance with Annex 16 of cGMP.
The qualified person also monitors and approves investigations and reports on deviations and cases where results are obtained outside the approved specification or out-of-trend results. In addition, it monitors quality non-conformities, complaints, withdrawals and recalls of a batch of a drug from the market. Participates in making decisions related to these processes.
The qualified person participates in the meetings held within the Change Control process.
This person performs control and coordination of all activities that ensure the quality of medicines, by checking the record of the batch of medicine (production protocol, packaging protocol and analytical file) with particular attention to the results of the process and control parameters. Monitors stability results of commercial and development batches.
If the validation batches are intended to be commercial batches, the Qualified Person performs a full inspection of them. It also performs a full inspection of samples/lots intended for clinical trials.
The qualified person monitors the quality of products from the manufacturer's drug portfolio through Periodic Product Quality Reviews. Approves specifications and analytical methods of drugs and validation reports of analytical methods.
The qualified person monitors the indicators of validation and monitoring, to monitor the status of each product, as well as the results of Microbiological monitoring of the space.
The qualified person is part of performing Internal Audits as part of the team. Performs education and mentoring on topics related to the process of batch certification and release of a batch of medicine. It continuously evaluates the possibility of improving the quality of medicinal products and processes.
This person follows and implements professional literature, regulations, and knowledge in the field of cGxP, certification and release of a batch of medicine and participates in the implementation of new projects/processes in the company according to the current regulation for medicines. (European Compliance Academy, 2007)

4. CONCLUSIONS

A qualified person in the pharmaceutical industry has a very responsible position in the pharmaceutical industry. This person is responsible for releasing of each batch of medicinal products on the market and is also responsible for ensuring the safety, quality, and efficiency of the medicinal products during their entire life cycle.
This person must justify this great responsibility by possessing numerous trainings, specific skills, and qualifications.
A person designated as a qualified person under the various regulatory requirements of the European Union and our country includes:
- Special requirements for previously completed education,
- Additional requirements regarding the work experience of this person,
- The possession of specific skills,
- Attending continuous trainings during his work in the position.

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