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Quality Control of Medicines and the Role of Quality Control Laboratory

Merita Kucuku*

Freelance Consultant, Albania

***Corresponding Author:** Merita Kucuku, Freelance Consultant, Albania.

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Abstract

"All substances are poisons there is none which is not a poison. The right dose differentiates a poison and a remedy"

- Paracelsus 1493-1541.

The medicines is very important to fill out 3 criteria for human use. First of all the medicines is necessary to have good quality, and must be safe and effective. The quality of medicines has an impact on public health and quality control should be guaranteed by National Regulatory Agency in the country. The medicines from manufacturer to customer pass in long procedure especially when the medicines are imported the procedure is longer. During this time the medicines can expose incorrect delivery and storage condition and any other mistake in the procedure can detected and avoided from the quality control of medicines in the control laboratory.

Keywords: *Quality Control; Medicines; Quality Control Laboratory; safety of medicines and regulatory system.*

Introduction

The pharmaceutical industry has evolved, and so has the concept of quality assurance of pharmaceutical products gradually evolved over time.

Quality assurance of medicines contributed to public health enabling standards of health care system.

Based on World Health Organization (WHO) recommendations quality assurance of medicines is achieved through:

1. The development of the norms, standards, and guidance of the Food and Drug Administration (FDA), European Medicines Agency (EMA), and World Health Organization (WHO) quality control and quality assurance of medicines.
2. Development of international pharmacopeia.
3. Creation of international chemical reference substances (ICRS).
4. Cooperation with different stakeholders.

Quality control of medicines in the control laboratory of medicines should have management and technical personnel, management of responsibilities for technical operations, and provisions of necessary resources to ensure the required quality of laboratory operations

and policies and procedures in the country to ensure the confidentiality of the information contained the marketing authorization, transfer the results or reports, protection of data in the archive (letter or electronically laboratory of medicines [1].

Material and Method

This research is based in literature for the quality control of medicines in different time in human history from the century 15th and continuously.

Results and Discussion

The strengthening of laboratory capacities, investments with state-of-the-art equipment and devices and the training of staff of laboratory with contemporary knowledge of medicines control, is very necessary and important because directly affects the quality of medicines to ensure the health of the population. This also is a way to avoid counterfeit medicine in the market which is very common today.

Pharmacopeia

The word Pharmacopeia is from Greek language: pharmakon (medicine or charm) and poiein (to make). In Italy, a physician from Florence Lodvice dal Pozzo Toshchanelli, prepared a little book with information for quality standards in drug therapy. This book will serve as guidance for pharmacists in the century 15th [3].

First Pharmacopeia was the European Pharmacopeia in the 16th century.

First Spanish Pharmacopeia issued in year 1581.

London Pharmacopeia established in England was in year 1618 and prepared the standards for the manufacture of the Mithridatum [4].

The responsibility of Pharmacopeia commission is the protection of the public health related to the medicines against error, ignorance or fraud. This responsibility defined from the standards must meet the medicines offered for the human use and the methods used for the compatibility assessment. Pharmacopeia used for ensuring safety of medicines used for human use.

Except for pharmacopeia for the safety of medicines also using control by legislation over the trainings and practice of pharmacists, control about the amounts of certain medicines with the prescriptions of doctors, control about the amounts of medicines sold from pharmacists especially in EU countries for all medicines except a small number, inspection of manufacturer of medicines for their conditions of productions, inspection and evaluation from the experts of the formulations produced from the manufacture, registration procedures of the medicines for sale and testing of medicines sample post marketing [5].

Pharmacopeia used for quality control of medicines

Pharmacopeia used today for quality control of medicines are European Pharmacopeia (Ph. Eur.), United State Pharmacopeia (USP), British Pharmacopeia (BP). The use of pharmacopeia has no territorial limits for applications. Pharmacopeia contains monographs on pharmaceutical preparations and methods for their testing. It is claimed that the pharmacopeia has a valid regulatory function to perform which is not incompatible with but complementary to that of the registration system.

The purpose of the European Pharmacopeia is to promote public health by the provision of recognized common standards for the quality of medicines and their components. Such standards are to be appropriate as a basis for the safe use of medicines by patients. In addition, their existence facilitates the free movement of medicinal products in Europe and beyond. European Pharmacopoeia monographs and other texts are designed to be appropriate to the needs of:

- Regulatory authorities;
- Those engaged in the quality control of medicinal products and their constituents;
- Manufacturers of medicinal products and their individual components.

The European Pharmacopeia is widely used internationally. As globalization and expansion in international trade present a growing need to develop global quality standards for medicines, the Commission works closely with all users of Pharmacopoeia worldwide [6].

Why necessary quality control of medicines?

In human history happened very different situations with using medicines to cure diseases because:

1. The tests on animals are not reliable in relation to the effects on a human subject.
2. In clinical trials, the number of selected people and the duration of the trial are limited and conditions of use are different.
3. The information about serious adverse events and chronic toxicity used in the group are so much abundant [7].

Using the medicines had negative effects for the reason mentioned above which have been fatal causing the death of people.

In the first year, 1937 over 100 people in the USA died of diethylene glycol poisoning following the use of sulfanilamide elixir, which used the chemical as a solvent without any safety testing.

The second Thalidomide sale in Western Germany the first in year 1956.

In the third years 1958-1960 thalidomide was presented in 46 countries estimated 10,000 babies were born with phocomelia and other deformities.

These and other cases in different countries over the world made it possible to strengthen and reshape the regulatory system in different countries.

The United Kingdom 1963 Committee on the Safety of Drugs (CSD) voluntarily had to report Adverse Drug Reaction (ADR).

United State America in 1962 passed by Congress FDA to approve all new medicines applications for the first time, should be safe and effective [8].

On 1975 European Community introduced 2 Council Directives:

- First was the approximation of the Laws of Member States relating to analytical, pharmacotoxicological, and clinical standards and protocols in respect of the testing of proprietary medicinal products (75/319/EEC).
- Second was the approximation of provisions laid down by law, regulation, and administrative action related to medicinal products.

The table 1 below shows the cases of recall of medicines from the market, produced by different pharmaceutical companies in different countries.

Date	Brand name	Product description	Product types	Recall description	Company name
2/08/2018	Amneal Pharmaceuticals LLC	Lorazepam Oral Concentrate, USP 2mg/mL	Drugs	Due to Misprinted Dosing Droppers	Amneal Pharmaceuticals LLC
2/08/2018	Baxter	Intravenous (IV) solutions: 0.9% Sodium Chloride Injection, USP, 250 mL VIAFLEX Plastic Container and 70% Dextrose Injection (2000 mL) USP	Drugs	Labeled as Eliquis5 mg was found to contain Eliquis 2.5 mg tablets	Baxter International Inc.
2/08/2018	Bristol-Myers Squibb	Eliquis (Apixaban)5 mg tablet	Drug	Potential Labeling Issue	Bristol-Myers Squibb
1/08/2019	Sun Pharma		Drugs, Generic Drugs	Potential Foreign Material	Sun Pharmaceutical Industries, Inc
1/08/2019	Rhino	Rhino 5K capsules	Drugs, Generic Drugs	Undeclared Sildenafil and Tadalafil	Happy Together, Inc
03/15/2019	Hospira	Sodium bicarbonate injection USP	Drugs, Generic Drugs	Presence of Particulate Matter	Hospira.Inc
05/23/2019	Pharm D Solutions	Sterile Compounded Drug Products	Drugs, Generic Drugs	Lack of sterility assurance	Pharm D Solutions, LLC

Table 1: *Table has examples of medicines recall for the reason of safety and effects in human health and not all cases are included in this presentation [9].*

April 1 2020 FDA sought the withdrawal from the market Ranitidine medicine as this contain NDMA (N-Nitrosodimethylamine caused cancer in patients. NDMA during the storage in room condition and duration of storage in the room condition can be a risk to health of the patient.

As long as there is no information about the duration of storage of medicines is best to withdraw this medicine from the market to ensure the health of patients.

The level of NDMA is going increasing during the storage in the room condition and over time and can be a risk for consumers [10].

Risk of quality of medicines

Medicines are not ordinary consumers products. Consumers are not able to decide when to use the medicines, which medicines to use, which dose, the benefit risk and the medicines are not totally safe. Healthcare professional even have no capacity to take informed deci-

sions about all aspects of medicines without special training and access for necessary information. Production of medicines, distribution requires special knowledges and expertise.

The use of ineffective, poor quality harmful medicines can results in therapeutic failure, exacerbation of diseases, resistance of medicines and sometimes and death.

This can undermine confidence of the healthcare system, pharmaceutical professionals, manufacturers and distributors.

Other problem is money spend for ineffective, poor quality, unsafe medicines from insurance scheme or from patients/ consumers.

Challenge of laboratory of quality control of medicines

The challenges that must be faced by the control laboratory in control of pharmaceutical quality for safe and effective quality medicines are different like:

- Techniques and methods that must be well defined and mastered by the laboratory staff.
- Strengthening the laboratory, which is a fundamental feature that must be achieved in the conditions when working under time and cost pressure, using routine equipment of different levels by experienced staff.

Strengthening laboratory capacity

The staff of laboratory for quality control of medicines is very important point.

The technical and human capacity should receive an important attention of the country's authorities for raising and strengthening the technical and human capacities in a drug control laboratory for National Regulatory Agencies. It request qualified personnel, periodic training, technical knowledge and experience. The staff of the quality control laboratory of medicines should have very clear responsibilities in this laboratory, ensuring and clarifying of competencies for each other. The training of staff of quality control laboratory should evaluate and supervised in adequate manner, by experts and no political personnel. One way of evaluation will be participation of laboratory staff in proficiency test which is and one request of ISO 17025: 2017 for accreditation of laboratory.

Quality system of control laboratory

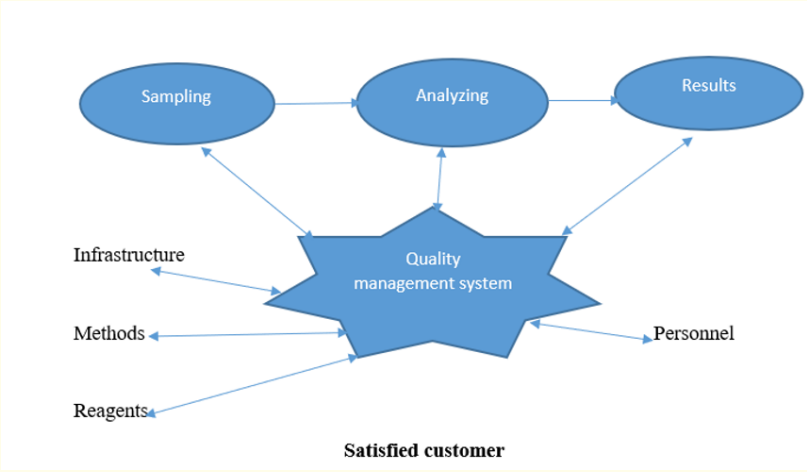

Figure 1: *Quality system of control laboratory.*

The figure 1 show how function the quality system in control laboratory. Sampling received in laboratory according the quality management system analyzing in laboratory with infrastructure using methods and reagents from the personnel which fill out the criteria of ISO 17025: 2017 to achieve the final goal satisfied customer for the safe and quality products.

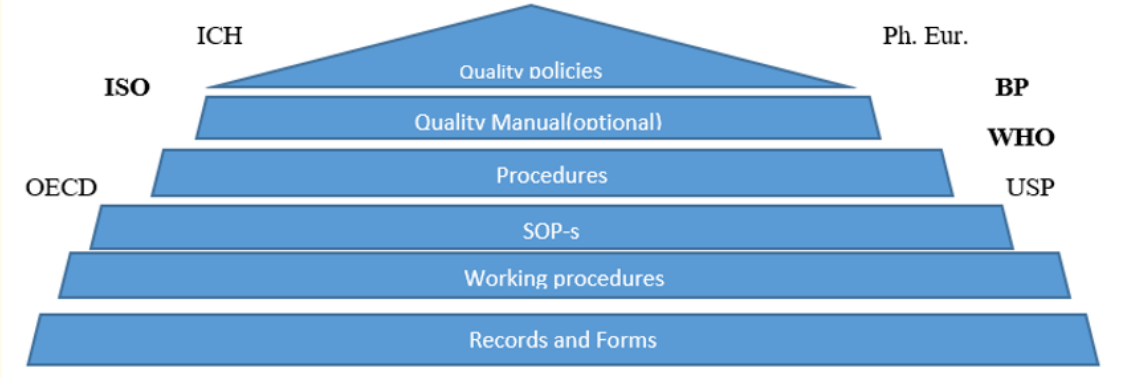

Figure 2: *Quality management scheme.*

Quality management system

1. Creation, implementation and maintenance of quality system management
2. Type of activities, range and volume of testing and validity and verification calibration
3. Policies, systems, programs, procedures and guidance
4. Understandable, possible, applicable system from the staff
5. Quality manual available from laboratory personnel [11].

International collaboration

The collaboration of laboratory of medicines control with homologies laboratory in different regulatory agencies of medicines in world is issue which should consider in objectives of laboratory as the exchange of information and practical experience is important for the newest development in pharmaceutical field and methods used in quality control laboratory.

OMCL Network (Official Medicines Control Laboratories) which is cooperation in the field of medical control traded products for human and veterinary use, activities that are partially funded by the European Commission [12].

TAIEX (Technical Assistance and Information Exchange Instrument) is the Technical Assistance and Information Exchange of the European Commission. TAIEX supports public administrations regarding the approximation and implementation of EU legislation, as well as facilitating the exchange of EU better practices. It is mainly directed by the needs of the places and offers the right expertise [13].

Conclusion

1. The role of the laboratory is very important for the quality control of medicines, not only for imported but and for the country of medicines production.

2. People very often discuss the efficacy of medicines and this answer can give from the laboratory.
3. Quality control of medicines has an impact on public health and this request a very qualified staff, proper equipment, and a laboratory building according to the technical condition for analyzing medicines.

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