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Important terminology in pharmaceutical quality assurance: Literature review

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Abstracts

The quality of pharmaceutical is the main concern since inception of world health organization certified and acknowledge the quality assurance terminology used in manufacturing and quality control laboratory. Company employees constitute the most important resource for improving quality. Each employee in all organizational units is responsible for ensuring that their work processes are efficient and continually improving. Quality assurance is the wide ranging concept covers all matters starting from raw material, finished products till to marketing. On the other hand, it is focused on providing confidence that quality requirements are fulfilled. As we all know medications are something that is used for disease or any illness in our body. Thus due to the reason, that the medication could also be harmful to the body, if the quality is not kept up to the requirements. Good Manufacturing Practice and Good Laboratory Practice is a very important aspect of QA, every methods and steps that is implemented should follow the GMP and GLP guidelines. Therefore the terminology used in quality assurance of pharmaceuticals aims to contribute to promoting understanding of the multiple layers of meaning which become apparent when we attempt to understand quality assurance across borders, and across languages. They do not offer a conclusion, but a point of departure for further research and reflection.

Keywords: Quality Assurance, Pharmaceuticals, Terminology, Good Manufacturing Practice, Good Laboratory Practice.

1. INTRODUCTON

The quality of pharmaceuticals has been a concern of the World Health Organization (WHO) since its inception. The setting of global standards is requested in Article 2 of the WHO Constitution, which cites as one of the Organization's functions that it should "develop, establish and promote international standards with respect to food, biological, pharmaceutical and similar products.Quality assurance" is a wide ranging concept covering all matters that individually or collectively influence the quality of a product. It is the totality of the arrangements made with the object of ensuring that pharmaceutical products are of the quality required for their intended use. Quality assurance therefore incorporates GMP and other factors such as product design and development [1].

High levels of quality are essential to achieve Company business objectives. Quality, a source of competitive advantage, should remain a hallmark of Company products and services. High quality is not an added value; it is an essential basic requirement. Quality does not only relate solely to the end products and services a Company provides but also relates to the way the Company employees do their job and the work processes they follow to produce products or services. The work processes should be as efficient as possible and continually improving. Company employees constitute the most important resource for improving quality. Each employee in all organizational units is responsible for ensuring that their work processes are efficient and continually improving [2].

Quality assurance functions primarily to monitor the fact that the quality function is being performed. Its role in process validation is readily associated with its main functions. It performs the tests that demonstrate the product's content uniformity. It may also perform the statistical evaluation of the test results to show that the process is reproducible. Quality assurance initiates the action to dispose of nonconforming product. It implements the inspection criteria and sets the specification for the product approval or rejection. It analyzes the product complaints to learn how effective its test program has been in preventing rejectable product from reaching the market place [3]

Quality assurance, on the other hand, is focused on providing confidence that quality requirements are fulfilled. As related to clinical trials, it includes all those planned and systemic actions that are established to ensure that the trial is performed and the data are generated, documented (recorded), and reported in compliance with GCP and the applicable regulatory requirements [2]. It is a very crucial aspect in every field of industry; it can be in the field of engineering, pharmaceutical products, food and beverage products. Name any field and quality is a must in it, the reason why QA is mentioned as a vital aspect is due to the fact that every products that are produce needs to meet a certain criteria of quality which will be safe and efficacy for the consumers [4].

As we all know medications are something that is used for disease or any illness in our body. Thus due to the reason, that the medication could also be harmful to the body, if the quality is not kept up to the requirements. Good Manufacturing Practice and Good Laboratory Practice is a very important aspect of QA, every methods and steps that is implemented should follow the GMP and GLP guidelines [5]. GMP ensures that the product is manufactured according to the standard to avoid any product related problem or any manufacturing related problem. In order for the production in a pharmaceutical industry to continue they have to obtain approval from the authorities and the particular authorities are keener on the GMP procedures that are used [6]. GLP is an important aspect for personnel's that are related to the lab works and analysis. Every methods and SOP should follow the GLP guidelines [7].

Therefore; the terminology used in quality assurance of pharmaceuticals aims to contribute to promoting understanding of the multiple layers of meaning which become apparent when we attempt to understand quality assurance across borders, and across languages. They do not offer a conclusion, but a point of departure for further research and reflection.

2. GENERAL DESCRIPTION OF QUALTY ASSURANCE IN PHARMACEUTICALS

Quality assurance is defined as the sum total of the organized arrangement made with the object of ensuring that the medicinal products are of the quality required for their intended use [4]. Quality assurance is a process that is done for validating and to ensure that the products that are released are safe and meets the requirements in every aspects, from the raw material till the product leaves the industry as a packed and finished product [9].

Quality Assurance is a management method that is defined as "all those planned and systematic actions needed to provide adequate confidence that a product, service or result will satisfy given requirements for quality and be fit for use". A Quality Assurance programme is defined as "the sum total of the activities aimed at achieving that required standard" [10]. Practically QA need to evaluate the whole system for its smooth operation while the major effect comes from the actions of the supporting department. In order to meet this objective the QA staff must interact and co-ordinate with their colleagues in the organization; Such as; finance, personnel, research and development, pack design, planning, purchasing, manufacturing, engineering, warehousing and distribution , marketing, etc. QA is a team work with a common goal for quality [11].

2.1. Components of quality assurance in pharmaceuticals industries

The components of a QA programme are often grouped into three levels, variously labelled: the strategic or organizational level (dealing with the quality policy, objectives and management and usually produced as the Quality Manual); the tactical or functional level (dealing with general practices such as training, facilities, operation of QA); and the operational level (dealing with the Standard Operating Procedures (SOPs) worksheets and other aspects of day to day operations) [12].

2.1.1. Setting up the system

There is no single method for establishing a QA system. Each organization has its own problems that will require special consideration and planning. However, once the decision to implement a QA system has been taken and the necessary funds and facilities have been made available, then a plan must be drawn up. For a new project the QA system can be drawn up before the start but if the project is already established then a QA system can be retrofitted. In the latter situation, existing practices must be evaluated with respect to QA needs and any QA checks and procedures that are already in place. It is better to build on procedures already in place and only to remove them if they are clearly unsatisfactory. If too many changes are imposed too quickly, especially where they are seen to increase work load, they are unlikely to be met with a favourable response and implementation will be poor. The QA programme must be seen to be practical and realistic and not to include trivial or unnecessarily time-consuming or difficult tasks [13].

2.1.2. The Quality Manual

The Quality Manual is composed of the management documents needed to implement the QA programme and includes;

- A quality policy statement, including objectives and commitments.
- The organisation and management structure of the project, its place in any parent organisation and relevant organisational charts.
- The relationship between management, technical operations, support services and the quality system.
- Procedures for control and maintenance of documentation.
- Job descriptions for key staff and reference to the job descriptions of other staff.
- Identification of approved signatories.
- Procedures for ensuring traceability of all paperwork, data and reports.
- The laboratory's scope for calibrations and tests.

- Arrangements for ensuring that all new projects are reviewed to ensure that there are adequate resources to manage them properly.

- Reference to the calibration, verification and testing procedures used.

- Procedures for handling calibration and test items.

- Reference to the major equipment and reference measurement standards used.

- Reference to procedures for calibration, verification and maintenance of equipment.

- Reference to verification practices including inter laboratory comparisons, proficiency testing programmes, use of reference materials and internal quality control schemes

- Procedures to be followed for feedback and corrective actions whenever testing discrepancies or departure from documented procedures are detected.

- Procedures to be followed for feedback and corrective actions whenever testing discrepancies or departure from documented procedures are detected.

- Complaints procedure.

- Procedures for protecting confidentiality and property rights.

- Procedures for audit and review [14].

2.1.3. Standard Operating Procedures

Standard Operating Procedures (SOPs) are the documents detailing all specific operations and m ethods, including sampling, transportation, analysis, use of and calibration of equipment, product ion of reports and interpretation of data. They are the internal reference manual for the particular procedure and should detail every relevant step. Anybody of the appropriate training level should be able to follow the SOP [15].

2.1.4.   The Quality Assurance manager

For larger projects, proper management of QA will require the appointment of a QA manager to l iaise with staff, to manage data archives, to conduct regular audits and reviews and to report on a ny QA issues. The manager is responsible for inspecting all aspects of the system regularly to ensure compliance, for reporting on such inspections and audits to management and for recomme nding improvements.These activities involve inspecting facilities and procedures regularly, traci ng samples and documents back through the system and ensuring that all appropriate records hav e been kept. Where QA is the responsibility of a separate section within an organization many of the management difficulties are minimised. Appointment of a full time QA manager is difficult i n a small organization and in these cases the responsibility for QA should be assigned on a part-time basis, to a suitable member of staff [10].

2.1.5.   Auditing and checking compliance

When all the documentation for the QA system is in place, it should be piloted. During this time, the QA manager should conduct a series of audits covering all aspects of the system. Traceability of data is a key component which can be checked by picking data at random and tracing them ba ck through all relevant paperwork to the sampling procedure. A review of the system with positiv e and negative areas clearly defined should be written at the end of the pilot phase. One method of implementation is to apply for accreditation from a recognized QA system. The ISO standard, ISO 9000, is suitable for the monitoring programme as a whole and is available in many countrie s. These systems are expensive but do allow the QA programme to be assessed independently against an agreed standard. Sometimes formal accreditation is required by regulatory and comme rcial bodies [14].
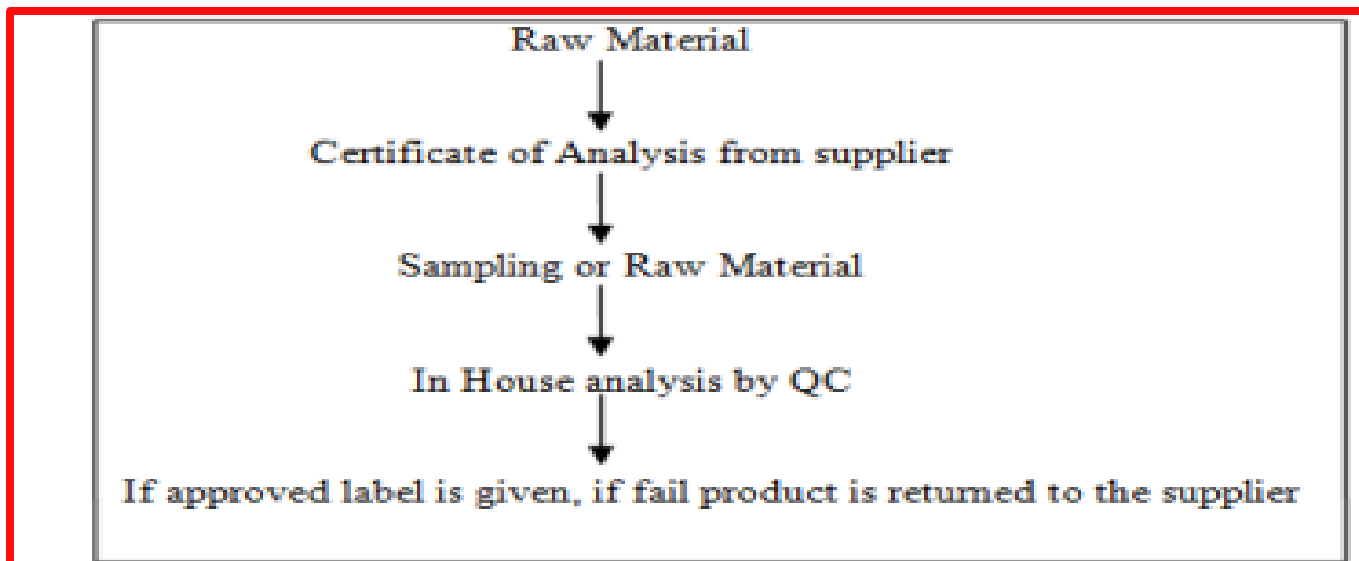
2.3. Vital role of quality assurance in pharmaceutical industry

A product that is not safe to be used will not be given authentication or approval to be marketed to the public. Looking at the scope that we are about to discuss is the field of pharmaceutical industry, as we know pharmaceutical industry produces medications, that is consume on a daily basis in our life by humans and even animal [2].

2.3.1. Drug Product Quality

The quality of a drug does not only means here on the finished product, the quality of the product starts from the raw material to the final day when the product leaves the industry, and the quality of the product is also monitored till the expiry of the product in the market. The responsibility of the quality assurance does not only stop when the product leaves the industry but it is maintained also as the product is the market. The product quality is measured as follows; the methods and process are all repeated for each batch, as the batch is released from the industry [16].

The QA plays a role here by ensuring the product that is obtained from the vendor has gone through the analysis that is required and make sure the product meets the regulatory requirement in the specification of the raw material. The industry will obtain the Certificate of Analysis (COA) from the supplier, once the COA is obtained then it is checked by QA to ensure it is up to the standard. Then the sampling team will also obtain sufficient amount of the raw material to do a in house analysis. The in house analysis is done to ensure that the content and the results obtain in the COA from the supplier is genuine [17].

Raw Material

↓

Certificate of Analysis from supplier

↓

Sampling or Raw Material

↓

In House analysis by QC

↓

If approved label is given, if fail product is returned to the supplier

Figure 1: steps of certificate of analysis of raw material

Manufacturing of medication, as the medications are manufactured it has to follow with the standard SOP to ensure the product meet the quality requirement. As each process of manufacturing is over and it goes to the next level of manufacturing it is monitored by the relevant staff to ensure that the product is up to the specifications that are required, this steps are repeated till the final stage of the drug. As the drug is completed then the sampling team will obtain the sample to be produced to the QC department, so further analysis is done on the finished product. The analysis is done based on the British Pharmacopeia or the United Stated Pharmacopeia all aspect of the analysis and assays is done to ensure that the product is safe and efficacy for the product to be released to the market for public use [17].
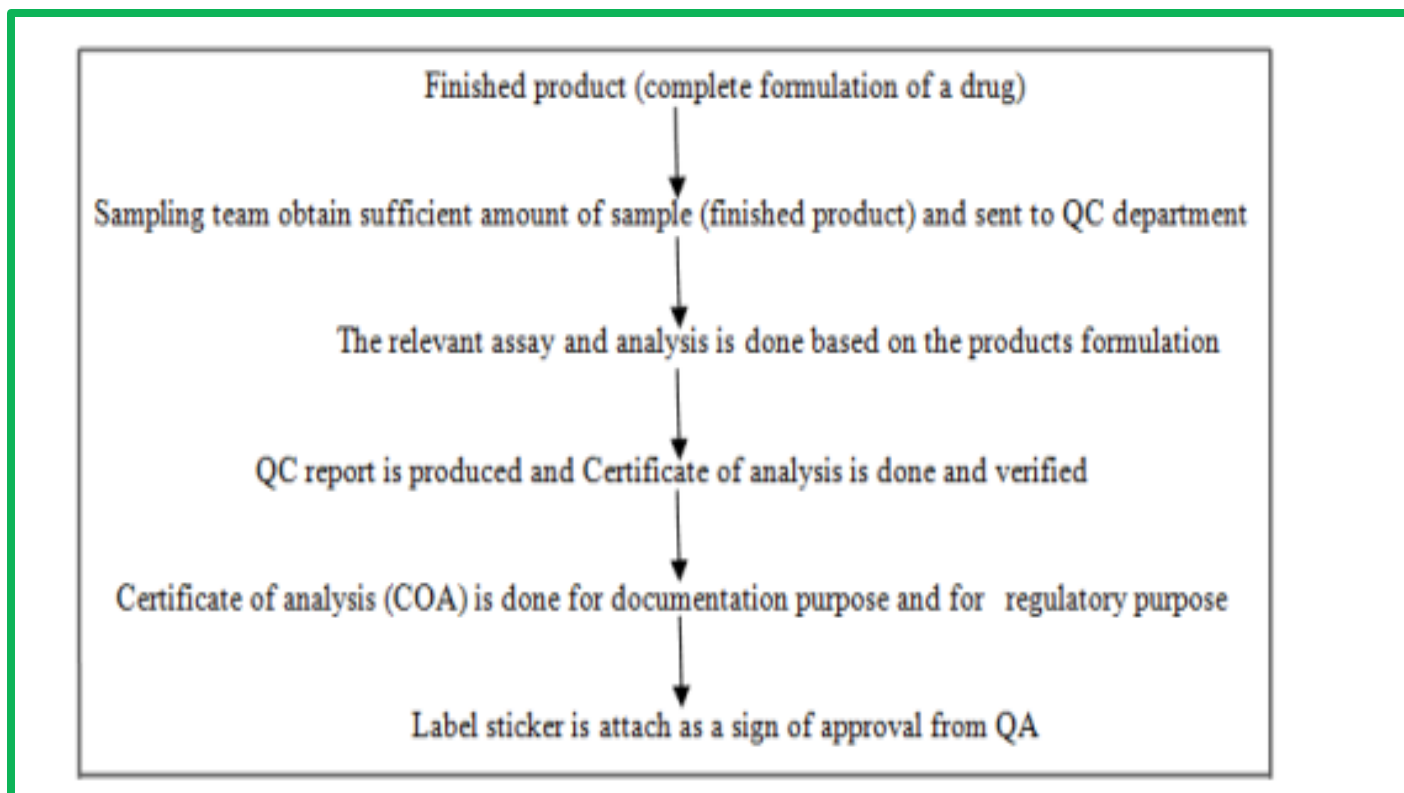
Figure 2: steps of finished products formulation and certification.

2.3.2. Validation and technical support in quality assurance

Validation as how it is mention in the heading it would give us a rough idea, as we all know validation it means of validating something. In pharmaceutical industry validation plays a very vital role under the QA department. This team here will validate each methods and each process that is carried out in the QA department to ensure that it gives results according to the standard th at is set, moreover this team also work on various angle in enhancing each methods to give more quality in the results that is obtain. The reason it is mention here as technical support also is due to the fact that this team supports the other for example validation team supports the QC team and also supports the stability team. But all of this comes under one major department which is known as Quality Assurance. Each assay method and the SOP are validated on a regular basis to ensure that the procedures that are used to carry out by the QC to obtain results are all effective [18].

2.3.3. Stability in Quality Assurance

Stability is that supports the quality assurance team by checking on the stability of the products t hat have been manufactured by the particular industry. Before the drug is released to the market t he drug is ensured with a good stability. The most interesting part of the stability team is that the y even do the stability testing on drugs that has been released to the market. This works a very di fferent concept where the retention team will support the stability team. Each drug that has been released to the market is stored by the retention team for the stability studies to be conducted. The stability study of the product that has been marketed is done on a 3months basis [19].

Any problem on the drug stability before it is released to the market or even after it is released to the market that particular product must be recalled, if the batch has not been marketed then it should be inhibited [21].

2.3.4. Quality Assurance in regulatory affairs of a pharmaceutical industry

A regulatory affair as it is mentioned on the heading the first thing that strikes us on the word regulatory is regulation and laws. In this section we are about to discuss on how does quality assurance is related to the regulatory affairs department and how they work hand in hand for the betterment of the particular pharmaceutical industry to give a better profit to the industry. Regula tory affairs particularly deal with the regulatory aspect of a medication and pharmaceutical industry thus in the regulation aspect also QA documentation in order to obtain clearance on any related regulatory issues. The overview on the job scope in the regulatory affairs is working close with the authorities to ensure product is registered according to the regulation guideline. Dossiers is a very important aspect in a regulatory affairs department this dossiers are generally used to register the manufactured products in other countries [22].

This dossier should contain details about every aspect of the drugs; the major aspect in a drug dossier is the Quality assurance details and the Certificate of Analysis (COA). The dossier prepar ed is sent to the specific countries authorities for registration of the drug in that particular country It will nearly take 2 years for a drug to be registered in a different country in a export basis.

Every detail of analysis and assay that is done in the QA department is given in the form as report to be attached in the drug dossier before it is sent for registration [23].

2.4. Important terminology in pharmaceuticals quality assurance

The ENQA workshop on the language of European quality assurance, hosted by the Quality Assurance Agency (QAA, UK) in Warwick, revealed a wide range of points of interest, discussion and challenge for all those attempting to work across language boundaries to translate, understand and implement quality assurance ideas, processes and procedures. The workshop brought together representatives from a wide range of agencies, representing 16 different countries and at least 12 different languages. The discussion focused predominantly on the use of English as a mediating' language for the European quality assurance community and the impact that this has on the clarity of communication. The intent of the workshop was not to produce a glossary' of quality assurance words but to open up the debate on language and raise awareness of the problems and pitfalls of working across language boundaries [8].

Quality control: is an essential operation of the pharmaceutical industry. Pharmaceutical products must be marketed as safe and therapeutically active formulations whose performance is consistent and predictable [24].

Good Manufacturing practice: is aimed at assuring the quality of the product by assuring the quality of the process. GMP should also: be part of process development (e.g. development reports and approval requirements); proceed through validation, manufacturing, controls and end product testing; and reach into the distribution network of the product. Process development is often seen as being incompatible with GMP compliance, as development requires flexibility. However, if examined more closely, compliance will always involve process improvement, as GMP regulations actually require procedures and processes to be 'state-of-the-art' design [25].

Validation: Confirmation by examination and provision of objective evidence that the particular requirement for a specified end use are fulfilled [10].

Verification: Confirmation by examination and provision of objective evidence that specified re quirements have been fulfilled [26].

Monitoring quality: Regular and systematic monitoring of quality is necessary to ensure that it is appropriate to the Laboratory's needs and all aspects of it are functioning properly. Monitoring may be carried out by external bodies or internally, using laboratory staff. Where there is a formal quality system internal assessment is conducted to formal procedures and known variously as audit or review [27, 28].

Equipment: Most biotechnological operations are run under aseptic conditions (i.e. free from viable organisms other than the production organism). The art of aseptic design has developed rapidly, but the need for hygienic design (i.e. the ability of equipment to be cleaned from undesie d matter, such as product residues is often underestimated. The potential carry over into subseque nt products is a major concern, particularly in multipurpose plants [29].

Better customer quality: Through proper validation, market recall is avoided which results in better customer care and quality of the product [30].

Design Qualification (DQ): The design qualification outline the key features of the system designed to address the user requirements, regulatory compliance and selection rationale of a part icular supplier. The more function that are specified in design qualification, the more work have t o be included in the Installation, operational and performance qualification processes [31].

Certification: Procedure by which a third party gives written assurance that a product, process or service conforms to specified requirements [32].

Accreditation: 'Procedure by which an authoritative body gives formal recognition that a body or person is competent to carry out specific tasks [32]

Registration: Procedure by which a body indicates relevant characteristics of a product, process or service, or particulars of a body or person, in an appropriate, publicly available list (ISO/CASCO 193 (Rev. 2), 1.10, & ISO Guide 2:1996, 12.10) [31].

Active Ingredient: A substance with a therapeutic, diagnostic or prophylactic activity used in a pharmaceutical product. Drug Substance" and "Active Substance" are synonymous to "Active Ingredient" [33]

Reference Standard/Substance: Authentic specimens that have been verified for suitability for use as comparison standards in compendia tests and assays [33].

Pharmacuetical product: Any preparation for human or veterinary use that is intended to modify or explore physiological systems or pathological states for the benefit of the recipient [33].

Calibrations: Set of operations that establish, under specified conditions, the relationship between values indicated by a measuring instrument or measuring system, or values represented by a material measure, and the corresponding known values of a measurand [34].

Certified reference material (CRM): Reference material one or more of whose property values are certified by a technical procedure, accompanied by or traceable to a certificate or other documentation which is issued by a certifying body [34].

Document control: Mechanism by which quality management system documents are created and amended, reviewed, approved, distributed and archived to ensure that all staff use the latest authorized versions [35].

Quality manual: Document stating the general quality policies, procedures and practices of an organization [36].

Procedure: Specified way to perform an activity or process. For quality assurance purposes the procedures should be written [37].

Quality assurance management: All activities of the overall management function that determine and implement quality policy, objectives and responsibilities [37].

Quality audit: Systematic and independent examination to determine whether quality activities and related results comply with planned arrangements and whether these arrangements are implemented effectively and are suitable to achieve the objectives [37].

Facilities: A number of regulatory requirements for biotechnological plants have been developed, including, for example, the requirements for containment measures and equipment systems [e.g. the heating, ventilation and air-conditioning systems (HVAC), water, steam and sterilization systems, material, equipment, product and waste flow, personnel flow, and personnel control [38].

Quality by Design and Product Development: Quality by design means designing and developing a product and associated manufacturing processes that will be used during product development to ensure that the product consistently attains a predefined quality at the end of the manufacturing process [39].

Personnel: Persons qualified, (at different levels, and sufficient in number) with adequate training and experience to carry out their assigned functions [40].
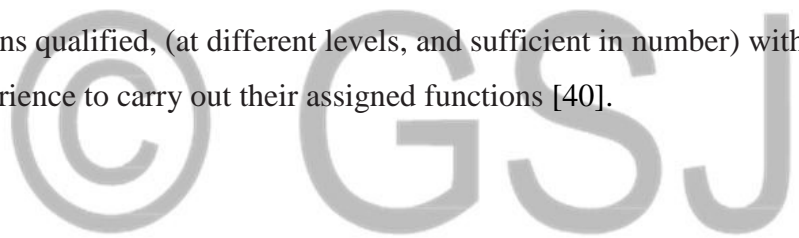
3. Conclusion

Quality Assurance is generally defined as the process used to ensure a product meets quality standards. It consists of activities that occur before and during the production process. This revie w covers what should be included in a quality assurance strategy and the considerations behind each pharmaceutical products. It's essential to explicitly define and communicate all key termino logy of quality assurance for the process to work efficiently. Quality Assurance can increase the revenue of the industry and it also explains on the work flow from the raw material till the finish ed product and the role of quality assurance in each flow. It gives a clear picture on how the quali ty assurance is manage and gives ideas on how to enhance the flow.

Acknowledgments

Abbreviation: COA: Certificate of Analysis; CRM: Certified Reference Material; DQ: Design Qualification; ENQA: European network quality Assurance; GCP: Good Clinical Practice; GLP: Good Laboratory Practice; GMP: Good Manufacturing Practice; HVAC: Heating,Ventilation and Air   conditioning; QA: Quality Assurance; SOP: Standard Operating Procedure; WHO: World Health Organization

Declaration: we declare that we have no conflict of interest in the publication process of this review
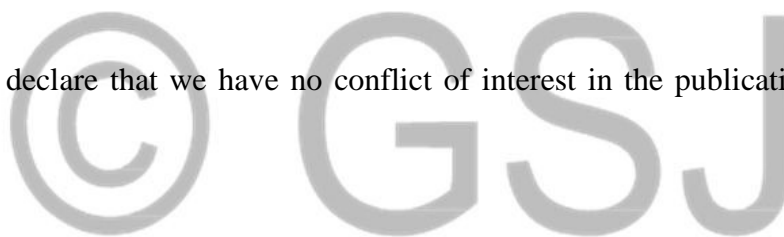
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