بسم الله الرحمن الرحيم

Sudan University of Science and Technology

College of Graduate Studies

Evaluation of Good Manufacturing Practice System Application in the Pharmaceutical Industry

(Case of Study: Pharmaland Company - Gezira state)

تقويم تطبيق نظام الممارسة التصنيعية الجيدة في الصناعة الدوائية

(دراسة حالة: شركة فارملاند للادوية - ولاية الجزيرة)

A Dissertation submitted in partial fulfillment of the requirements of M.Sc. in Total Quality Management and Excellence

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الإستهلال

بسم الله الرحمن الرحيم

قَالَ تَعَالَىٰ:

﴿ يَٰٓأَيُّهَا ٱلَّذِينَ ءَامَنُوٓاْ إِذَا قِيلَ لَكُمۡ تَفَسَّحُواْ فِي ٱلۡمَجَٰلِسِ فَٱفۡسَحُواْ يَفۡسَحِ ٱللَّهُ لَكُمۡۖ وَإِذَا قِيلَ ٱنشُزُواْ فَٱنشُزُواْ يَرۡفَعِ ٱللَّهُ ٱلَّذِينَ ءَامَنُواْ مِنكُمۡ وَٱلَّذِينَ أُوتُواْ ٱلۡعِلۡمَ دَرَجَٰتٖۚ وَٱللَّهُ بِمَا تَعۡمَلُونَ خَبِيرٞ ١١ ﴾

صدق الله العظيم

سورة المجادلة الآية (11)

Dedication

TO MY:

PARENTS

Wife And

Brother

Acknowledgement

Praise all amity for Allah, giving me the courage, ability and strength to complete this work.

My special and deepest thanks to my supervisor Dr. Elfatih Ahmed Hassan for his continuous support, guidance, and encouragement through this study

ABSTRACT

This study was carried out in Pharmaland company, during the period from January 2018 to June 2018. The study aimed to evaluate the applications of good Manufacturing practice (GMP) system in the Pharmaland company, Questionnaires were designed and distributed to the (16) employees of the laboratories that apply GMP and then collected and responses were analyzed using SPSS program.

The type of staff to whom the questionnaire was distributed was different in terms of their functions, expertise and gender, and most them were chemists in the Quality Control department, because the study aimed to scrutinize Application.

The number of employees is 16, 11 of them are analytical chemists, which is (68.8%) of the sample, and quality managers are 4 employees, which is (25%), other type of employee was just one, which represent (6.3%) the total number of questions was 80.

The study revealed the following results:

The employees responded positively to 46 questions, while the number of question they disagreed with was 34.

Gender disparities as the following:

Male employees were nine employees at (56.3%) Female employees were seven employees at (43.8%).

From the results it is positive conclude that the staff responded to 46 questions by answering (Yes), (57.5%) of them disagreed 34 questions. This shows that the Pharmaland plant applies industrial practice to an average fair level. The company need to address which to improve the level of GMP compliance.

المستخلص

أجريت هذه الدراسة الوصفية في شركة فارملاند للادوية ، خلال الفترة من يناير 2018 حتى يونيو 2018 ، هدفت الدراسة إلى تقويم تطبيق نظام الممارسة التصنيعية الجيدة في شركة فارملاند .وقد تم تصميم استبيان لجمع المعلومات المطلوبة لهذه الدراسة. و قد استهدف موظفي الجودة وبشكل خاص علي موظفي المختبرات. وزع الاستبيان على (16) موظفاً في الشركة. ثم جمع الاستبيان وحللت بياناته باىستخدام برنامج SPSS.

كان التباين والاختلاف بين الموظفين علي حسب المسميات الوظيفية كالأتي: عدد الموظفين الكلي 16 موظف ، المحللين الكيميائين عددهم 11 موظف بنسبة(68.8%) ، مدراء الجودة عددهم 4 موظفين بنسبة(25%) و موظفين التأكد من الفعالية والصحة موظف واحد بنسبة (6.3%).

كان التباين والاختلاف من حيث الجنس كالأتي: الموظفين الذكور عددهم تسعة موظفين بنسبة(56.3%) والموظفين الاناث بعدد سبعه موظفات بنسبة(43.8%).

كشفت الدراسة النتائج التالية : كان العدد الكلي لأسئلة الاستبيان 80 سؤال ، وكانت اجابات الموظفين بالخيار(نعم) عددها 46 سؤال لم يختلفوا فيها واجمعوا عليها. بينما كان عدد الاسئله التي اختلفوا فيها بالخيارات (لا) و(لا يمكن تطبيقه) 34 سؤال.

كان نوع الموظفين الذين وزع عليهم الاستبيان مختلفين من حيث مسمياتهم الوظيفية وجنسهم، وقد كان الاغلبية منهم من المحللين الكيميائين في قسم ضبط الجودة؛ وذلك لأن الدراسة تستهدف تطبيق الممارسة التصنيعية الجيدة داخل المعمل.

من هنا نستنتج ونستخلص ان الموظفين اجمعوا علي عدد اسئله 46 سؤال بالاجابه (نعم) وذلك نسبته(57.5%) واختلفوا في عدد من الاسئلة وقدره 34 سؤال بنسبة(42.5%). وهذا يدل ان معمل فارمالاند يطبق الممارسة التصنيعية بنسبة تفوق المتوسطة.

علي المؤسسه الاهتمام ببعض التوجه لمعالجة بعض المسائل لرفع مستوى التزامها بالممارسه التصنيعيه الجيده.

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LIST OF ABBREVIATIONS

FDA Food and drug administration
PLP Pharmaland pharmaceutical
GLP Good laboratory practice
GMP Good manufacturing practice
cGMP Current Good manufacturing practice
OECD Organization for economic co-operation and development
QA Quality assurance
SOP Standard operating procedure
CNS Central nervous system
NMPB National medicines and poisons board
CFR Code of Federal Regulation
WHO World health organization
MHRA Medicines and healthcare products regulatory agency
MENA Middle east and north Africa
EU European union
R&D Research and development
US FDA United states food and drug administration
ISO International organization for standardization
OHSAS Occupational health and safety management
QC Quality Control
TQM Total Quality Management
RFQ Requests for Qualifications
RFP Requests for Proposals
DOT Department Of Transportation
CAPA Corrective and Preventative Action
ICH International Conference on Harmonization
PIC/S Pharmaceutical Inspection Cooperation Scheme
OOS Out of Specification
CNS central nervous system
USP United State Pharmacopeia
BP Britch Pharmacopeia

CHAPTER ONE

Introduction

1.1 Introduction

Quality Control is very much important in pharmaceutical industry. Doctors always need a good quality product for treatment. Pharmacist and pharmaceutical industry is responsible for delivering good quality product. All factors that contribute either directly or indirectly to the purity , safety , effectiveness and reliability of the product will be included under the term "QUALITY". To achieve all these characters there is need to undertake quality control. A typical total quality control starts from the procurement of raw materials to the finished product until it gets consumed by the patient. When a drug is administered to the patient it should not show any undesirable /toxic effects.

*Quality control ensures that a drug will have the following characteristics:

- Genuine quality as well as good nature.

- Physically and chemically pure.

-It contains same amount of ingredients as mentioned on the label.

-It must be in such a form that after administration it is effective.

-Quality in terms of shelf life /stability.

-No toxic impurities.

The drug is tested for both quality, and quantity by the quality control department. Every country should have an official pharmacopoeia which will give the standards of quality for all medicines along with the methods to be used for quality control. Revised supplements are published periodically to stay up-to-date pertaining to drug quality.

Every test or criterion that is prescribed as a standard in pharmacopoeia is a parameter. (E.g. Assay, solubility, limit test for arsenic). The number of parameters indicates the rigidness of the standard and reliability.

However, we do not need too many parameters. To ensure good quality few critical and important parameters are enough. Too many parameters lead to confusion, tedious analytical process and also increase the cost of production. In order to avoid these problems pharmacopoeia should select some critical tests and prescribes them.

Quantitative analysis depends on the drug characteristic and its formulation. The analytical methods include some physicochemical methods. Other methods include separational techniques.

The basis of all these tests is to ensure that quality drugs are made available to patients.

1.2 Quality Management in the Pharmaceutical Industry

Alongside with other industries where safety is critical, the pharmaceutical industry is heavily regulated and for obvious reasons: mistakes in product design or production can have severe and even fatal consequences. Manufacturer should establish and implement effective pharmaceutical quality assurance (QA) system, involving active participation of management and personnel of the service involved. To ensure quality and safety of the products, pharmaceutical companies build their quality approach around good manufacturing practices (GMP).

1.3 Concept of Total Quality Management (TQM):

A philosophy of management is driven by customers' needs and expectations, and focuses on continual improvement in work process

TQM is system of practices, tools and training methods for managing companies to provide customer satisfaction in a rapidly changing world . Quality has been an important issue for organizations for many years. The early focus on quality evolved from inspection to quality control and later to quality assurance.

1.4 Purpose for Quality

All personnel at every level and function, share a responsibility to strive for and maintain a high standard of work quality. Quality is as much a concern to project level professionals, and support staff, as it is to administrators. It is the purpose of this chapter to define a comprehensive and integrated program for incorporating awareness and achievement of quality into the work activities of all staff.

The quality assurance/quality control (QA/QC) process is based on the following concepts:

1. Quality is a responsibility of each individual employee and not solely a management responsibility.
2. Quality is a continuous process, not an intermittent concern to address deficiencies that surface. Quality is proactive, not reactive. Quality is a journey, rather than a destination.
3. Quality is a specific, not an ambiguous concept. Quality is reflected in criteria and standards of performance and accomplishment.
4. Quality is customer oriented. The process has a diverse set of customers, including property owners, displaces, and the Maine DOT units that use or depend on the completion of services. Thus, each function must identify its customers and define quality performance in relation to their needs.

1.5 Quality Defined:

Quality is the measurement of the level of work performance of each employee, and the project team as a group as it relates to the Quality Standards and customer satisfaction. High levels of quality result in a project that the Department is proud to deliver, and the customer is pleased to receive. Following are the essential elements of work quality:

1. Level of Service. Quality in delivering requires a high level of knowledge of the body of laws, regulations and procedures that control right of way acquisition, and skill in performing specific functions (e.g., appraisal, relocation). The skills, knowledge and abilities of right of way personnel are critical to delivering a high level of service.
2. Timeliness. The process is responsible for delivery of property rights needed for construction and operation of highways. The timely delivery of to meet project schedules is a primary customer need for which Property Office and Program personnel are responsible.
3. Quantity as other functions in Maine DOT, has limited staff resources to carry out its mission. This requires that all employees work diligently and use efficient work practices. Work production levels are valid evaluation factors in unison with applicable difficulty factors. Evaluation will consider complexity and level of difficulty of individual cases and projects, and it is not appropriate to measure individual production solely in terms of units delivered over a time period.

1.6 Objective:

The objective is to establish responsibility and define actions for continuously improving the performance in delivery of services. Tasks to assure quality in each function are set forth. Also, methods (4) of quality

control for oversight and improvement of the function as a whole are identified.

1.7 Responsibilities:

1.7.1 Property Office Staff:

Every employee has a responsibility for improving the quality of the process. They are responsible to perform, and the timeliness, work quantity and level of service they provide. Following are important factors in carrying out this responsibility:

1. Identify improvement factors within personal control.
2. Contribute to joint efforts to improve quality delivery as a member of a project team, office or other group.
3. Discuss perceived obstacles to quality with management.
4. Accept opportunities to improve knowledge and skills through training, new assignments and accepting team leadership responsibilities.

Every staff member needs a clear understanding of job performance expectations in order to carry out the above responsibilities. This includes a current job description, job performance standards and a yearly evaluation of performance. If any of these elements are not provided, the individual should bring this to the attention of management.

1.8 Quality Control:

1.8.1 Quality Control General:

Quality control is a process improvement activity that is undertaken at the operational or project level. Each staff member has an individual as well as a shared responsibility to actively contribute to the delivery of quality products by performing tasks appropriate to their assignment and span of organizational influence. The concept of quality control is distinct from quality assurance, which is a program management responsibility.

The organizational placement of functions within the Department relies on individual initiative and responsibility. It is performed in context of multidisciplinary project teams. Personnel are directed by project team objectives and accomplish these objectives without on-site operational supervision. This structure requires the skills of a highly experienced and motivated professional staff. It enables efficient and on-time delivery of while allowing a high degree of professional independence and decision authority. A major element in success is the self-assessment by operational staff of the quality of the process that they control.

Quality control activities will be undertaken in each function on a continuing basis. The specific activities will vary with each discipline and will be scaled to accommodate the significance of the function in the current program, vulnerability of the function, the staff resources available to carry out quality assessment and the potential efficiencies to be gained. Each Senior Property Officer in the right of way function will be assigned to perform one or more quality control tasks biennially. The tasks, and the form and timing of reporting, will be developed and directed by the Property Office.

1.8.2Quality Control Tasks:

Staff in each discipline will assess the qualitative aspects of operations by performing tasks that are appropriate to the function being examined. The following listings of assessment tasks for each function are examples and not an exclusive list of assessment tasks.

a) Valuation

Quality control in the valuation function is a process of self-assessing performance and improving methods of producing appraisals and other valuation products. Quality assurance is a shared responsibility of all

persons involved in the valuation function, including staff and contract appraisers, review appraisers and support services personnel.

Quality control in the appraisal function may include the following activities and tasks:

1. Develop effective coordination methods with Project Team members responsible for other projects.
2. Appraisal staff self-assess appraisal-related training needs.
3. Valuation staff identify critical path tasks involving appraisals to eliminate barriers to timely completion of these activities.
4. Evaluate performance of consultant appraisers after project assignments are completed concerning quality of documentation, analysis of data and timely delivery of appraisal products.
5. Perform effective evaluation and feedback of work of staff valuation personnel.
6. Review and refine appraisal contract procedures, including maintenance of the Appraiser Register. This includes culling the list periodically for appraisers that are no longer available for assignment.
7. Secure feedback from contract appraisers as to how the process involving them can be more effective and efficient (360-degree evaluation).
8. Quality control is a focus on achieving improvement in performing the appraisal function using the tools of policy, training, evaluation and communications.

(b) Waiver Valuation

Personnel assigned responsibility for Waiver Valuation will actively examine the process to ensure that it is fulfilling its goals as set forth and identify opportunities for improvement.

The following items are examples of specific quality control activities that may be undertaken:

1. Conduct follow-up phone interviews with owners after construction is complete.
2. Identify training opportunities that would expand knowledge and skill in right of way acquisition.
3. Suggest refinement in acquisition practices that will make the process more efficient and effective.
4. Participate in informal workshops to exchange experiences and practices with other professionals involved in administrative acquisition.
5. Perform spot checks of closed files to identify successful and unsuccessful practices.
6. Conduct a letter survey of owners after acquisition.
7. Each involved staff member will develop the quality assurance actions to be undertaken, in consultation with the Senior Property Officer, or as otherwise directed by the Property Office.

c) Acquisition

Quality control in the acquisition function include the policy guidance, program management tools and specific training necessary to ensure that responsible personnel are conducting operations in an effective and efficient manner. The various activities used to test and evaluate program activities form the basic elements of the QA function.

personnel involved in the acquisition function shared responsibility to strive and improve operational quality. This could be advanced by such tasks as:

1. Owners phone call Followed up after the acquisition process is complete. The purpose would be determined overall satisfaction with the

process and secure suggestions that will be useful in future project acquisition activities.

2. Negotiations records Tracked and analyzed, and completed to identify practices that result in successful settlements. Patterns that indicate successful practices could be determined by examination of a completed group cases that might not be apparent in day-to-day work activities.

3. Best practices shared with other staff. Experienced property acquisition staff members bring a wide range of skills, knowledge and techniques to the job that contributes to a higher rate of settlements. The knowledge and successful practices may be shared by such means as workshop sessions or one-on-one mentoring of less experienced acquisition staff.

4. Personnel training needs identified acquisition. Acquisition knowledge and skills are best identified by a formalized process because this is a human focused and subjective area of work. Training opportunities and resources should be prioritized based on objective discovery of employee training needs.

(d) Property Management

The goal of quality control in property management is to secure and protect acquired property, generate income from sale or rental and achieve other objectives. Responsibilities for quality control in Property Management include the following:

1. Policies reviewed regularly. Revise as necessary to reflect best property management practices and more effective compliance with applicable law and regulations.
2. Project and field staff Provided advice and guidance to that will enhance their knowledge and skill in performing the elements of property management for which they are responsible.

3. Field personnel of standards Provided specific advice and instruction to performance in areas such as building inspection and security, building disposals and property rental.
4. Activities at the Department level Reviewed property management, including work by staff and by private contractors. The purpose of the reviews is to ensure compliance with laws, regulations, policies and professional standards and to identify opportunities to improve performance. The Property Manager under direction of the Legal Services Office and the Property Office will determine the form and frequency of reviews.

(e) Relocation

Quality control in relocation is an inclusive process of evaluating performance and developing ways to continuously improve accomplishment of program goals. This is accomplished by performing spot checks that monitor the function as to the following performance elements.

1. Effective coordination with project team members responsible for other project development activities.
2. Timely and relevant assistance provided to displaces, with special focus on those having needs, including elderly and disabled.
3. Assessment of relocation related needs of relocation personnel.
4. Identification of critical path tasks involving relocation, including prioritizing so that more time is available to those having more serious relocation problems;
5. Evaluation of consultant staff that are employed by the Department to perform relocation services.
6. Participation in process and performance evaluations, including 360-degree evaluations; and

7. Participation in the continuous refinement of relocation practice and policy to reflect best practices in the field of work.

(f) Contracting Services

Quality control includes activities that are incorporated into the contracting process for services to measure progress, monitor progress performance and evaluate the performance of completed work.

This includes the following activities:

1. Review and refine Requests for Qualifications (RFQ) and Requests for Proposals (RFP). The initial development of RFQs and RFPs should not be regarded as a final product. Each need for republication of these documents should be an occasion for review and revision based on knowledge gained from past experience.
2. Develop more effective means to inform service contractors policy concerning functions provided under contract and provisions of law that applies specifically to operations.
3. Develop improved ways to attract qualified professionals to submit qualifications and proposals for work contracted by. Develop ways to maximize participation by minorities and women.
4. Perform post project reviews and evaluation of provider's performance under every professional function that is contracted to private sources.

(g) Local Agency Acquisition

1. The following activities are appropriate quality control measures that can be undertaken by the municipality performing real property acquisition: Perform a second-party internal review of all documents before they are delivered to the property owner. This includes appraisals, agreements, instruments of conveyance, offer letters, etc.

2. Provide relevant training to agency personnel who are engaged in specialized activity (e.g., appraisal, negotiations, titles, relocation).
3. Perform quality spot checks of completed work concurrent with any ongoing project acquisition activity.
4. Perform peer reviews of work activity when there is more than one staff member involved in property acquisition.
5. Conduct phone or mail surveys of property owners following acquisition.
6. Develop internal procedures or policy to apply to specific recurring situations or circumstances to ensure consistency and equitable treatment
7. Perform joint project reviews between main DOT and local agency management staff.

(h) Mapping

The following tasks may be performed by staff to contribute to improving the quality of the Main DOT mapping function:

1. Develop a peer review process of evaluating mapping work products with the aim of constructively identifying opportunities for improvement.
2. Perform formal evaluations of the quality and timeliness of consultant work products.
3. Perform 360-degree evaluations of specific mapping processes. This would include participation of all parties involved in the process.
4. Survey Departmental and external "customers" as to the effectiveness of specific Mapping and Research policies and practices.

1.9Literature Review:

- **GMP:** Protect the integrity and quality of manufactured product intended for human use.
- **GLP:** Protect the integrity and quality of laboratory data used to support a product application.

What is Quality?

- The ability to consistently produce the same product to meet the same specifications time after time!
- Stronger, purer, higher assay, or higher yield is not better!
- Current Good Manufacturing Practices (GMP or cGMP)
- Must be both current and good!
- Apply to all aspects of preparation when any product entity is intended to use in humans or animals.
- Do not apply when drug is in Pre-Clinical Trials (animal testing).
- Good Laboratory Practices (GLP)
- Apply when a non-clinical laboratory study (e.g. Pre-Clinical animal testing) is intended to support an application for an FDA-regulated product.

1.10 GMPS and the Concepts of Modern Quality Systems:

The FDA believes that several key concepts are critical for any discussion of modern Quality systems. The following concepts are used throughout this guidance as they Relate to the manufacture of pharmaceutical dosage forms Current Good Manufacturing Practice

Quality For the purposes of this guidance, the phrase achieving quality means Achieving the identity, strength, purity, and other quality characteristics designed to ensure safety and effectiveness.

Quality by Design and Product Development This means designing and developing a product and its associated manufacturing processes that will be used to ensure that the product consistently attains a predefined quality at the end of the manufacturing process.

Quality Risk Management This component of a quality systems framework can help guide the setting of specifications and process parameters for dosage form manufacturing, assess and mitigate the risk of changing a process or specification, and determine the extent of discrepancy investigations and corrective actions.

Corrective and Preventative Action (CAPA) This is a regulatory concept that focuses on investigating, understanding, and correcting discrepancies while attempting to prevent their recurrence.

CAPA Concepts:

• Remedial corrections of an identified problem

• Root cause analysis with corrective action to help understand the cause of The deviation and prevent recurrence of a similar problem

• Preventative action to prevent recurrence of similar problems

Change Control this process focuses on managing change to prevent unintended Consequences.

Quality Unit While the GMPs refer to a quality unit, current industry practice is to divide the responsibilities of this unit between two groups:

• Quality control (QC) usually involves

(a) Assessing the suitability of incoming components and the finished products.

(b) Evaluating the performance of the manufacturing process.

(c) Determining the acceptability of each batch for release and distribution

• Quality assurance (QA) involves

(a) review and approval of all procedures related to manufacturing and maintenance,

(b) review of records(c) Auditing and performing/evaluating trend analyses.

Six - System Inspection Model the FDA's instruction manual for its investigators is a system - based approach to inspection consistent with this guidance. The FDA defines six interlocked systems:

(1) The quality system which encompasses all the other systems.

(2) A materials system.

(3) A production system.

(4) A packaging and labeling system.

(5) A facilities and equipment system, and

(6) A laboratory controls system. The agency believes that use of this overall system approach will help firms achieve better control.

1.11Quality Systems Model:

This section was written to describe a model for use in pharmaceutical manufacturing that can supply the controls to consistently produce a product of acceptable quality. The model is described by four major factors:

Good Manufacturing Practices and Related FDA Guidelines

• Resources

• Manufacturing operations

• Evaluation

Management Responsibilities the FDA feels that a robust quality system model calls for management to play a key role in the design, implementation, and management of the quality system.

Resources Sufficient resources should be provided to create a robust quality system that complies with the GMP regulations. Senior management or a

Designee should be responsible for providing adequate resources.

Facilities and Equipment the technical experts who have an understanding of pharmaceutical science, risk factors, and manufacturing processes related to the product are responsible for defining specific facility and equipment requirements.

The equipment must be qualified, calibrated, cleaned, and maintained to prevent contamination and product mix - ups. It is important to remember that the GMPs place as much emphasis on process equipment as on testing equipment while most quality systems focus only on testing equipment.

Control Outsourced Operations Quality systems call for contracts with outside suppliers that clearly describe the materials or service, quality specification responsibilities, and communication mechanisms.

Manufacturing there is an overlap between the elements of a quality system and the GMP regulation requirements for manufacturing operations. One should always remember that the FDA's enforcement programs and inspectional coverage are based on the GMPs. The FDA feels that the following factors are essential in a manufacturing quality system:

1. Design, develop, and document product and processes
2. Examine inputs
3. Perform and monitor operations
4. Address nonconformities

1.11.1Evaluation Activities include the following:

1. Analysis data for trends
2. Conduct internal audits
3. Quality risk management
4. Corrective action
5. Preventative action
6. Promote improvements

1.12 GMP ISSUES: CHANGE CONTROL AND PROCESS VALIDATION

Changes are unavoidable in a manufacturing setup. Manufacturers make changes at some stage of manufacturing during and after approval of a product. However, consistent quality of a drug product can only be assured through well - defined validation procedures. When a change is made in the manufacturing process of a drug product, sponsors are responsible for evaluating the effect of any change on the safety, efficacy, quality, stability, and potency of a drug product and ensuring that these properties are not influenced by the change. In a manufacturing setup, various disciplines like sales, marketing, medical, regulatory affairs, manufacturing,

electrical, and technical services work together. Hence, any kind of change in one discipline will have direct consequences on other disciplines. Each company should have a procedure with regard to handling a change. Quality control and quality assurance departments usually keep track of various changes occurring in a GMP environment. Therefore, it is required that personnel performing the job are trained enough to assess the effect of any kind of change or variation and take appropriate action for its evaluation or control. Supporting data should be

generated and once evaluated can confirm whether further clinical or nonclinical studies are required.

1.13 Change Control

When a change is made in a manufacturing setup, it is important to assess its impact. As a change can have impact on regulatory filling, manufacturing parameters, specifications, and technical services, it is important to consider the concerns and objections of various disciplines involved and only through well - defined standard operating procedures should it be properly validated, evaluated, and finally implemented.

A properly defined order of evaluation of a change with strategic input of trained personnel is key to delivering a consistent quality product.

When a change is the processed, the manufacturer should have protocols in place with regard to assessing the change. Therefore, "control of change" is important.

Control can be implemented effectively only through well – defined standard operating.

Systematic process in place to accurately evaluate a change using specific tests. Moreover, it aims to measure the effects on quality safety and efficacy before a change is implanted. Change control and its evaluation through proper documentation should include**:**

(a) Description and purpose of change

(b) Inputs from research and development (R & D) department

(c) Evaluation steps for impact assessment, such as evaluation of stability, validation requirements, and in vivo bioequivalence requirement

(d) Need and extent of regulatory documentation and approval

(e) Implementation schedule

(f) Clear definition of personnel authorized for change approval

(g) Monitoring protocol for change implementation and periodic review of Impact Following the informal proposal of a change, it should be reviewed by the responsible initiator, who will then generate a formal proposal. The proposal should describe accurately what the change is concerned with, how to validate the (change, and the time frame within which the change should be implemented. The final proposal should be reviewed and assessed by all functional groups involved. Once the change is approved, it can be implemented and the change cycle is completed describes responsibilities of different departments of a pharmaceutical company,

1.13.1 Process Validation:

Process validation is an important part in the implementation of a post approval change. It establishes the documented evidence of conformance of a pharmaceutical operation in accordance with specifications. FDA "Guideline on General Principles of Process Validation" describes in detail the principles and practices of process validation and documentation required by the regulatory authority. In general terms, process validation may be defined as the procedure which generates sufficient

Assurance and documented evidence that a operation is operating and producing drug products in accordance with the specifications and process controls

1.14 International GMP:

The first predecessors of manufacturing and quality requirements, which later evolved into good manufacturing practices (GMPs), were issued in the 1940s in the United States by the Food and Drug Administration (FDA) [1]. In the general meeting of the World Health Organization (WHO) held in 1969, the World Health Assembly issued a

recommendation for the introduction of GMPs Since then, most industrialized countries have passed laws on control procedures essential for the manufacture of drug products. In some countries GMPs are integrated into national legislation as a part of laws or regulations on production, distribution, marketing, and use of drug products (GMP regulations). In other countries, GMPs are separate guidelines outside the national drug legislation (GMP codes). In addition to national GMPs, also some international organizations and trade blocks have issued their own international GMP guidelines to harmonize the requirements for drug production in different countries. However, regardless of their origin, the main purpose of GMPs is to ensure that manufactured drug products have the safety, identity, potency, purity, and quality that they are presented to have. To fulfill this aim, most GMPs usually cover quality management, personnel, premises, equipment,

documentation, materials management, production and in - process controls, packaging and labeling of intermediate and finished products, laboratory controls, validation, and change controls.

1.14.1 NATIONAL GMP REGULATIONS AND CODES:

- United States:

In the United States the production of drug products is controlled under the federal Food, Drug and Cosmetic Act, which states that a drug product will be deemed to be adulterated unless the methods used in or the facilities or controls used for its manufacture, processing, packaging, or holding conform to or are operated or administered in conformity with current **GMP:** The actual GMP regulations are issued as a part of the Code of Federal Regulations and as such they are a federal law. The current set of GMP regulations is based on the 1978 revision [6, 7] of the original GMP regulations, which were first promulgated in 1963. The GMP regulations

Are updated every year in April [8] ; however, no major changes have been implemented since 1978. As an addition to GMP regulations, the FDA also publishes

Other GMP - related guidance documents covering various issues of drug manufacturing On the other hand, although these documents reflect current views and TABLE 1 Contents of Part 211 of U. S. GMP Regulations [7](18)Section Subject :

Subpart A General provision

Subpart B Organization and personnel

Subpart C Buildings and facilities

Subpart D Equipment

Subpart E Control of components and drug product containers and closures

Subpart F Production and process controls

Subpart G Packaging and labeling control

Subpart H Holding and distribution

Subpart I Laboratory controls

Subpart J Records and reports

Subpart K Returned and salvaged drug products

1.14.2 NATIONAL GMP REGULATIONS AND CODES 121

Expectations of the agency, they only provide guidance on principles and practices that are not legal requirements a member of the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceutical for Human Use (ICH), the United States has adopted the ICH guidance document Q7, Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, and published it as guidance for industry document [10].

The U.S. GMP regulations are divided into two parts: 210 [6] and 211 [7]. Part 210, “Current Good Manufacturing Practice in Manufacturing,

Processing, Packing or Holding of Drugs — General," provides the framework for the regulations [6], and Part 211, "Current Good Manufacturing Practice for Finished Pharmaceuticals," states the actual requirements. Part 211 is further divided into 11 subparts, which cover the requirements for personnel, premises, equipment, control of materials, production and process controls, packaging and labeling control, holding and distribution, laboratory controls, documentation, and returned and salvaged products [7].

1.14.3 The contents of Part 211 are presented in in Canada:

The production of drug products (drugs) in Canada is controlled under the Food and Drugs Act, which states that distributors and importers are not allowed to sell a drug product unless it has been manufactured according to the requirements of GMP. The principles of GMP are laid down by Division 2 in Part C of the Food and Drug Regulations, which is a part of the Food and Drugs Act. The Health Products and Food Branch Inspectorate has also issued a guidance document (GMP code), which has been prepared to assist in the interpretation of GMP regulations.

The current set of the Canadian GMP code was issued in 2002 and has not been revised since. It has been written with a view to harmonization with GMP standards of other countries and international organizations [WHO, Pharmaceutical Inspection Cooperation Scheme (PIC/S), ICH]. Canadian Healthcare authorities have also published several annexes to the basic GMP code covering topics such as GMP for medical gases, biological drug products, blood products, and production of investigational new drugs. In addition to the GMP code and its annexes, the Canadian Contents of Part 211 of U. S. GMP Regulations [7]

Section Subject

Subpart A General provision

Subpart B Organization and personnel

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1.15 Good Manufacturing Practice for Products

Good Manufacturing Practice is that part of Quality Assurance which ensures that Medicinal products are consistently produced and controlled quality standards appropriate to their intended use and as required by the marketing authorization or product specification.

Good Manufacturing Practice is concerned with both production and quality control.

1.16 The basic requirements of GMP are:

a) All manufacturing processes are clearly defined, systematically reviewed in the light of experience and shown to be capable of

consistently manufacturing medicinal products of the required quality and complying with their specifications and/or marketing authorization;

b) Critical steps of manufacturing processes and significant changes to the process are validated;

c) All necessary facilities for GMP are provided including:

i. appropriately qualified and trained personnel;

ii. adequate premises and space;

iii. suitable equipment and services;

iv. correct materials, containers and labels;

v. approved procedures and instructions;

d) Instructions and procedures are written in an instructional form in clear and unambiguous language, specifically applicable to the facilities provided.

e) Operators are trained to carry out procedures correctly;

f) Records are made, manually and/or by recording instruments, during manufacture which demonstrate that all the steps required by the defined procedures and instructions were in fact taken and that the quantity and quality of the product was as expected. Any significant deviations are fully recorded and investigated.

g) Records of manufacture including distribution which enable the complete history of a batch to be traced, are retained in a comprehensible and accessible form.

(h) The distribution (whole sales) of the products minimizes any risk to their quality.

i) A system is available to recall any batch of product, from sale or supply.

j) Complaints about marketed products are examined, the causes of quality defects investigated and appropriate measures taken in respect of the defective products and to prevent re-occurrence.

1.17 Quality Control

Quality Control is that part of Good Manufacturing Practice which is concerned with sampling, specifications and testing, and with the organization, documentation and release procedures which ensure that the necessary and relevant tests are actually carried out and that materials are not released for use, nor products released for sale or supply, until their quality has been judged to be satisfactory.

The basic requirements of Quality Control are that:

a) Adequate facilities, trained personnel and approved procedures are available for sampling, inspecting and testing starting materials, packaging materials, intermediate, bulk, and finished products, and where appropriate for monitoring environmental conditions for GMP purposes.

b) Samples of starting materials, packaging materials, intermediate products, bulk products and finished products are taken by personnel and by methods approved by Quality Control.

c) Test methods are validated.

d) Records are made, manually and/or by recording instruments, which demonstrate that all the required sampling, inspecting and testing procedures were actually carried out. Any deviations are fully recorded and investigated.

(e) The finished products contain active ingredients complying with the qualitative and quantitative composition of the marketing authorization, are of the purity required, and are enclosed within their proper containers and correctly labeled.

f) Records are made of the results of inspection and that testing of materials,

Intermediate, bulk, and finished products is formally assessed against specification. Product assessment includes a review and evaluation of relevant production

Documentation and an assessment of deviations from specified procedures;

g) No batch of product is released for sale or supply prior to certification by unauthorized person that it is in accordance with the requirements of the relevant authorizations.

h) Sufficient reference samples of starting materials and products are retained to permit future examination of the product if necessary and that the product is retained in its final pack unless exceptionally large packs are produced.

1.18 Product Quality Review

Regular periodic or rolling quality reviews of all licensed medicinal products, including export only products, should be conducted with the objective of verifying the consistency of the existing process, the appropriateness of current specifications for both starting materials and finished product to highlight any trends and to identify product and process Improvements. Such reviews should normally be conducted and ocumented annually ,taking into account previous reviews, and should include at least:

a) A review of starting materials including packaging materials used in the product, especially those from new sources.

b) A review of critical in-process controls and finished product results.

c) A review of all batches that failed to meet established specification(s) and their investigation.

d) A review of all significant deviations or non-conformances, their related Investigations and the effectiveness of resultant corrective and preventative actions taken.

e) A review of all changes carried out to the processes or analytical methods.

f) A review of Marketing Authorisation variations submitted/ granted/ refused, including those for third country (export only) dossiers.

g) A review of the results of the stability monitoring programme and any adverse trends.

h) A review of all quality-related returns, complaints and recalls and the investigations performed at the time.

i) A review of adequacy of any other previous product process or equipment corrective actions.

j) Review of post-marketing commitments and pharmacovigilance, where applicable.

k) The qualification status of relevant equipment and utilities, e.g. HVAC, water, compressed gases, etc.

l) A review of any contractual arrangements to ensure that they are up to date.

The manufacturer and marketing authorisation holder should evaluate the results of this review and an assessment made of whether corrective and preventative action or any revalidation should be undertaken. Reasons for such corrective actions should be documented. Agreed corrective and preventative actions should be completed in a timely and effective manner. There should be management procedures for the ongoing management and review of these actions and the effectiveness of these procedures verified during self-inspection.

Quality reviews may be grouped by product type, e.g. solid dosage forms, liquid dosage forms, sterile products, etc. where scientifically justified.

Where the marketing authorization holder is not the manufacturer, there should be a technical agreement in place between the various parties that defines their respective responsibilities in producing the quality review. The authorized person responsible for final batch certification together with the marketing authorization holder should ensure that the quality review is performed in a timely manner and is accurate.

1.19 Quality Risk Management

Quality risk management is a systematic process for the assessment, control, communication and review of risks to the quality of the product. It can be applied both proactively and retrospectively. The quality risk management system should ensure that:

a) The evaluation of the risk to quality is based on scientific knowledge, experience with the process and ultimately links to the protection of the patient and users.

b) The level of effort, formality and documentation of the quality risk management process is commensurate with the level of risk.

c) The general quality risk management process and integration in to the product quality can be referred in ICHQ9.

1.20 cGMPs and The CONCEPTS Of MODERN QUALITY SYSTEMS:

Several key concepts are critical for any discussion of modern quality systems. The following concepts are used throughout this guidance as they relate to the manufacture of pharmaceutical products.

A. Quality

Every pharmaceutical product must have an established identity, strength, purity, and other quality characteristics designed to ensure the required levels of safety and effectiveness. For the purposes of this guidance document, the phrase achieving quality means achieving these product characteristics.

B. 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. Quality by design, in conjunction with a quality system, provides a sound framework for the transfer of product knowledge and process understanding from drug development to the commercial manufacturing processes and for post-development changes and optimization. The CGMP regulations, when 5 See ICH-Q8 Pharmaceutical Development.

C. Quality Risk Management

Quality risk management is a valuable component of an effective quality systems framework. Quality risk management can, for example, help guide the setting of specifications and process parameters for drug manufacturing, assess and mitigate the risk of changing a process or specification, and determine the extent of discrepancy investigations and corrective actions.

D. CAPA (Corrective and Preventive Action)

CAPA is a well-known CGMP regulatory concept that focuses on investigating, understanding, and correcting discrepancies while attempting to prevent their recurrence. Quality system models discuss CAPA as three separate concepts, all of which are used in this guidance.

Remedial corrections of an identified problem

Root cause analysis with corrective action to help understand the cause of the deviation and potentially prevent recurrence of a similar problem

Preventive action to avert recurrence of a similar potential problem .

E. Change Control

Change control is another well-known CGMP concept that focuses on managing change to prevent unintended consequences. The CGMP regulations provide for change control primarily through the assigned responsibilities of the quality control unit. Certain major manufacturing changes (e.g., changes that alter specifications, a critical product attribute or bioavailability) require regulatory filings and prior regulatory approval. Effective change control activities (e.g., quality planning and control of revisions to specifications, process parameters, procedures) are key components of any quality system. In this guidance, change is discussed in terms of creating a regulatory environment that encourages change towards continual improvement. This means a manufacturer is empowered to make changes subject to the regulations based on the variability of materials used in manufacturing and process improvements resulting from knowledge gained during a product's lifecycle.

1. 21Problematic Research:

Quality has become increasingly important to companies as stakeholder groups, interest groups and members of the public required that their concerns about certain aspects of companies' operations are considered by managers of the companies. As highlighted above, unforeseen consequences raise people's and authorities' awareness.

Both are especially interested in GMP principles, though different reasons which approach the complex of problems in a different sides.

1.22 Aim of this study:

To explore the reasons why companies, adopt Good Manufacturing Practice.

This specifically identify the advantages and disadvantages of adopting principles GMP for companies/laboratories, and how quality is improved by adopting GMP principles.

- To study the impact of the laboratory optimization project for the laboratory utilization, work safety, work practices and quality requirement.

Plan for GMP Compliance master plan

- Guide line for effective and consistent implementation of GMP regulation
- Documents the laboratory's approach for compliance
- Ensures efficiency AND consistency
- Useful for audits to explain the laboratory's approach towards compliance Project Plan
- Outlines steps, tasks, deliverables and owners

1.22.1 Develop procedures and other documents:

- Policy master plan

- Training maintenance validation, audits.
- Test procedures, operation manuals, QC procedures.
- Product test records, batch records, validation results, training records, chromatograms.

  (Present…<https://pdfs.semanticscholar.org).

1.22.2Preparing for the Inspection

- Preparing the Laboratory for the Inspection
- Areas to “troubleshoot”
- Laboratory Equipment
- Calibration
- Preventative Maintenance
- Validation

1.22.3Standard Operating Procedures SOP’s

- Laboratory Records
- Logs
- Data Sheets
- Out of Specification (OOS)
- Laboratory Errors
- Investigations
- Documentation
- Investigation Timeframes
- Training
- Documented Program
- Analytical Method Validation
- Reagents, Solutions and Reference Standards
- Development “work” - GMP “work”
- Documentation
- Laboratory Notebooks

1.22.4 Laboratory Equipment

- Is all the QC equipment controlled and utilized by QC personnel
- Is there a Equipment List
- Is the Laboratory Area (with all the equipment) of a suitable size 211.42 (a)
- Calibration Program
- Is it written down
- Suitable calibration intervals
- Provisions for remedial Action
- Tracking capabilities
- Is Equipment “tagged”
- Maintenance
- Is there a program
- Responsibility
- Record Keeping
- Validation

Does the lab have equipment that requires Validation (PQ)

- Master Validation Plan

Standard Operating

1.22.5 Procedures – SOP’s

- SOP’s in QC Laboratory
- Accessible to QC staff
- Current version
- Laboratory Records (raw laboratory data)
- Bound or prenumbered sheets
- Not lose or scraps of paper
- Review of data (acceptability)

- Laboratory Logs

"Sequence" dates in log – analysis

Dates versus manufacturing dates

- Equipment usage logs for all
- Equipment usage logs current

1.22.6 Out of Specification (OOS)

- **Laboratory Errors**

Laboratory Errors should be relatively rare**.** frequent errors suggest a problem**:**

• Inadequate training

• Poorly maintained equipment

• Improperly calibrated equipment

- Laboratory Investigations
- Analyst and Supervisor – "roles"
- Informal Investigation
- Formal Investigation –extending

- **Beyond the QC laboratory**
  - Investigation Documentation
  - Investigation or Failure Report
  - Corrective Action
  - Investigation Timeframes
  - All failure investigations should be
- **Performed within 20 business daysOf the problem.**
  - Includes implementation time
- **Frame for corrective action**
  - **Training**
  - GMP's require an "active" training
  - **program**
  - Documented evaluation of the

- **training of QC analysts – "Task Training"**

- **Analytical Method**
- **Validation**
  - Compendial Methods – must
  - **demonstrate that the method**
  - **works under actual conditions of use.**
  - System suitability does not
  - **constitute method validation**
  - **Reagents, Solutions**
  - **Reference Standards**
  - Proper storage of
  - Reuse of solutions –stability
  - Appropriate identification
  - Expiration "justifications"
  - Reagent and Solution preparation
  - Complete and accurate
  - **documentation**
  - Highly unlikely that analysts can

"accurately and consistently weigh" to the same gram or microgram

1.22.7 Development vs. GMP

- Use of Laboratory Notebooks
- Documented methods
- Documented materials
- Traceability to equipment

1.22.8 Preparing QC Personnel for the Inspection

- Training the staff

1.22.9 Preparation for an Inspection

- Clean and organize your work area

- Don’t store items on the floor
- No loose data, post-its, or writing data on your hand
- Know where SOPs, logbooks, and

1.22.10 controlled forms applicable to your work are kept

- Clean lab coats
- Neatness counts

1.22.11 Conduct of the Inspection

- Inspectors are looking for issues &
- **Deficiencies, despite how they present**
- **Their approach to the inspection**
- Inspectors can inspect all areas of the Labs that apply to the scope of the Inspection; accompanied by your QA
- May read SOPs, review data, watch analyses, question analysts The inspection covers the lab, the data, and the compliance program, not the individuals in the lab
- The inspection should never be taken personally
- **Questions by the inspectors**
- Inspectors may ask questions to learn how the lab or compliance program operates
- May ask the same question in different ways
- Remember: the inspectors have to learn the processes of a lab that is new to them, prior to making an assessment of the lab
- **Answering the Questions**
- Think before you answer
- Answer questions accurately and truthfully
- Don’t be intimidated or defensive
- Know your work and be confident of your answers
- Be professional

- If you don’t know the answer, it is acceptable to ask your supervisor
- Acceptable to reply that don’t know, but you can find out

▪ **Your role in the Inspection**

- Things not to do:
- Don’t have food in the lab
- Joke with inspectors
- Have clutter in your work area
- Quote what the SOP says, unless

you’re 200% certain you know what you’re talking about

1.22.12 Laboratory Controls

▪ **General Requirements**

(a) “The establishment of any specifications, standards, sampling plans, test procedures, or other laboratory control mechanisms required by this subpart, including any change in such ..., shall be drafted by the appropriate organizational unit and reviewed and approved by the quality control unit. The requirements in this subpart shall be followed and shall be documented at the time of performance. Any deviation... shall be recorded and justified.”

(b) “Laboratory controls shall include the establishment of scientifically sound and appropriate specifications, standards, sampling plans, and test procedures designed to assure that components, drug product containers, closures, in-process materials, labeling, and drug products conform to appropriate standards of identity, strength, quality, and purity. ”Note subpart (4): “The calibration of instruments, apparatus, gauges, and recording devices at suitable intervals in accordance with an established written program...”

- **Testing and Release for Distribution**

(a) "For each drug product, there shall be appropriate laboratory determination of satisfactory conformance to final specifications for the drug product ..." (e) "The accuracy, sensitivity, specificity, and reproducibility of test methods employed by the firm shall be established and documented [validated]."

- **Stability Testing**

There shall be a written testing program designed to assess the stability characteristics of drug products. The results of such stability testing shall be used in determining appropriate storage conditions and expiration dates."

- **Special Testing Requirements**

(a) sterile and/or pyrogen-free product

(b) ophthalmic products

(c) controlled release products

- **Reserve Samples**
- **Penicillin Contamination**

If a reasonable possibility exists that a non-penicillin drug product has been exposed to cross-contamination with penicillin, the non-penicillin drug product shall be tested for the presence of penicillin. Such drug product shall not be marketed if detectable levels are found when tested according to procedures specified ..."

1.23 About Pharmaland:

Pharmaland pharmaceuticals is a subsidiary of Hikma pharmaceuticals PLC, the fast growing multinational pharmaceutical group that operates

in the US, Europe and across the MENA region and has different manufacturing facilities in 11 countries, 5 of them are FDA approved.

Hikma pharmaceuticals PLC acquired Pharmaland in Sudan in 2011. The acquisition reflects Hikma commitment towards improving healthcare in Sudan through the transfer of the highest manufacturing technology.

Pharmaland pharmaceuticals is committed to improve people's health and well-being in Sudan and the region by providing patients with better access to high -quality, affordable medicines in the different therapeutic categories.

1.24 **Manufacturing facilities:**

Pharmaland manufacturing facilities composed of three different plants, each one is dedicated towards a specific group of products: General formulations plant, Penicillin-based formulations plant and cephalosporin-based formulations plant.

Our facilities hold a license for manufacturing different dosage forms including tablets, hard gelatin capsules, dry suspensions, liquid syrup and suspensions. Moreover, Pharmaland obtained a license for secondary packaging of oncology products and injectables.

The plant is located in AL-Bagair industrial area, Jazeera state, about 45 km in the south of Khartoum city.

1.25 **Commitment to Quality:**

Hikma pharmaceuticals PLC manufacturing facilities have a strong reputation for quality products. Hikma has been the first company in the region to obtain USFDA and UKMHRA quality certificates. As part of Hikma group, Pharmaland is strongly committed to implement and maintain a Quality Management System and to continuously improve its effectiveness in accordance with the requirement of ISO 9001:2008

international standard with high adherence to the WHO/ICH guidelines by:

- Proper implementing of current Good Manufacturing Practices (cGMP).
- Continuous improving its manufacturing technology.
- Recruiting employees with best knowledge and high-quality performance.

The request of cGMP certificate from national regulatory authority (NMPB) is currently under process.

1.26 Pharmaland Vision:

"Pharmaland **pharmaceuticals** is committed to improve people's health and well-being by providing high-quality, affordable medicines in the different therapeutic categories. Pharmaland vision is to become a pharmaceuticals leader in East Africa region."

1.27 Diversified Portfolio:

Pharmaland has been building a smart and Diversified product range in the growing therapeutic categories through different models including technology transfer from other Hikma manufacturing facilities, R&D and in-licensed products.

Pharmaland focuses in developing in-invectives, cardiovascular, diabetes, central nervous system (CNS), oncology and respiratory portfolios.

Our current portfolio contains 70 molecules in 121 dosage strengths, beside many other products in the pipeline :

- Anti - infectives.
- Anti - parasitic products.
- Cardiovascular products.
- .Musclo - skeletal products.

- Central nervous system products.
- Respiratory system products.
- Alimentary Tract and Metabolism Products.
- Oncology products.

1.28 R&D capabilities:

Pharmaland is highly concerned with developing its R&D in terms of highly qualified personnel and advanced equipment.
R&D will play a crucial rule in enriching the company Portfolio.

1.29 Partnership:

Developing successful Partnerships is a key to accessing new products and new technology that will enhance and expand our business. Pharmaland is committed to develop Partnerships with global pharmaceutical companies to enrich its Portfolio.

Pharmaland is currently manufacturing Prospan, the No (3) cough syrup globally, under licensed from Engelhard Arzneimittel GmbH & Co, Germany.

1.30 Pharmaland suppliers:

Pharmaland exercises an extensive supplier selection process that ensures that chosen suppliers have the GMP (Good Manufacturing practices) certificate or its equivalent and our main suppliers are ISO 14001 and OHSAS 18001 certified.

1.31 Expanding Geographic Reach:

Pharmaland has an ambitious plan to expand its geographical reach outside Sudan to include Sub - Saharan African countries.

The plant products are currently registered in Sudan, Republic of South Sudan, Eritrea and Chad. The future plan includes registration in other countries especially in the region of East Africa.

1.32 **WHO - Qualification:**

Pharmaland will start a WHO - prequalification program for its facilities and some of its portfolio in order to establish quality system approved by international standard, and to supply NGOs that work in Sub - Saharan Africa.

1.33 **Pharmaland values:**

Pharmaland is committed to highest ethical principles and endeavored to ensure that all employees conform to the highest possible standards of integrity and honesty in everything we do.

Pharmaland treats all people equally, and doesn't judge people by ethnicity, gender, religion, or on political bases. Pharmaland consider diversity as one of the strength of the company community.

1.34 **Customer - Focused Culture:**

Pharmaland has a customer - focused culture that considers maintaining sustainable relation with customers as a key strategy.

Pharmaland will always honor the agreements with its customers & has an active complaints system to keep performance up to the customer's expectations.

1.35 **Social Responsibility:**

Pharmaland consider its contribution to the community as an integral part of the company policy. The company is highly committed to play a major role in the development of the communities where it operates. Pharmaland conducted different development projects for Al - Bagair local community including education and health projects.

Archaization chart

The Pharmaland Pharmaceuticals with the aid of organizational charts defines the organization and management structure of the manufacture and the relationships between management, production operations, support services and the quality management system.

1.36 **Staff expertise and competencies:**

The establishment and maintenance of a satisfactory system of quality assurance and the correct manufacture and control of pharmaceutical products and active ingredients rely upon people. For this reason, there are sufficient qualified personnel to carry out all the tasks for which the manufacturer is responsible. Individual responsibilities are clearly defined and understood by the persons concerned and recorded as written descriptions.

1.37 **Qualifications of key technical employees:**

The Pharmaland Pharmaceuticals have an adequate number of personnel with the necessary qualifications and practical experience.

CHAPTER TOW

Materials and Methodology

CHAPTER TOW

RESEARCH METHODOLOGY

2.1 Introduction:

The idea of this research is to evaluate the role of good manufacturing practice within the Pharmaland pharmaceutical industry through the distribution of a questionnaire to the laboratory staff, which collected the greatest possible results, whether the laboratory staff are applying the system of manufacturing practice to the required form. The requirements of this system will be met and illustrated to us by this descriptive instruction.

2.2 The society:

The society consists of the sample of the quality control staff who were sur 20 employees, questionnaire distributed to16 of them, they are responded as the following:

4: Quality Managers

1: Validation

11: Chemical analyst.

2.2.1 The divisions of the lab into four sections:

* The raw materials have five employees.

* The Microbiology contains four employees.

* The R & D have two employees.

* The final product contains five employees.

2.3. Sample Design:

Table 2.1: Gender

	Frequency	Percent
Male	9	56.3
Female	7	43.8
Total	**16**	**100.0**

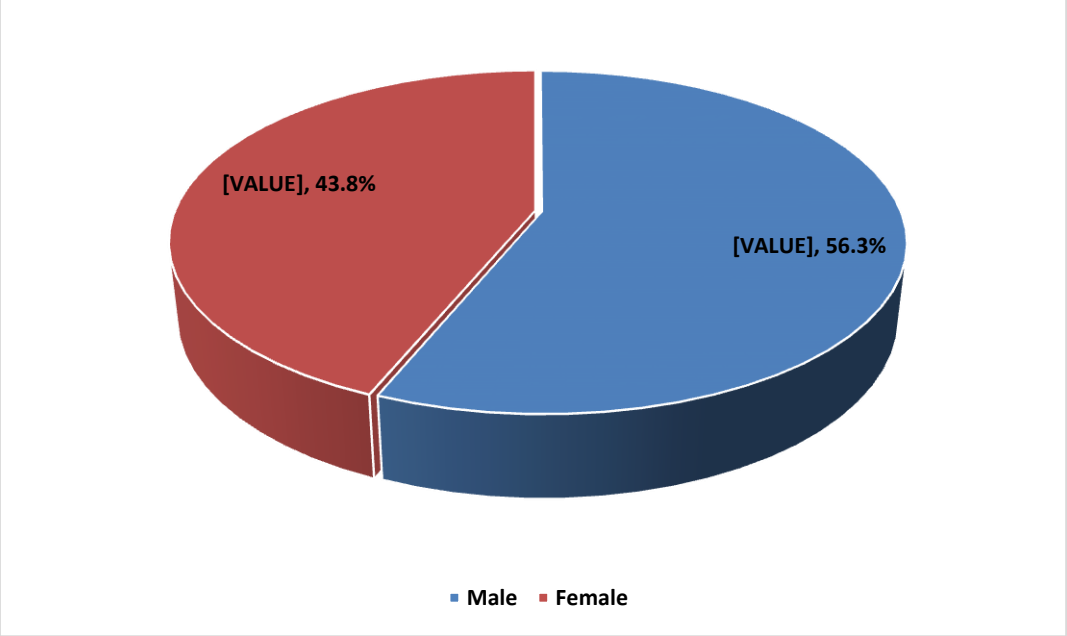
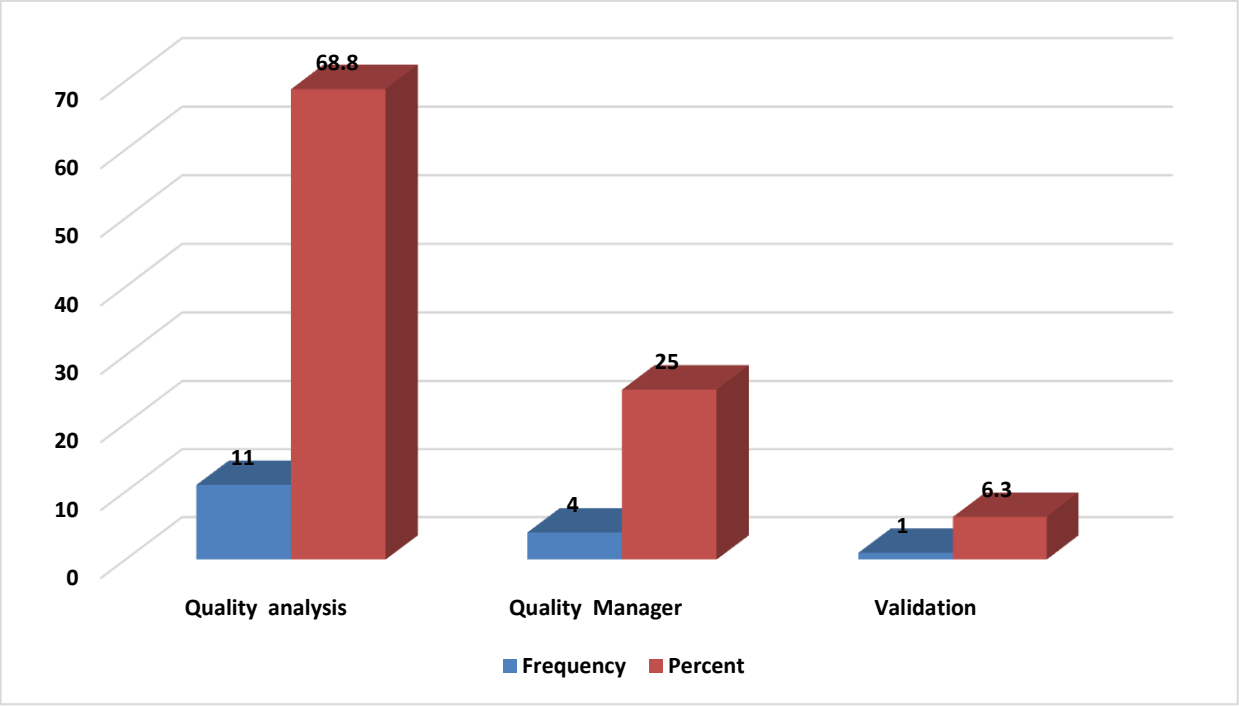


Table 2.2: Qualification:

	Frequency	Percent
Quality analysis	11	68.8
Quality Manager	4	25.0
Validation	1	6.3
Total	**16**	**100.0**



2.4. Tools:

Use a questionnaire consisted of 80 questions and a list of questions for good manufacturing practice and scores were given for answer

Table: 2.3:

cGMP ASSESSMENT CHECKLIST

Participant name (Optional): ……
Date: ……
Job title: ……
Instruction: Please Check ☑ in the 'Y' column if information is collected, confirmed. Check ☑ in the 'N' column
if it is not. Check ☑ in the 'N/A' column if it does not apply. Comments are optional.

Item	Question	Y	N	NA	Comment
1.	Does the staff wear laboratory coats or other protective clothing including eye protection?	☐	☐	☐	
2.	a.Do washing facilities include: Hot and cold water? b. Soap and detergent? c. Clean toilet facilities that are easily accessible to working area d. Clean hand drying facilities? Are the premises satisfactory with respect to? a. Neatness and cleanliness b. State of repair, e.g. paint work, cracks in floors, ceiling or walls, door seals, etc? c. Exposed piping or electrical wiring? d. Blocking of air ducts? e. Equipment blocking corridors or exists?	☐	☐	☐	
3.	Do adequate drains exist? Are they designed with an atmosphere break to prevent back-siphon age from sewer?	☐	☐	☐	
4.	Are areas clearly defined and appropriately controlled.	☐	☐	☐	

5.	Do controlled entry requirements exist Quality control areas?	☐	☐	☐	
6.	Is there a medical monitoring programme to ensure protection of staff and product? Vaccination where applicable? For all employees? For contractors?	☐	☐	☐	
7.	Are staffs instructed to report health or medical problems that may have an adverse effect on the product?	☐	☐	☐	
8.	Are appropriate protective apparel required? Is there gowning SOP for qc staff? For other staff entering production areas? (Engineering/Maintenance; Cleaners; QC samplers; QA auditors) For staff in the Quality Control Lab?	☐	☐	☐	
9.	Is there training in containment procedures? By written procedures? Are records maintained?	☐	☐	☐	
10.	Does a GMP training programme exist? For new employees? Annual update for all staff? Are records maintained	☐	☐	☐	
11.	Are training and education records available?	☐	☐	☐	
12.	Are there on the job training procedures for new employees?	☐	☐	☐	
13.	Are they skilled/trained in fields such as biology, microbiology, chemistry, veterinary medicine, chemical or industrial engineering, etc?	☐	☐	☐	

14.	Are there sufficient key personnel to supervise assigned functions?	☐	☐	☐	
15.	Is there a clear separation of responsibility for production from QC?	☐	☐	☐	
16.	Are they appropriate to the activities of the department?	☐	☐	☐	
17.	Are there job descriptions for key personnel?	☐	☐	☐	
18.	What departments are identified?	☐	☐	☐	
19.	Is there an organizational chart?	☐	☐	☐	
20.	Are equipment and chemicals used in cleaning appropriately maintained and stored?	☐	☐	☐	
21.	Information to be recorded?	☐	☐	☐	
22.	Are adequately constructed waste containers located in appropriate areas?	☐	☐	☐	
23.	Are there records of pesticide usage?	☐	☐	☐	
24.	Is their use controlled so as to avoid product contamination?	☐	☐	☐	
25.	Are pesticides used?	☐	☐	☐	
26.	Is there a pest control programmed? Is it in writing and is it followed?	☐	☐	☐	
27.	Are SOPs available for the transport of microorganisms in closed systems or containers to and from the area?	☐	☐	☐	
28.	Are biohazard signs used and posted where applicable?	☐	☐	☐	
29.	Is there a health and medical surveillance program?	☐	☐	☐	
30.	Are showers available where applicable?	☐	☐	☐	
31.	Are there SOPs for dress codes specified for containment levels applicable and is access controlled and secured? Is there a	☐	☐	☐	

	list displayed of authorized staff for entry?				
32.	Do personnel have specific training in the procedures for handling the pathogenic agents used and the method of using containment equipment?	☐	☐	☐	
33.	Is there a list displayed of responsible individuals to be contacted in the event of an emergency?	☐	☐	☐	
34.	Are standard operating procedures available and displayed outlining emergency procedures in the event of a spill or accidental release of contaminate?	☐	☐	☐	
35.	Is the equipment tested regularly for integrity of containment capability	☐	☐	☐	
36.	Are there standard operating procedures for decontamination of process equipment and facilities? Have these procedures been validated and is the performance monitored?	☐	☐	☐	
37.	Is the process equipment designed to minimize aerosol generation (including sampling devices)?	☐	☐	☐	
38.	Are the appropriate classes of biosafety cabinets used for the relevant microorganisms, and are they certified annually?	☐	☐	☐	
39.	Is the equipment designed, constructed and installed to permit ease of decontamination and cleaning?	☐	☐	☐	
40.	Is the primary containment equipment designed to limit or prevent contact between operators and microorganisms?	☐	☐	☐	
41.	Is there a system for inspection of contractors in respect of any manufacturing or testing activities	☐	☐	☐	

	contracted out?				
42.	Following the national control authority's (NCA) inspection of the manufacturer, is there a system to follow up any recommendations received from NCA?	☐	☐	☐	
43.	Are the inspections followed up to ensure that appropriate action was taken to correct deficiencies?	☐	☐	☐	
44.	Is there a system for regular self-inspection of each manufacturing and test area?	☐	☐	☐	
45.	Is the QC Laboratory involved in all decisions that may concern the quality of the product?	☐	☐	☐	
46.	Is QC monitoring consistency of production using trend analysis?	☐	☐	☐	
47.	Does the QC laboratory have SOPs describing sampling, testing, documentation and précised criteria for release?	☐	☐	☐	
48.	Are all QC tests validated?	☐	☐	☐	
49.	Is the QC department independent from production?	☐	☐	☐	
50.	Are archive facilities provided to ensure the secure storage and retrieval of all documents?	☐	☐	☐	
51.	Is the design adequate to protect the contents from deterioration and is access restricted to authorized personnel	☐	☐	☐	
52.	Are separate storage facilities maintained for the secure storage of samples, retained samples and reagents?	☐	☐	☐	
53.	Are environmental conditions appropriate to the functions and operations to be performed?	☐	☐	☐	
54.	Is there a formal evaluation after	☐	☐	☐	

	training?				
55.	Are there on the job training procedures for new employees?	☐	☐	☐	
56.	Are training and education records available?	☐	☐	☐	
57.	Is staff undergoing training appropriately supervised?	☐	☐	☐	
58.	Is there an SOP for identifying training needs and providing the necessary training on a regular basis	☐	☐	☐	
59.	Are there job descriptions for personnel?	☐	☐	☐	
60.	Are records maintained for 2 years after the expiry dates?	☐	☐	☐	
61.	Does revised document includes reference to previous document?	☐	☐	☐	
62.	Is a system of change control in place to inform staff of new and revised document?	☐	☐	☐	
63.	All relevant staff are trained for new and revised SOPs?	☐	☐	☐	
64.	Is there a system for distribution of SOPs?	☐	☐	☐	
65.	Are the SOPs available at the relevant location?	☐	☐	☐	
66.	Are revisions of SOPs approved by an authorized person?	☐	☐	☐	
67.	Are there SOPs written and approved for all testing activities?	☐	☐	☐	
68.	Are the SOPs reviewed on a regular and defined schedule?	☐	☐	☐	
69.	Is there a policy for handling out-of-specification (OOS) results?	☐	☐	☐	
70.	Is there an internal quality audit programmed?	☐	☐	☐	
71.	Does top management hold periodic reviews to confirm continued	☐	☐	☐	

	conformance to the quality system?				
72.	Is there a quality manual?	☐	☐	☐	
73.	Does the laboratory have a quality manager?	☐	☐	☐	
74.	Does the laboratory have organizational charts?	☐	☐	☐	
75.	Does the laboratory nominate substitutes or subordinates trained for key management?	☐	☐	☐	
76.	Does the laboratory's documentation specify the responsibility and authority of all personnel?	☐	☐	☐	
77.	Does the laboratory ensure adequate information flow between staff at all levels?	☐	☐	☐	
78.	Are staff members aware of the relevance and importance of their activities?	☐	☐	☐	
79.	Does the laboratory have a policy and procedure to ensure the confidentiality of the information?	☐	☐	☐	
80.	Pest control programmed.	☐	☐	☐	

3.5 Statistical Methods:

Statistical analysis was used in the analysis of the results by means of frequency and percentage ratios

CHAPTER THREE

Results and Discussions

CHAPTER THREE

RESULTS:

Applying the Good Manufacturing Practice

Table: 3.1:

The GMP Practice	Frequency	Percent	Valid Percent	Cumulative Percent
Good	44	55.0	55.0	55.0
Poor	36	45.0	45.0	100.0
Total	**80**	**100.0**	**100.0**	

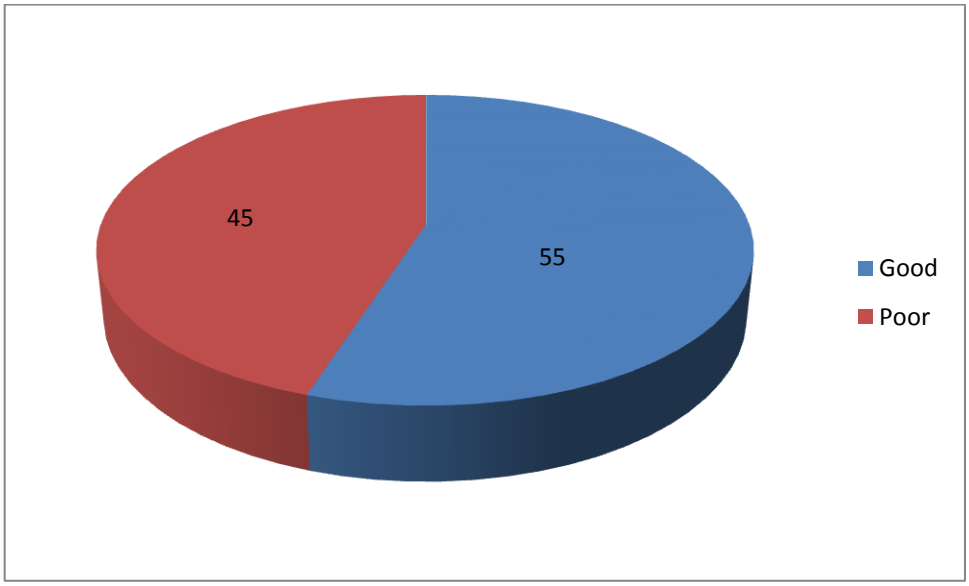


Table: 3.2:

q	Comment		Frequency	Percent
		Yes	No	NA
1	Does the staff wear laboratory coats or other protective clothing including eye protection	16	0	0
		100%	0%	0%
2	Do washing facilities include: (all question)	16	0	0
		100%	0%	0%
3	Do adequate drains exist? Are they designed with an atmosphere break to prevent back-siphon age from sewer	15	1	0
		93.8%	6.3%	0%
4	Are areas clearly defined and appropriately controlled.	16	0	0
		100%	0%	0%
5	Do controlled entry requirements exist Quality control areas?	16	0	0
		100%	0%	0%
6	Is there a medical monitoring programmed to ensure protection of staff and product? Vaccination where applicable? For all employees? For contractors?	16	0	0
		100%	0%	0%
7	Are staffs instructed to report health or medical problems that may have an adverse effect on the product?	16	0	0
		100%	0%	0%
8	Is appropriate protective apparel required? Is there gowning SOP for qc staff? For other staff entering production areas? (Engineering/Maintenance; Cleaners; QC samplers; QA auditors) For staff in the Quality Control Lab?	16	0	0

		100%	0%	0%
9	Is there training in containment procedures? By written procedures? Are records maintained?	15	1	0
		93.8%	6.3%	0%
10	Does a GMP training programmed exist? For new employees? Annual update for all staff? Are records maintained	16	0	0
		100%	0%	0%
11	By written procedures?	15	1	0
		93.8%	6.3%	0%
12	Are there on the job training procedures for new employees?	16	0	0
		100%	0%	0%
13	Are they skilled/trained in fields such as biology, microbiology, chemistry, veterinary medicine, chemical or industrial engineering, etc.?	16	0	0
		100%	0%	0%
14	Are they appropriate to the activities of the department?	16	0	0
		100%	0%	0%
15	Are there job descriptions for key personnel?	16	0	0
		100%	0%	0%
16	What departments are identified?	16	0	0
		100%	0%	0%
17	Is there an organizational chart?	16	0	0
		100%	0%	0%
18	Are equipment and chemicals used in cleaning appropriately maintained and stored?	16	0	0
		100%	0%	0%

19	Is there a clear separation of responsibility for production from QC?	16	0	0
		100%	0%	0%
20	Are they appropriate to the activities of the department?	16	0	0
		100%	0%	0%
21.	Information to be recorded?	16	0	0
		100%	0%	0%
22.	Are adequately constructed waste containers located in appropriate areas?	16	0	0
		100%	0%	0%
23.	Are there records of pesticide usage?	16	0	0
		100%	0%	0%
24.	Is their use controlled so as to avoid product contamination?	16	0	0
		100%	0%	0%
25.	Are pesticides used?	16	0	0
		100%	0%	0%
26.	Is there a pest control programme? Is it in writing and is it followed?	16	0	0
		100%	0%	0%
27.	Are SOPs available for the transport of microorganisms in closed systems or containers to and from the area?	16	0	0
		100%	0%	0%
28	Are biohazard signs used and posted where applicable?	16	0	0
		100%	0%	0%
29	Is there a health and medical surveillance program?	15	1	0
		93.8%	6.3%	0%
30	Are showers available where applicable	16	0	0
		100%	0%	0%

31	Are there SOPs for dress codes specified for containment levels applicable and is access controlled and secured? Is there a list displayed of authorized staff for entry?	15	1	0
		93.8%	6.3%	0%
32.	Do personnel have specific training in the procedures for handling the pathogenic agents used and the method of using containment equipment?	16	0	0
		100%	0%	0%
33.	Is there a list displayed of responsible individuals to be contacted in the event of an emergency?	16	0	0
		100%	0%	0%
34.	Are standard operating procedures available and displayed outlining emergency procedures in the event of a spill or accidental release of contaminate?	16	0	0
		100%	0%	0%
35.	Is the equipment tested regularly for integrity of containment capability	16	0	0
		100%	0%	0%
36.	Are there standard operating procedures for decontamination of process equipment and facilities? Have these procedures been validated and is the performance monitored?	16	0	0
		100%	0%	0%
37.	Is the process equipment designed to minimize aerosol generation (including sampling devices)?	16	0	0
		100%	0%	0%
38	Are the appropriate classes of biosafety cabinets used for the relevant microorganisms, and are they certified annually?	15	1	0
		93.8%	6.3%	0%

39.	Is the equipment designed, constructed and installed to permit ease of decontamination and cleaning?	16	0	0
		100%	0%	0%
40.	Is the primary containment equipment designed to limit or prevent contact between operators and microorganisms?	16	0	0
		100%	0%	0%
41.	Is there a system for inspection of contractors in respect of any manufacturing or testing activities contracted out?	16	0	0
		100%	0%	0%
42	Following the national control authority's (NCA) inspection of the manufacturer, is there a system to follow up any recommendations received from NCA?	15	1	0
		93.8%	6.3%	0%
43.	Are the inspections followed up to ensure that appropriate action was taken to correct deficiencies?	16	0	0
		100%	0%	0%
44.	Is there a system for regular self-inspection of each manufacturing and test area?	16	0	0
		100%	0%	0%
45.	Is the QC Laboratory involved in all decisions that may concern the quality of the product?	16	0	0
		100%	0%	0%
46.	Is QC monitoring consistency of production using trend analysis?	16	0	0
		100%	0%	0%
47.	Does the QC laboratory have SOPs describing sampling, testing, documentation and précised criteria for release?	16	0	0
		100%	0%	0%
48	Are all QC tests validated?	15	1	0
		93.8%	6.3%	0%

49	Is the QC department independent from production	15	1	0
		93.8%	6.3%	0%
50.	Are archive facilities provided to ensure the secure storage and retrieval of all documents?	16	0	0
		100%	0%	0%
51	Is the design adequate to protect the contents from deterioration and is access restricted to authorized personnel	15	1	0
		93.8%	6.3%	0%
52	Are separate storage facilities maintained for the secure storage of samples, retained samples and reagents ?	15	1	0
		93.8%	6.3%	0%
53	Are environmental conditions appropriate to the functions and operations to be performed?	15	1	0
		93.8%	6.3%	0%
54	Is there a formal evaluation after training?	15	1	0
		93.8%	6.3%	0%
55	Are there on the job training procedures for new employees?	15	1	0
		93.8%	6.3%	0%
56	Are training and education records available?	15	1	0
		93.8%	6.3%	0%
57	Is staff undergoing training appropriately supervised?	15	1	0
		93.8%	6.3%	0%
58	Is there an SOP for identifying training needs and providing the necessary training on a regular basis	15	1	0
		93.8%	6.3%	0%

59	Are there job descriptions for personnel?	15	1	0
		93.8%	6.3%	0%
60	Are records maintained for 2 years after the expiry dates?	15	1	0
		93.8%	6.3%	0%
61	Does revised document includes reference to previous document?	15	1	0
		93.8%	6.3%	0%
62	Is the a system of change control in place to inform saff of new and revised document?	15	1	0
		93.8%	6.3%	0%
63	All relevant staff are trained for new and revised SOPs?	15	1	0
		93.8%	6.3%	0%
64	Is there a system for distribution of SOPs ?	15	1	0
		93.8%	6.3%	0%
65	Are the SOPs available at the relevant location?	15	1	0
		93.8%	6.3%	0%
66	Are revisions of SOPs approved by an authorized person?	15	1	0
		93.8%	6.3%	0%
67	Are there SOPs written and approved for all testing activities?	15	1	0
		93.8%	6.3%	0%
68	Are the SOPs reviewed on a regular and defined schedule?	15	1	0
		93.8%	6.3%	0%
69	Is there a policy for handling out-of-specification (OOS) results?	15	1	0
		93.8%	6.3%	0%
70	Is there an internal quality audit programme?	15	1	0
		93.8%	6.3%	0%

71	Does top management hold periodic reviews to confirm continued conformance to the quality system?	15	1	0
		93.8%	6.3%	0%
72	Is there a quality manual ?	15	1	0
		93.8%	6.3%	0%
73	Does the laboratory have a quality manager?	15	1	0
		93.8%	6.3%	0%
74	Does the laboratory have organizational charts?	15	1	0
		93.8%	6.3%	0%
75	Does the laboratory nominate substitutes or subordinates trained for key management ?	15	1	0
		93.8%	6.3%	0%
76.	Does the laboratory's documentation specify the responsibility and authority of all personnel?	16	0	0
		100%	0%	0%
77.	Does the laboratory ensure adequate information flow between staff at all levels?	16	0	0
		100%	0%	0%
78.	Are staff members aware of the relevance and importance of their activities?	16	0	0
		100%	0%	0%
79.	Does the laboratory have a policy and procedure to ensure the confidentiality of the information?	16	0	0
		100%	0%	0%
80.	Pest control programme.	16	0	0
		100%	0%	0%

3.1 Discussion

This study, which was conducted on Pharmaland laboratories, a member of a group of hikma. The study was based on a questionnaire composed of questions posed to the laboratory staff. These questions set to be analyses of the basic requirements of the good manufacturing practice system.

One of the good points that the laboratory staff wear uniforms in the laboratory and committed to follow the safety procedures. There are some points that needed to be improved such as the development of drainage system within the laboratory and the isolation of materials that harm the environment in a special place and disposal through competent authorities and in a manner not harmful to the environment.

The study also showed some good things that the system of identification of areas and control in the laboratory is good and effective. The study also showed that medical services are provided to all employees and a medical report employee shows his health status. Also good things found that there are methods of operation written and approved, Access to the laboratory is available to every employee.

The study also revealed that there is a weakness in the training system for staff needs to develop and be more effective. The good thing is that the new staff are train on good manufacturing practice, but it must be according to written methods. The study also showed that the employees who are selected according to specific systems, who are skilled and highly qualified. One of the excellent things that the study has shown the devices and tools that used inside the laboratory are well cleaned and storage. There is also a good division of sections within the laboratory. Information is also well recorded and stored in the laboratory. There is an appropriate place to store the waste. When pesticides are used, they are

used for insect control. There are measurements to determine the degree of pollution and all that is written. here are standard operating methods that illustrate dealing with microorganisms within the laboratory. There are also posters showing the degree of risk of these materials. But the study showed that there is no clear medical program followed during the year.

Also through the study it is noted that there is a water shower used in emergencies and injuries. One of the things that is not good in the study is that there are no written operational methods that explain the processes of entry and exit within the system of the laboratory of the definition of responsible persons and the distinction between sections within the laboratory. One of the good things about BD training is that the specific and custom sections are done. The study also showed that the employee in charge of the ambulance staff is well trained and available to all in the case of injuries and there is a first aid box, a standard method of operation that shows how the ambulance is performed. The study showed that there is a documentation section and all documentation within the laboratory. The study also indicated that biosafety cabinets needed to be developed within the microbiology laboratory.

The study showed that there is a documentation section and all documentation within the laboratory. The study also indicated that bio-reservoirs needed to be developed within the microbiology laboratory. The study also showed that the devices used are easy to wash and use and can be prevented from pollution.

The study showed that the laboratory is subjected to inspection visits and this is good but there is a lack of commitment to follow up the minor points written during the inspection.

One good thing is that the QA department of the laboratory is involved in every decision taken in the product as the laboratory uses clear methods

of analysis for the samples but some of these methods need to be updated. The good thing is that there is monitoring of the repetition of the results and explaining the cause. The study found that the management of quality control is independent of the production management.

A good thing is that there is a place reserved for archiving and archiving, but one of the negative observations that the study showed is that there is a weakness in the staff.

In addition to retain samples are kept in the concerned laboratories and it is not under the control of the QC department.

The study showed that optimum conditions within the laboratory for work need to be improved to create a better environment. There is also a weakness in the evaluation of training for new employees and must be provided by supervisors and not a lower level. The method must be designed in a standard way to describe in detail how the training is done. The study also showed that the job description of each employee is unclear. The study also indicated that the documents must be kept for two years after the completion date.

There are some standard operating methods that must be reviewed every year. The study showed that there are no clear policies to deal with the results outside the specifications. The study also showed that the internal audit system need to be improved. There is also no periodic review of the quality system by high management.

It is necessary to establish a quality manual and establish an effective organizational structure for the employees according to job title because the study clearly showed weakness in that.

The alternative staff system is not used and trained to replace the basic staff member in his / her absence. There is some weakness in the responsibilities specified in some places in the laboratory. The flow of information and communication within the laboratory needs to be

improved. Lab staff awareness about the policies and management structure and job description should be improving to allow for fulfill of each of the staff his prescribed tasks and duties completely.

The study also revealed that the updates for the previous document must be trained to the staff, and it is necessary to create a system that distributes these updated documents to their respective places. The contents of the documents must be ascertained and approved because they contain all the activities, however the study showed the opposite.

The study showed that Pesticides Control Program needs clear policies.

3.2 Conclusion:

From this study it's possible to conclude that some variables were well establish such as the organization and management, documentation, personnel, materials, equipment and instruments ,working procedures and safety other variables are not well establish such as quality management system and computer systems .

3.3 Recommendations:

On the bases of this study it's recommend that:

- Laboratory access should be established.
- Software and analytical methods should be validated.
- Procedure for disaster recovery should be established.
- Quality manual should be established.
- Attention must be paid to the internal audit program.
- The laboratory management should train staff to act improve output.

- The internal environment needs to be better prepared than the current one to do the job better.
- Special place should be established for chemical waste.
- The quality system should be activated better, and periodic reviews should be made.
- The data must be archived on better places than current ones.
- The quality system should be activated better, and periodic reviews should be made.
- High efficiency drains should be designed and the harmful substances should be isolated and disposed of authorized team.
- The training should be implemented by specialized, effective and sophisticated manner so that the capacity of the staff is properly constructed.
- An effective documentation system must be established that includes a clear description of each method used in the work, written and available to the employee and must keep all documents in a safe place.
- A medical monitoring program and an annual and semi-annual examination of staff and new employees should be established.
- Design clothes to distinguish employees according to the section in which it works and create accounts to enter the system for each one alone and secure it with a password.
- Customize the system within the quality system to review all the points discovered by the auditors who visit the factory and the system is required to follow all these points.
- All laboratory tests must have official and recognized references such as USP, BP .... etc.

- An appropriate form must be designed for the laboratory to preserve its contents and the entry and exit of it shall be in a clear and recorded system.
- The management of the lab must be separate from production until the results are unquestionable.
- Appropriate places should be allocated to retain chemicals according to their type and suitability to the place where they are stored, and should be defined by a clear labeling .
- It must be ideal conditions for work by distributing and coordinating tasks and collaborating in their implementation.
- Staff should be evaluated after training to determine the utilization rate of the training.
- New staff should be trained under intensive supervision.
- It must be a training file for each employee and be available for all the time.
- The performance of staff should be assessed periodically, and their abilities and training improved based on evaluation.
- There must be a clear job description for each employee.
- Old records must be kept for two years after the completion date.
- When documents are updated, there should be a section indicating the previous update.
- The QA department should review documents, update them in a timely manner and keep them well.
- All staff should be trained on updated documents and distributed among the departments and available in their places. The original documents should be kept in one place at the QA department.
- The operational procedures must be written, approved, and updated according to a regular schedule.

- The internal audit program should be used in accordance with a regular program and the recommendations that come out of it must be followed up and implemented.
- There must be clear policies to deal with results out of specifications and out of trend.
- Top management should hold periodic reviews to ensure continuous compliance with the quality system.
- The organizational chart of the laboratory must be complete and there must be an alternative to replacing each person in case of absence.
- The system of work must ensure adequate flow of information among the staff at all levels and each employee must know the importance of his job.
- Must be followed by a clear sense inside the laboratory to ensure the preservation of information and confidentiality.

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