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RECENT RULES AND REGULATIONS RELATED TO MANUFACTURING DRUG PRODUCT IN QUALITY CONTROL AS PER CENTRAL DRUG STANDARD CONTROL ORGANIZATION (CDSCO) IN INDIA COMPARISON WITH UGANDA

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ABSTRACT

The Central Drugs Standard Control Organisation (CDSCO) is India's national regulatory body for cosmetics, pharmaceuticals and medical devices. Its headquarters is located in Delhi and it has 6 zonal offices, 4 sub zonal offices, 13 port offices and 7 laboratories spread across the country. Good manufacturing practices (GMP) are complex and thorough. Wide array of regulatory requirements needs to be followed. Following GMP results in high quality products. GMP is mandatory in countries with a regulated pharmaceutical market and in the WHO prequalification programme too. GMP covers all aspects of production; from the starting materials, premises and equipment to the training and personal hygiene of staff. Detailed, written procedures are essential for each process that could affect the quality of the finished product. Comparing the manufacturing regulatory requirements of India and Uganda helps to recognize the pharmaceutical manufacturing market size.

KEYWORDS: CDSCO (central Drugs Standard Control Organisation); GMP (good manufacturing practices); Pharmaceutical marketing; regulatory requirements; quality of product.

1. INTRODUCTION

Quality control is a set of activities for ensuring the required quality in the product. The activities focus on identifying defects in the manufactured products. It is a set of procedures intended to ensure that a manufactured product adheres to a defined set of quality criteria or meets the requirements of the customer. The aims and objectives of QC is improvement of quality, efficient use of men and machines, economy in use of materials, reduction in cost unit, scientific evaluation of quality and production, reduction of customer complaints, to prevent the poor-quality product reaching to customer. Pharmaceutical manufacturing is the process of industrial-scale synthesis of pharmaceutical drugs as part of the pharmaceutical industry. The process of drug manufacturing can be broken down into a series of unit operations, such as milling, granulation, coating, tablet pressing, and others. The importance of QC in manufacturing is the industry can ensure that the final drug products meet the required standards for safety, efficacy, and pass stability testing; to verify and test the medicine at the various stages of production, to ensure every product is of the highest quality; to verify and test the medicine at the various stages of production, to ensure every product is of the highest quality; QC also involves identifying any defects in products and fixing the problems with corrective techniques and measures.

Good manufacturing practice (GMP) is a system for ensuring that products are consistently produced and controlled according to quality standards. GMP covers all aspects of production; from the starting materials, premises and equipment to the training and personal hygiene of staff. Detailed, written procedures are essential for each process that could affect the quality of the finished product. Poor quality medicines are not only a health hazard, but a waste of money for both governments and individual consumers. A poor-quality medicine may contain toxic substances that have been unintentionally added. A medicine that contains little or none of the claimed ingredient will not have the intended therapeutic effect. GMP helps to boost the pharmaceutical export opportunities, most countries will only accept import and sale of medicines that have been manufactured to internationally recognized GMP. Governments seeking to promote their countries' export of pharmaceuticals can do so by making GMP mandatory for all pharmaceutical production and by training their inspectors in GMP requirements. Good quality must be built in during the manufacturing process; it cannot be tested into the product afterwards. GMP prevents errors that cannot be eliminated through quality control of the finished product. Without GMP it is impossible to be sure that every unit of a medicine is of the same quality as the units of medicine tested in the laboratory.

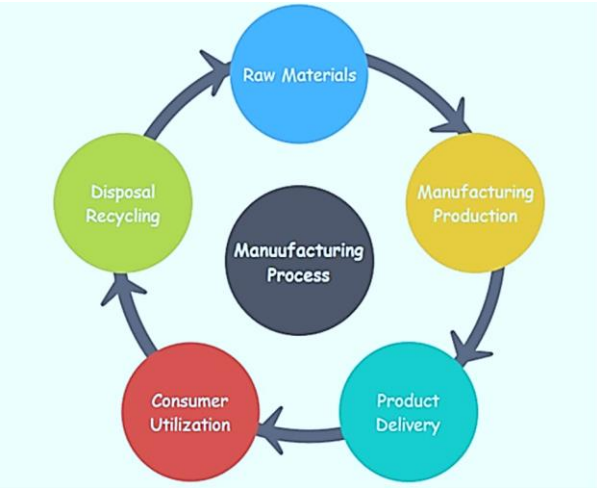

Figure 1: Manufacturing process.

GMP covers all aspects of production; from the starting materials, premises and equipment to the training and personal hygiene of staff. Detailed, written procedures are essential for each process that could affect the quality of the finished product.

2. Good manufacturing practices

Premises: Premises must be located designed, constructed, adapted and maintained to suit the operations to be carried out.

Design and construction: The design construction and manufacture of building should be in a manner that allows the production under hygienic conditions. An adequate area for placement of materials equipment and movement of personnel. The design, construction and maintenance in such a manner that it is protected from pests, birds and animals. Smooth, waterproof and crack free walls and flooring to allow easy cleaning, painting and disinfection. Adequate lighting, proper ventilation and handling system to maintain temperature and humidity at construction or building area.

Location: Location of factory and its surroundings should be good and free from contaminations like dust and smoke. A location should be far away from any other factory which produces any disagreeable odour, fumes, dusts, smokes, any biological emissions.

Water systems: Water tanks should be regularly cleaned to ensure freedom from microbial growth and the record of such cleaning should be maintained by manufacturer. The purified water used should be in accordance with the IP specifications. potable water can be used only for cleaning and washing and for other operations.

Management of waste: There should be adequate area for the storage and disposal of waste materials. Any waste water or residue is likely to cause any harm to the health of the workers or to the general public should be treated before to its disposal.

Plant layout: It refers to the arrangement of physical facilities such as machinery, equipment, furniture etc within the manufacturing area in such a manner so as to have quickest flow of material at the lowest cost. The importance of plant layout is It provides optimum relationship among output, floor area and manufacturing process; It allows easy production flow; It provides flexibility of operations; It makes the economic use of buildings; It provides safety and comfort at work.

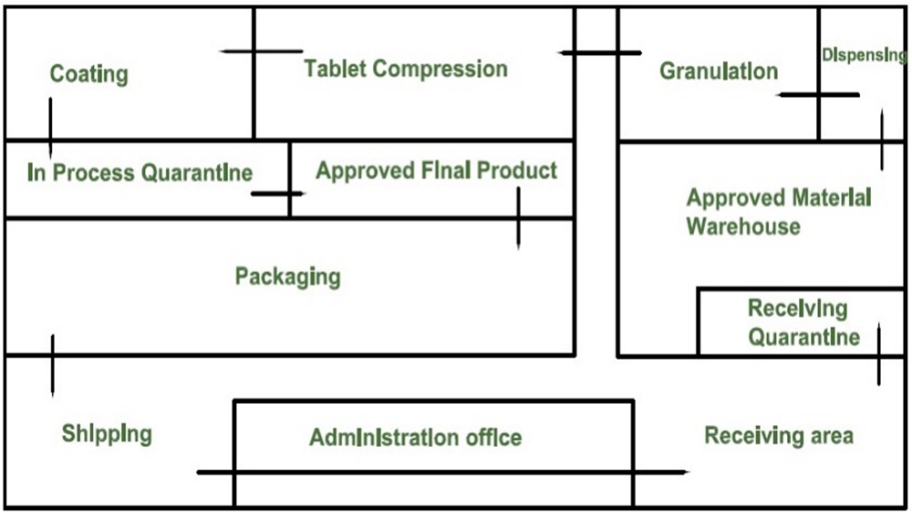

Figure 2: Plant layout.

Maintenance: Buildings used in manufacturing, packaging or warehousing of drug products should be properly maintained. A deteriorated building presents a poor image of the facility and also affects the product quality. Any cracks or holes in the walls, floors or ceilings of warehouse provide the entry of insects, birds, dirt or microbes and can result in cross contamination and microbial growth. Water leaking from the cracked roofs significantly damages the stored materials and equipment and can also cause electrical failures and fires. Written procedures for cleaning, sanitizing, fumigating agents should be maintained.

Sanitation: Building used for manufacturing, processing, packaging or storing of drug products should be maintained under clean and sanitary conditions. Buildings should be cleaned regularly and thoroughly in according to approved written program. Growth of microbes should be monitored regularly. Disinfectants and detergents should be monitored and it is used in grade A and B areas should be sterilized before and after use.

Equipment: It may be defined as physical entity which is used to carry out a general or specific activity in the pharmaceutical plant. Ex – Tablet compressor, weighing machines, filling machines etc. The equipment should be selected based on requirements like equipment must be designed, constructed and maintained in such a way that it suits the operations. The layout and design of equipment must aim to minimize the risk of errors a permit effective cleaning. Maintenance of equipment is necessary in order to avoid cross contamination. Production equipment should be thoroughly cleaned on a scheduled basis. Laboratory equipment and instruments should be suited to testing procedures done. Equipment should be calibrated before used as per guidelines. Equipment in the production area should not be reactive to the products or affect the quality of the product.

Raw materials: Raw materials are the products that are purchased in their raw state for the purpose of processing them into industrial goods. It is a starting material that include buffers, common solvents, substituents, elements and materials required for the manufacturing of drug. Raw materials are materials or substances used in the primary production or manufacturing of goods. Raw materials should be purchased from the authentic seller who have all the proper up to date documentation. Purchasing should be done under the supervision of experienced personnels. For each consignment, the containers should be checked for at least integrity of the packages and seal. If any problem is observed it can be sent to QC department for verification. The labels attached to the containers of raw materials should not be destroyed or rewritten. Raw material received should be quarantined in the quarantine area before accepting or rejecting the goods. QC department examines the raw materials according to suitable guidelines and decides whether to accept or reject the goods. After the tests, the goods are differentiated into accepted, rejected and under test areas. The rejected goods should have proper documentation of reasons for the rejection and the goods are sent back to the respective seller.

Personnel: The establishment and maintenance of a suitable quality assurance system for pharmaceutical products depends on the person. A person who is responsible for manufacturing, processing, packaging and handling of drug products should be provided with adequate education, training and experience is defined as personnel. Personnel are the most significant part of a manufacturing system. They should be provided with standard training to maintain a high level of safety, identity, strength, quality and purity in the work area. The personnel also have their own responsibilities like personnel involved in manufacturing, processing, packaging and handling of drug products should wear clean clothing or uniform; the personnel should cover his/ her head, face, hand and arms in order to protect the products from contamination; the company should provide appropriate uniforms or protective clothing to the personnels; the personnel should follow good sanitization and healthy habits; the personnels should not wear cosmetics or jewelleries in production or QC areas as it can lead to contaminations; eating, drinking, chewing, alcohol, smoking should be avoided in production and storage areas; only authorized and trained personnels should enter the company areas; personnel should be physically fit to work; tests should be conducted on regular basis; if any personnels have illness or open wounds that may affect the safety and quality of drug products so he/she should avoid coming in contact with the drug products. The manufacturer should provide training in accordance with written program for all the employees or personnels whose duties are in manufacturing areas and laboratories. Newly recruited personnel should receive training appropriate to the duties assigned to them. Personnel working in areas where highly active, toxic, infectious areas should be given specific training. The concept of quality assurance should be fully discussed during the training sessions. Continuous training should be given and its practical effectiveness should be evaluated. Visitors or untrained personnels should not be allowed to enter production and QC areas, if its unavoidable they should be given protective clothing.

Personnel hygiene: All personnels should be trained in the personal hygiene. A high level of personal hygiene should be observed by all the personnel working in company. All personnel should undergo health examination, personnel should be instructed to wash their hands before entering production areas, smoking, eating, drinking, chewing should not be permitted in production areas, laboratories and storage areas, direct contact should be avoided between the starting materials, primary packaging materials, intermediate materials and bulk products, to protect the products from contamination the personnel should wear clean body covering appropriate to their duties, protective clothing should apply to all personnels entering production areas, whether they are temporary or full time employees or non-employees, if person shows any illness signs, then they should not be allowed to handle starting materials, primary packaging materials, in process materials or drug products until the condition is no longer judged to be a risk, a personnel should be instructed and encouraged to report to their supervisor in any mistake or condition, a personnel used clothes if reusable then store the clothes in separate closed containers until properly laundered.

Figure 3: Personnel hygiene.

Quality management systems (QMS): A quality management system (QMS) is defined as a formalized system that documents processes, procedures, and responsibilities for achieving quality policies and objectives. A QMS helps coordinate and direct an organization's activities to meet customer and regulatory requirements and improve its effectiveness and efficiency on a continuous basis. ISO 9001:2015, the international standard specifying requirements for quality management systems, is the most prominent approach to quality management systems. Implementing a quality management system affects every aspect of an organization's performance. Benefits of a documented quality management system include meeting the customer's requirements, which helps to install confidence in the organization, in turn leading to more customers, more sales, and more repeat business, meeting the organization's requirements, which ensures compliance with regulations and provision of products and services in the most cost- and resource-efficient manner, creating room for expansion, growth, and profits. The additional advantages, including: Defining, improving and controlling processes reducing waste, preventing mistakes, lowering costs, facilitating and identifying training opportunities, engaging staff, setting organization-wide direction, communicating a readiness to produce consistent results.

ISO 9001: 2015: ISO 9001 is defined as the international standard that specifies requirements for a quality management system (QMS). Organizations use the standard to demonstrate the ability to consistently provide products and services that meet customer and regulatory requirements. ISO 9001 is based on the plan-do-check-act methodology and provides a process-oriented approach to documenting and reviewing the structure, responsibilities, and procedures required to achieve effective quality management in an organization. Specific sections of the standard contain information on many topics, such as requirements for a QMS, including documented information, planning and determining process interactions, management of resources, including human resources and an organization's work environment, product realization, including the steps from design to delivery, measurement, analysis, and improvement of the QMS through activities like internal audits and corrective and preventive action.

Elements and requirements of a QMS: Each element of a quality management system helps achieve the overall goals of meeting the customers' and organization's requirements. Quality management systems should address an organization's unique needs; however, the elements all systems have in common include the organization's quality policy and quality objectives, quality manual, procedures, instructions, records, data management, internal processes, customer satisfaction from product quality, improvement opportunities and Quality analysis.

Figure 4: Quality management principles.

3. Uganda national bureau of standards (UNBS):
The Uganda National Bureau of Standards (UNBS), was established as a semi-autonomous body by an Act of Parliament in 1983. It has a National Standards Council (NSC) as its policy making body. The Executive Director together with the management team is charged with the administrative and operational responsibilities. The UNBS Information Resource Centre is a national repository for information on Standardization, Quality Management, Metrology, Inspection and Testing. The Centre provides information to: MSMEs, industries, business community, government ministries, departments and agencies, civil society, researchers, NGOs, academia, and the general public. The objective of the Information Resource Centre is to provide an efficient information service on national, regional, foreign and international standards; quality management; metrology; product and system inspections, laboratory testing.

Responsibilities: The role of UNBS is the formulation and promotion of the use of standards; enforcing standards in protection of the public health and safety and the environment against dangerous, counterfeit and substandard products; ensuring fairness in trade and precision in industry through reliable measurement systems; strengthening Uganda's economy by enhancing competitiveness of local industries and promotion of quality exports through standardization, quality assurance, testing and metrology.

Comparison of manufacturing regulations of India with Uganda:

	INDIA	**UGANDA**
Industrial Clusters	Major 6 industrial clusters *Minor industries *Major industries	The government has established over 20 industrial parks in the country, which enjoy various investment incentives. There are few capital goods industries and agriprocessing firms account for about 39% of manufacturing.
Main Industries	Steel, Textile, Jute, Sugar, Cement, Iron, Paper, Petrochemical, Pharmaceutical, Auto mobile	Electronics, autos and machinery were traditionally some of the largest manufacturing export categories, but these sectors have all seen exports fall significantly since 2011. Autos, pharmaceuticals, iron and steel are three of the brightest manufacturing export sectors.

Labour Supply	As per 2022 473.2 million people	As per 2022 22.3 million people
Labour wages	(US$65) INR 5340 Per month	UG 13,000 per month
Logistics infrastructure	Rail ways, Water ways, Air ways, more utilization of road Ways & railways	Railways, water ways, Air ways, less utilization of rail ways
Pharmaceutical Industries	There are 3,000 pharmaceutical enterprises in India Mainly Sun pharmaceutical industries Divis laboratory ltd Cipla ltd Dr Reddy's laboratories Etc.	21 registered pharmaceuticals Industries in Uganda in 2019 Of which majority are small scale industries
Transportation of drugs	India pharmaceutical market export the drug to several countries In march 2022 exportUS$2.4Billion worth of drugs and pharmaceuticals	Uganda pharmaceutical market import 90%of medicines from mainly India and China
Tax Incentive	Tax incentives are eligible to be claimed from taxable income. The incentives can be based on income, investment, expenditure	From a tariff barrier perspective, Uganda is relatively competitive in the region as an export and import market, having the third-lowest average applied tariff rate
Total pharmaceutical net worth	In India was valued at an estimated US$42 billion in 2021and is estimated to reach $130 billion by 2023	Valued at $450 million, the pharmaceutical sector makes up approximately 0.16%of Uganda GDP at current market prices, according to the Uganda pharmaceutical manufacturers association (UPMA)
Authority	Central drug standard control organisation (CDSCO)	National drug authority (NDA)
Manufacturing challenges	Lack of technology and infrastructure: One of the biggest challenges facing Indian manufacturing is the lack of technology and infrastructure. Many Indian manufacturers still rely on outdated technology and methods, which makes it difficult for them to compete with their global counterparts	The main challenges facing domestic and foreign manufacturers operating in Uganda include high costs of infrastructure, limited availability of technical and managerial skills and lack of financial sources, especially in terms of longer-term financing

4. CONCLUSION

GMP is designed to ensure that mistakes do not occur. Implementation of GMP is an investment in good quality medicines. This will improve the health of the individual patient and the community, as well as benefiting the pharmaceutical industry and health professionals. Making and distributing poor quality medicines leads to loss of credibility for everyone: both public and private health care and the manufacturer. Good quality must be built in during the manufacturing process; it cannot be tested into the product afterwards. GMP prevents errors that cannot be eliminated through quality control of the finished product. Without GMP it is impossible to be sure that every unit of a medicine is of the same quality as the units of medicine tested in the laboratory. By comparing the good manufacturing practices of India with Uganda we can know about the differences and similarities in both the markets.

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