REPORT OF THE WORKSHOP ON ICH Q7 GOOD MANUFACTURING PRACTICE FOR PHARMACEUTICAL INGREDIENTS WHICH HELD ON 25RD – 26TH JULY, 2024 AT MARRIOTT HOTEL, IKEJA, LAGOS.

The workshop was a significant event that brought together key stakeholders in the pharmaceutical industry and regulators across West African Sub-region. The workshop aimed to address critical aspects of Good Manufacturing Practice (GMP) for pharmaceutical ingredients with the aim of building capacity for manufacturers and regulators.

Day 1 (25th July 2024)

Topic 1: Introduction to GMP for APIs and ICH Q7 for Pharma and Biologic Products

The workshop commenced by welcoming the resource person, Dr. Jared Auclair who provided an overview of Good Manufacturing Practices (GMP) for Active Pharmaceutical Ingredients (APIs), highlighting the importance of quality, safety, and consistency in pharmaceutical manufacturing.

He also touched on some key principles include Quality by Design (QbD) whereby quality is built into a material or product right from the design stage through the development stages to the final step of the manufacturing process to ensure consistent outcomes. The presentation underscored the significant roles personnel, good documentation practices and quality control plays in ensuring a quality pharmaceutical ingredient is consistently achieved.

Topic 2: Introduction to Quality Management

The presentation provided an overview of Quality Management (QM) principles and responsibilities in pharmaceutical manufacturing. It emphasized that quality is everyone's responsibility and mandates an effective system involving management and manufacturing personnel.

Key principles include establishing independent Quality Assurance (QA) and Quality Control (QC) functions, documenting and explaining deviations, and ensuring no materials are used without satisfactory evaluation. Quality units are tasked with various responsibilities, such as reviewing and approving all quality documents, investigating deviations, performing internal audits, and ensuring proper equipment maintenance and calibration. It also include regular quality reviews of APIs, conducted annually, assess process consistency, and implement corrective actions as necessary. The presentation underscored the importance of maintaining rigorous standards to ensure API quality and compliance with regulatory requirements.

Topic 3: Personnel

The presentation on personnel in pharmaceutical manufacturing emphasizes the importance of qualified and trained staff for ensuring quality assurance and proper production of medicinal products. The responsibilities of all personnel must be clearly documented, with regular training conducted by qualified individuals, covering both specific operations and Good Manufacturing Practices (GMP).

An adequate number of qualified personnel is essential for supervising manufacturing processes. Specific training is required for those working in contamination-prone areas. Hygiene standards must be strictly followed, including wearing appropriate protective clothing and maintaining good sanitation habits. Personnel should avoid direct contact with intermediates or APIs, and restrictions should be placed on smoking, eating, and drinking in designated areas. Those with infectious diseases or open lesions should be excluded from activities that could compromise product quality. Consultants should have sufficient qualifications, and records of their credentials and services should be maintained.

Topic 4: Building and Facilities

The presentation on buildings and facilities in pharmaceutical manufacturing outlined critical aspects for ensuring a clean, safe, and efficient production environment. Buildings should be designed to facilitate cleaning, maintenance, and operations, minimizing contamination risks. Adequate space and proper layout prevent mix-ups and ensure a smooth flow of materials and personnel.

Specific areas should be designated for activities such as receiving, sampling, storage, and production to control contamination. Utilities impacting product quality must be monitored and maintained, with ventilation systems in place to control air quality. Water used in production should meet stringent quality standards, and special facilities are required for handling highly sensitizing or toxic materials to prevent cross-contamination.

Lighting must be sufficient for all activities, avoiding shadows and glare, with emergency lighting available. Proper disposal of waste and maintenance of sanitary conditions are essential, with written procedures for cleaning and using sanitizing agents.

Topic 5: Process Equipment

The presentation on "Process Equipment" covers essential guidelines for equipment used in the manufacture of intermediates and APIs. It emphasizes that equipment must be appropriately designed, adequately sized, and suitably located for its intended use, ensuring it does not alter the quality of intermediates and APIs.

The equipment should be used within its qualified operating range and identified clearly. It highlights the necessity of cleaning, sanitizing, and maintaining equipment to prevent contamination. Cleaning procedures should be detailed, reproducible, and include responsibilities, schedules, and methods. The presentation also addresses the importance of equipment calibration, emphasizing that critical instruments must be calibrated with traceable standards, and records maintained.

It includes guidelines for validating GMP-related computerized systems to ensure data integrity and security. Systems must have controls to prevent unauthorized access, data omissions, and ensure proper documentation of any changes. The presentation underscores that incidents affecting data quality should be recorded and investigated.

Topic 6: Documentation and Records

The "Documentation and Records" presentation highlights the importance of maintaining proper documentation and records as specified by cGMP regulations. Key points include the necessity of documentation to track past and present manufacturing activities, aiding in future planning. Regulatory inspectors scrutinize these records during inspections, as effective documentation enhances the visibility and reliability of the quality assurance system.

The presentation detailed different types of documents, such as the quality manual, policies, SOPs, batch records, test methods, specifications, and logbooks. It emphasized the control of document issuance, revision, and retention, ensuring all production, control, and distribution records are kept for specified periods. Records must be legibly and accurately maintained in indelible ink, with proper initialing and dating by individuals making entries. The presentation also covered procedures for handling entry errors, using footnotes, and the importance of third-party reviews to ensure thorough and unbiased documentation management.

Topic 7: Materials Management

The presentation on Materials Management covered various aspects crucial to the handling of materials in the pharmaceutical industry. It started with an overview of different types of materials, including raw materials, packaging materials, intermediate and bulk products, and finished products, among others. The slides emphasized the importance of procedures for the receipt, identification, quarantine, storage, handling, sampling, testing, and approval or rejection of materials.

Key points include ensuring materials are purchased from approved suppliers, verifying the identity of materials upon receipt, and proper storage to prevent contamination and degradation. The presentation also highlighted the necessity for robust systems to evaluate suppliers and the importance of quarantine procedures to prevent unauthorized use of rejected materials. Additionally, it discussed the sampling and testing of incoming production materials, storage requirements, and the re-evaluation of materials to ensure their suitability for use.

Topic 8: Production and In-Process control

The presentation on Production and In-Process Controls outlined key procedures and guidelines for managing raw materials and production processes in intermediate and API manufacturing. It emphasized the importance of accurate weighing, measuring, and proper identification of materials. Critical activities and deviations must be documented and investigated. The presentation highlighted the need for time limits in production, appropriate storage conditions, and re-evaluation of intermediates. In-process controls are essential to monitor and adjust processes to ensure product quality, with specific procedures for sampling

to prevent contamination. Blending processes should be controlled and documented, ensuring homogeneity and stability of batches. Residual materials can be carried over if adequately controlled, and precautions should be taken to avoid contamination during production operations.

Topic 9: Packaging and Identification Labelling of APIs and Intermediates

The presentation on Packaging and Identification Labelling of APIs and Intermediates outlined essential procedures for managing packaging and labelling materials. It emphasized the need for written procedures for the receipt, identification, quarantine, sampling, examination, testing, and release of these materials. Containers must protect against deterioration and contamination and be cleaned appropriately. Access to label storage should be restricted, with procedures for reconciling label quantities and managing discrepancies. Obsolete labels must be destroyed, and printing devices controlled. Labels should include essential information such as product name, batch number, and storage conditions, and should ensure no mix-ups during labelling operations. Facilities should be inspected before use to ensure no unnecessary materials are present, and labelled products should be examined to ensure correct labelling. Containers transported outside the manufacturer's control should be sealed to indicate any tampering.

Topic 10: Storage and Distribution

The presentation outlined essential guidelines and challenges related to storage and distribution in warehouses, particularly for pharmaceuticals. Key points include the necessity for controlled conditions such as temperature, humidity, and light to maintain the efficacy of drugs. Separate storage areas are required for quarantined, rejected, returned, or recalled materials. Warehouse management faces challenges like inventory management, temperature maintenance, and security. Detailed procedures for handling, distribution, and labeling of products, including unique identification codes, are crucial. The use of modern technology and automated systems was emphasized to enhance efficiency and compliance with legal standards. Additionally, stringent security measures are essential to prevent theft and ensure data protection. Good Manufacturing Practices (GMPs) mandate proper storage, labelling, and quality control checks before distribution, highlighting the importance of following regulatory guidelines to ensure product safety and integrity.

Day 2 (26th July 2024)

Day 2 commenced with the review of events from the previous day before proceeding with the business of the day where several topics were covered as outlined below.

Topic 1: Laboratory Control

The presentation on laboratory controls emphasized the importance of quality management and standardized procedures in pharmaceutical laboratories. Key elements include the necessity for adequate laboratory facilities, documented sampling and testing procedures, and scientifically

sound specifications for raw materials, intermediates, APIs, and packaging. Out-of-specification results must be investigated and documented. Reference standards should be maintained, with primary and secondary standards properly prepared, tested, and stored. Each batch of intermediates and APIs should undergo appropriate laboratory tests, including impurity profiling and microbiological tests. Certificates of Analysis must be issued, detailing test results, batch information, and expiry or retest dates. Stability monitoring programs are essential to confirm storage conditions and product longevity. Retention samples should be stored for future evaluation. Overall, adherence to regulatory guidelines ensures product safety and quality.

Topic 2: Validation

The presentation on validation provided a comprehensive overview of validation in pharmaceutical processes, ensuring consistency and quality. It covered validation policy, documentation, and qualification of equipment through Design Qualification (DQ), Installation Qualification (IQ), Operational Qualification (OQ), and Performance Qualification (PQ). Three approaches to process validation were highlighted: prospective, concurrent, and retrospective, each applicable under specific conditions. The presentation emphasized the importance of periodic review of validated systems and the necessity for cleaning validation to avoid contamination. Validation of analytical methods was also discussed, detailing the need for methods to detect residues and contaminants effectively. The presentation underlined the importance of maintaining accurate records, adhering to regulatory guidelines, and continuously monitoring validated processes to ensure they meet quality standards.

Topic 3: Change Control

The presentation on change control in the pharmaceutical industry detailed a systematic approach to managing modifications affecting production and control of intermediates or APIs. It outlines a formal change control system that includes identifying, documenting, reviewing, and approving changes in raw materials, specifications, methods, and equipment. The process involves evaluating the impact on product quality, safety, and efficacy, and ensuring changes are communicated and documented across departments. Types of changes include minor (low impact), major (moderate to high impact), and critical (profound impact). Key steps in the process include identifying and justifying changes, conducting preliminary and detailed evaluations, and deciding approval or rejection by a change control board. Implementation involves updating documents and executing changes per SOPs, followed by verification through testing, inspections, and audits. Finally, the process concludes with formal closure, post-implementation review, feedback collection, and continuous improvement to ensure long-term effectiveness and compliance.

Topic 4: CDMO

The section on "Rejection and Re-use of Materials, Complaints and Recalls, Contract Manufacturers" covers handling non-conforming materials, quality complaints, and contracting manufacturing standards. Rejection involves quarantining and potentially

reprocessing or reworking intermediates and APIs, with detailed documentation. Reworking includes investigation, testing, and validation to ensure quality. Material and solvent recovery is permitted if procedures ensure their suitability. Returned intermediates or APIs are quarantined and evaluated for quality before reuse or disposal, with comprehensive records kept.

Quality complaints are recorded and investigated per written procedures, with detailed documentation and trend analysis to identify corrective actions. Recall procedures define evaluation, initiation, and handling processes, involving regulatory authorities if necessary.

Contract manufacturers must comply with GMP, prevent cross-contamination, and maintain traceability. Written contracts detail GMP responsibilities and allow audits. Sub-contracting requires prior approval, and records must be maintained at the activity site for accessibility.

Topic 5: Agents, Brokers and Traders

This session outlined guidelines for agents, brokers, traders, distributors, re-packers, and re-labellers handling APIs and intermediates. These parties must comply with GMP, ensuring complete traceability of products by maintaining comprehensive documentation, including the identity and address of the original manufacturer, purchase orders, transportation records, and certificates of analysis. Quality Management System must be established and documented, with re-packaging and re-labelling conducted under appropriate GMP controls to prevent contamination and maintain product integrity. Stability studies are required if re-packaging involves different containers than those used by the manufacturer. All quality and regulatory information must be communicated between the original manufacturer and customers. Complaints and recalls must be recorded and investigated, with necessary actions taken in collaboration with the original manufacturer. Handling of returns should follow specified procedures, and all related documentation must be maintained for traceability and compliance.

Topic 6: Specific Guidance for APIs Manufactured by Cell Culture/Fermentation

This session provided guidance for APIs manufactured by cell culture or fermentation. It emphasized GMP compliance, highlighting the different levels of control needed for biotechnological processes versus classical fermentation. Key points include maintaining traceability of cell banks, ensuring environmental and equipment controls to prevent contamination, and monitoring critical parameters such as cell growth and viability. The guidelines stress the importance of aseptic techniques, proper sterilization of culture media, and appropriate handling of contamination events. Harvesting and purification processes should be designed to maintain product quality, with specific measures to prevent viral contamination as per ICH Q5A guidelines. The use of dedicated equipment and additional controls for multiproduct facilities is recommended to minimize cross-contamination risks. Detailed records of contamination and cell bank usage should be maintained to ensure consistent quality.

Topic 7: APIs use in Clinical Trial

The presentation on APIs for clinical trials outlined the adaptation of Good Manufacturing Practices (GMP) to the unique requirements of investigational APIs. It emphasized flexibility in processes and test procedures to accommodate changes during development stages. Quality Control is maintained through independent quality units overseeing batch approvals, raw material testing, and labelling for investigational use. Facilities and equipment must be clean, calibrated, and appropriate for use, with procedures in place to minimize contamination. Documentation is crucial, capturing production details and scientific observations. Process validation is generally inappropriate for clinical trial APIs due to frequent changes. Analytical methods should be sound but not necessarily validated. A system for retaining reserve samples and documentation is essential to support ongoing development and regulatory compliance. Changes in production or testing procedures must be well-documented, ensuring traceability and quality throughout the clinical trial phases.

Conclusion:

The workshop on ICH Q7 Good Manufacturing Practice on Active Pharmaceutical Ingredients (API) was a significant step toward enhancing the capacity of Regulators and Manufacturers in the pharmaceutical industry in Nigeria and West African sub-region.

It provided valuable insights into best practices in both regulatory frameworks, GMP practices and quality assurance.

This workshop couldn't have come at a better time than now when a good number of manufacturers of FPP have advanced in their quest to establish manufacturing outfits for APIs in Nigeria. This commitment of the Nigerian Government, regulatory bodies, and industry experts to promote local API production will certainly contribute to better healthcare outcomes that will benefit the teaming population of Nigeria and Africa in general.

The emphasis on collaboration, adherence to best practices, and continuous learning highlighted during the workshop are vital for ensuring that safe, quality, and efficacious medicines are available to the public.

As Nigeria and the broader African continent work towards achieving medicine security through local API manufacturing, the insights and expertise gained from this workshop will be instrumental in reaching this important objective.

The workshop not only served as a platform for knowledge exchange but also as a catalyst for ongoing improvement and innovation in the pharmaceutical sector.