WHO PUBLIC INSPECTION REPORT Finished Product Manufacturer

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(WHOPIR)

Finished Product Manufacturer

Part 1: General information

Name of Manufacturer	Evans Medical Plc
Unit number	NA
Production Block	NA
Physical address	Evans Medical Plc, Km 32, Lagos Badagry Expressway, Agbara Industrial Estate, Agbara, Ogun State. Telephone No: 234-1-7740595, 7749178, 7901409, 7912723, 7912733 Email: evansmedicalplc@yahoo.com
Contact person and email address.	Mr Mike Ajufo, e-mail: maajufo@gmail.com
Date of inspection	05 -07 October 2013 – Initial audit (WHO + NAFDAC) 05 – 07 May 2014– follow-up (WHO + NAFDAC 10 – 11 September 2014 – CAPA verification (NAFDAC)
Type of inspection	WHO PQP Pre-submission Audit
Dosage forms(s) included in the inspection	Oral Solid Dosage forms (Tablets)
WHO product numbers covered by the inspection	No submission yet but there are products under development with WHO-PQT Technical Assistance.
Summary of the activities performed by the manufacturer	• Manufacturing, Packaging, Quality Control and Batch release of Finished Pharmaceutical Products (FPPs) in oral solid (tablets) and liquid dosage forms. • Toll manufacturing of FPPs in oral solid dosage forms (tablets) • Importation and distribution of FPPs

Part 2: Summary

General information about the company and site

Evans medicals Plc commenced manufacturing and distribution of Pharmaceuticals and Nutraceuticals since 1954 under the corporate name Allen and Hansburys Nigeria Limited. The company changed to Evans Medicals Plc when it was sold off by Glaxo Nigeria Limited in 1994. The facility of Evans Medicals Plc which is situated in Agbara Industrial Estate at km 42, Lagos - Badagry expressway, Ogun State, South West Nigeria has 3 manufacturing plants within 8.3 hectares land area. These 3 plants are:

- Facility 1 - Pharma Plant I: Pharmaceuticals (Floor Area 4233m^2)
- Facility 2 - Nutraceuticals Plant (Floor Area 4505m^2)
- Facility 3 - Pharma Plant II: Beta lactam (Floor Area 670m^2)

The Beta lactam plant is located 400m away from the Pharma plant I and has a separate air handling system with dedicated personnel, facilities and warehousing.

The company has been involved in production of tablets, capsules, liquids, powder since 1982, creams and ointment since 1988 and toll manufacture since 1989 and have a total of 58 stock keeping units in 11 therapeutic areas.

The Company is working towards WHO pre-qualification for selected products manufactured in Pharma Plant I.

History of WHO and/or regulatory agency inspections

Evans Medicals Plc has been inspected by the National Agency for Food and Drug administration and Control (NAFDCAC) and Pharmacist Council of Nigeria for regulatory certifications. The company has to date locally registered a total of 58 pharmaceutical products. Between 2011 and 2012, a series of audits have been carried out in the company. These include Advisory Visits by WHO, WHO/NAFDAC gap analysis visits and periodic verification audits by NAFDAC. A WHO Pre-Inspection audit was also carried out between 5th - 7th October 2013 by the WHO PQT and NAFDAC as observers. This inspection was a follow up to that pre-inspection.

Focus of the inspection

The inspection focused on the production and control of tablet formulated products. The inspection covered the sections of the WHO GMP text, including premises, equipment, documentation, materials, validation, sanitation and hygiene, production, quality control and utilities.

Inspected Areas

Day 1 (Morning Session)

a) Opening Meeting

- Official introductions from both the auditees and auditors
- Company Presentation which included company overview, site description, production and QC capacities, quality management and assurance systems, summary of manufacturing processes, major equipment and product range, inspection history, major changes since the last inspection.
- Production plan for the 3 days audit and confirmation of same

b) Quality Management System Review

- Personnel Policies: Organization charts, Job descriptions and Training.
- SOP Preparation, review, approval and control
- Batch Numbering System
- Product Quality Review SOP and reports for 2013
- Deviations and Change control SOPs + Registers for 2013/4
- OOS SOPs + Registers for 2013/4
- Complaints handling systems SOPs + Register for 2013/4
- Product Master files, codes, specifications for APIs and FPPs plus list of approved vendors.

Day 1 (Afternoon Session)

a) Inspection of Receiving and Storage Areas + Procedures

- Receiving, quarantine, sampling and storage of starting materials, packaging materials and components
- Temperature + RH mapping and monitoring
- Vendor approval, qualification and maintenance system

Day 2 (Morning Session)

a) Review of list of observations made on day 1 + Feedback from Company

b) Inspection of Production Activities

- Site layout
- Dispensing

Day 2 (Afternoon Session)

- Production (Tableting Area), Packaging and in-process controls

Day 3 (Morning Session)

a) Brief Review of Validation Master Plan

b) Inspection of Quality Control Laboratory

- Documentation
- Sample receipt, storage and allocation
- Testing of packaging materials and components
- Wet chemistry laboratory
- Instrumental laboratory (Qualification, calibration and preventive maintenance of IR, UV Spectrophotometers and HPLC)
- Laboratory materials management (Samples, Reagents, Stock Solutions, Reference and Working Standards)
- Finished products specifications, testing and release.

Day 3 (Afternoon Session)

a) Review of HVAC System

- HVAC system schematic drawing and summary of specifications for HVAC
- Qualification, Monitoring of HVAC system
- Inspection of the HVAC + Dust extraction technical area

b) Review of Purified Water generation and distribution system

- Inspection of Water Generation and Purification System installations
- Sampling and Trend Analysis

c) Preparation of closing meeting (WHO PQT + NAFDAC observers only)
d) Summary of observations for the day and closing meeting with company representatives.

2.1 PHARMACEUTICAL QUALITY SYSTEM

The company has a pharmaceutical assurance system in place with adequate commitment of the top management and dedication of staff in all departments and at all levels within the company. The Company's quality objectives were clearly defined with a comprehensively designed system of quality assurance which incorporates GMP and quality control. Nonetheless gaps still existed particularly in the aspects of ensuring consistency of documents, clear allocation of reporting relationships and proper design of some documents to ensure clarity and avoid ambiguities. Appropriate corrective measures were subsequently put in place and their implementation was verified to have been effected.

2.2 GOOD MANUFACTURING PRACTICES (GMPs) FOR PHARMACEUTICAL PRODUCTS

Manufacturing processes were defined and those reviewed were found to be appropriate. The necessary resources required for compliance of GMP standards including qualified and trained personnel, adequate premises and space, suitable equipment and services, approved procedures and instructions as well as adequately equipped laboratories and equipment for in-process controls were generally in place. Generally the company's personnel demonstrated a good knowledge of GMP with a demonstrable potential for improvement.

2.3 SANITATION AND HYGIENE

Sanitation and hygiene was commensurate with the level of activity that goes on in the company. The scope of company's sanitation as documented covers the entire relevant components expected in a GMP environment. There were concerns with sanitization of drains in core processing areas and at the water treatment plant which needed a clearly defined and documented procedure to eliminate this potential source

of contamination. Corrective measures were subsequently put in place and their implementation was verified.

2.4 QUALIFICATION AND VALIDATION

A brief review of the Validation Master Plan (VMP) showed that the company had a robust validation matrix and approved schedule in place. Key elements of qualification and validation program were clearly defined and documented in the VMP. Future audits may need to review adherence to the sighted VMP matrix and schedule.

2.5 COMPLAINTS

Company's complaint procedure required intensive review. As at the time of inspection the complaints procedure was lumped together in the procedure for handling of deviations which created room for ambiguities and there was no appropriate system in place to differentiate Complaints from Incidents and deviations, OOS and OOT. The complaint log or register was not referencing the in the appropriate SOP. Appropriate corrective measures were subsequently put in place and their implementation was verified to have been effected.

2.6 PRODUCT RECALLS

The company SOP on handling of recalled goods was adequate but company had no register for recall as at the time of the audit. Subsequently, this was verified to have been put in place.

2.7 CONTRACT PRODUCTION AND ANALYSIS

The company has been involved in toll manufacturing for over two decades. Information available at the time of inspection showed that no documentary evidence was in place to audit the contract giver who supplies starting material for the range of products that were contract manufactured by the contract accepter (Evans Medicals Plc). Most of these materials were accepted without further analysis. The essence is to prevent the introduction of non-conforming materials into the accepter's GMP environment.

2.8 SELF INSPECTION AND QUALITY AUDIT

This was adequately covered during the previous inspection; it was not covered during the inspection.

2.9 PERSONNEL

The company had adequate number of qualified and trained personnel who demonstrated commitment and the requisite experience required. There were job descriptions and reporting relationships. However, the documentation of organogram and job descriptions was not done with care to ensure consistency, clear allocation of responsibilities and reporting relationships. There was no policy on deputisation of key personnel when they are absent or not available. In addition, some members of staff were noted to have two job descriptions and there was no documented evidence on how to counter concentration of too many roles in one person. These issues were subsequently addressed and the appropriate implementation of CAPAs verified.

2.10 TRAINING

The manufacturer has a written training program for all personnel. A comprehensive training matrix and training plan had been put in place however samples selected (training in statistical interpretation of analytical report and change control management) indicated that the plan was not strictly followed.

2.11 PERSONAL HYGIENE

Personnel health records were not examined during audit. The company claimed that health examination reports of all personnel were in custody.

There was a system and facilities for staff to change from street clothing to factory gowning appropriate to the level of operations. There were facilities and procedures for staff to wash hands before entering production areas.

It was strictly prohibited to bring food and drinks to production, quality control and warehousing areas and there were separate facilities designated for the same.

2.12 PREMISES

The layout and design of Evans Medicals Plc conforms to minimum GMP requirements. The premise is situated in an environment that protects the manufacturing environment and present minimum risk of causing any contamination or cross-contamination or materials and product. The level of maintenance and sanitisation were adequate.

2.13 EQUIPMENT

Most of the pieces of equipment sighted during inspection were of the appropriate design and installed to minimize potential risk of contamination and all service piping was adequately marked. A major concern during the audit was the unduly high man-material contact at the primary packaging process of one of the tablet products. This same observation was made in the previous inspection of 5th - 7th October 2013. To address this concern, the company had acquired a new blistering machine with the appropriate design to address this observation. The URS and DQ protocol were sighted while IQ was ongoing at the time of inspection.

The company had a qualification program in place and qualification was ongoing for newly acquired equipment at the time of inspection.

There were procedures and program for equipment cleaning and maintenance and logs were in place to records compliance with these procedures and programs.

2.14 MATERIALS

The company had formal procedure for receiving, quarantine, sampling and storage of starting materials, packaging materials and components. However, there were still gaps that could not assure consistent use of materials as approved and of adequate quality. For example, vendor evaluation focussed more on suppliers and financial issues and less on manufacturers and technical issues. Material codes used did not focus on manufacturers and were not consistent with the suppliers in the approved vendor list. The manufacturer has subsequently proposed appropriate CAPAs to

address these concerns and their implementation was verified to have been initiated. This will have to be closely monitored in subsequent inspections.

2.15 DOCUMENTATION

Documents were designed, prepared, reviewed and distributed as expected but a number documents reviewed were not reviewed with care to ensure clarity and avoid ambiguities. In certain instances, the title and scope did not match the content of SOP and procedures in several others were not designed to facilitate a logical sequence of steps in implementation (e.g. SOP on handling of incidents and deviations). These documents have been revised to address the observations.

2.16 GOOD PRACTICES IN PRODUCTION

Audit of the production system of the company showed good practices. Handling of materials was done with written procedures. All materials, bulk containers and major items of equipment carried appropriate status labels. In addition access to core processing areas was restricted to unauthorized personnel. The beta lactam plant (Pharma plant II) was located at a distance of 400m away from the Pharma plant I having dedicated personnel and AHUs. Line clearance procedures were also followed and processing operation as sighted during inspection was designed to prevent possibility of mix ups.

The observed concerns were associated with inadequate adherence of production personnel to approved procedures and where adherence was not observed, deviations were not always raised to address such observations. Robust CAPAs was proposed and its implementation was verified to have been initiated. This is another area to monitor for continuous improvement.

2.17 GOOD PRACTICES IN QUALITY CONTROL

The organisation structure and records reviewed plus the practices witnessed gave confidence that Quality Control (QC) functions are totally independent of production and other departments. QC laboratory was adequately equipped to the level of manufacturing operations. QC personnel exhibited a high level of understanding of procedures for sampling, inspecting, testing and release of starting materials,

packaging materials and intermediate, bulk, finished products. Measures to ensure data integrity, security, traceability and attribution needed to be strengthened. The company has proposed adequate CAPAs and subsequent on-site verification has confirmed that implementation has been initiated. This is another area for monitoring for continuous improvement.

Part 3: Conclusion

Based on the areas inspected, the people met and the documents reviewed, and considering the findings of the inspection, including the observations listed in the Inspection Report, as well as the corrective actions taken and planned, **Evans Medical Plc, Km 32, Lagos Badagry Expressway, Agbara Industrial Estate, Agbara, Ogun State** was considered to be operating at an acceptable level of compliance with WHO GMP guidelines.

All the non-compliances observed during the inspection that were listed in the full report as well as those reflected in the WHOPIR, were addressed by the manufacturer, to a satisfactory level, prior to the publication of the WHOPIR

This WHOPIR will remain valid for 3 years, provided that the outcome of any inspection conducted during this period is positive.