TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

TMDA
Tanzania Medicines & Medical Devices Authority

SHANGHAI DAHUA PHARMACEUTICAL CO. LTD, SHANGHAI, CHINA
PUBLIC GMP INSPECTION REPORT

11th December, 2020

Part 1: General information about the company

Manufacturers details	
Name of manufacturer	Shanghai Dahua Pharmaceutical Co., Ltd.
Corporate address of manufacturer	N/A
Inspected site	
Name & address of inspected manufacturing site	Chongming 400 709, 3503 Changzheng Road, Changzheng Farm, Chongming County, Shanghai, China
Unit/ block/ workshop number (be specific)	N/A
Inspection details	
Date of inspection	15-16th June 2018
Type of inspection	Renewal GMP inspection
Introduction	
General information about the company and site	Shanghai Dahua Pharmaceuticals Co. Ltd is a Pharmaceutical company located at Shanghai Chongming Changzheng Economic park. It started its operation in December, 2003 for manufacturing and packing of implant (Levonorgestrel Silastic implant (II), 75mg popularly known as Sino- implant (II)). The facility has been licensed by Shanghai Food and Drug Administration with license No. HU20160096.
History	The site has been inspected by several medicine regulatory authorities and was issued GMP Certificates including NAFDAC - Nigeria, NDA-Uganda, ANVISA-Brazil, INVIMA-Colombia, PPB (Kenya), FDA- Ghana, NDA-Uganda and FMHACA- Ethiopia. This was renewal GMP inspection conducted on 15th – 16th June 2018 to verify if the facility still

	operated under GMP requirements.
Brief report of the activities undertaken	
Areas inspected	This inspection focused on the production and control of the hormonal drug and covered all the sections including external environment, utilities, raw materials and packaging materials warehouse, sampling and dispensing areas, production areas, finished products warehouse, quality control and document review.
Restrictions	None
Out of scope	none
Production lines inspected by TMDA	Manufacturing and packaging of implant
Abbreviations	**Meaning**
ANVISA	Agencia National de Vigilancia Sanitaria
BMR	Batch Manufacturing Records
EAC	East African Community
FDA	Food and Drug Authority
FMHACA	Food, Medicine and Health Care Administration and Control Authority
GMP	Good Manufacturing Practices
HVAC	Heating, Ventilation and Air Conditioning
INVIMA	Instituto Nacional de Vigilancia Medicamentos y Alimentos
NAFDAC	National Agency of Food and Drug Administration and Control
NDA	National Drug Authority
PW	Purified water
RLAF	Reverse Laminar air flow
RO	Reverse Osmosis
SOP	Standard Operating Procedure
TMDA	Tanzania Medicines and Medical Devices Authority
TPIR	TMDA Public Inspection Report
UV	Ultraviolet
VMP	Validation Master Plan
WFI	Water for Injection

WHO	World Health Organization (not in text)

Part 2: Brief summary of the findings and comments

1. Personnel

The company had adequate number of qualified and experienced staff to perform various activities in the facility. Review of Company Organization Chart and job descriptions evidenced that the head of Production and quality control responsibilities were independent from each other. Personnel at the factory were subjected to medical examination prior to and during employment once in a year where among other test performed included hormonal levels test. Induction and on job GMP training were provided to employees as per the SOP, records were verified and were acceptable.

2. Premises

Shanghai Dahua Pharmaceuticals Co., Ltd consisted of a general block for raw materials, production, packing and finished goods, quality control laboratory and utilities.

i. Layout and Design

The facility was designed to ensure logical flow of materials and personnel. The building was made of steel and cement concrete materials with brick walls. Floor in material production were made up of epoxy resin with covings at all edges and angles between floor, ceiling, walls and windows to facilitate easy cleaning and prevent accumulation of dust or dirty. Electrical fittings were embedded to avoid creation of recesses that are difficult to clean.

Warehouses for storage of materials were spacious, well equipped and properly maintained to allow orderly storage of various categories of materials including materials under quarantine, released, and rejected. Dedicated ventilation system, reliable electrical supply and sufficient lighting were appropriate for manufacturing activities and functioning of equipment.

In general, the premises were properly designed, constructed and maintained to comply with GMP requirements.

ii. Sanitation and Hygiene

The facility was situated in an environment which was clean, properly maintained and free from contaminants. Personal hygiene was observed to all employees working in different departments and manufacturing processes. Separate gents and ladies change rooms were available and were provided with change instructions hand washing facilities and sanitizers.

Personnel were found wearing clean uniforms as required in clean zones. Direct contact of operator's hand with materials and products was avoided. Review of cleaning SOP, cleaning protocol, and record confirmed that cleaning of premises and equipment was performed as per requirements. Insect catcher and barrier were available to prevent the rodents from entering the facility.

3. Production

Only one product i.e. levonorgestrol implant was manufactured by the facility. There was a unidirectional flow of production from where raw materials were received and stored through manufacturing operations up to finished goods store. Production areas were spacious to allow logical movement of personnel and materials thus preventing cross contamination. The warehouse was designed and equipped to permit orderly storage of various categories of materials, putting into consideration materials under quarantine, released and rejected.

A common sampling booth for active and non- active materials was available and was provided with RLAF. Operation areas, bulk containers, major equipment and packaging lines were adequately labelled for identification and indication of stage of production. Review of manufacturing Batch Manufacturing Record (BMR) at different stages indicated that production operation followed written procedures. Check on yields and reconciliation of quantities were carried out to ensure that there were no discrepancies outside acceptable limits. It was observed that in-process controls and active environmental monitoring (air sampling) were performed within the production area as per respective SOP, records were verified and were acceptable.

4. Quality Control Laboratory

The facility had Quality Control laboratory manned by personnel with appropriate qualifications and experience; and equipped with instruments and procedures for sampling and testing of materials and products. The laboratory was subdivided into instrumentation, chemistry and microbiology sections.

Each section was spacious enough to minimize mix-up errors and cross contamination. Instruments were properly kept in a separate room to protect them against electrical interference, vibration, contact with external moisture and other external factors. The same were suitably qualified and calibrated and was confirmed from the records reviewed.

Reference and working standards were also found to be stored and maintained according to storage instructions. Qualification and validation was performed, records were maintained, deviation and out of specification were properly recorded and investigated. Zone 1V B climatic condition stability chambers were qualified and

operating at specified temperatures and relative humidity. Records for stability studies were verified and found to be satisfactory.

5. Equipment

The facility had sufficient number of equipment which were located, designed, constructed adapted and maintained to suit the operations carried out. The layout and equipment design minimized the risk of errors and permitted effective cleaning and maintenance in order to avoid cross contamination. All balances were calibrated and were provided with calibration status labels. Cleaning, maintenance, qualification and calibration records were reviewed and confirmed to be adequate.

6. Water Treatment System

The facility had Water treatment systems for generation of purified water (PW) and water for injection (WFI). PW generation system comprised of sand filter, activated carbon, softeners, ion exchange, RO, and UV. PW storage tanks and distribution pipelines were of SS-316L grade and were sanitized as per the procedure. WFI generation consisted of PW as source water and multi distillation columns.

To ensure consistent production of water of the required quality routine sampling and testing for chemical and microbiological attributes were performed.
Generally, water treatment system was properly functioning, suitably designed, maintained and monitored.

7. Heating, Ventilation and Air Conditioning

The facility had two separate ventilation systems which supplied production and non-production areas. The unit supplying the production areas was provided with three efficient level filters to filter the air before entering production areas. Pressure differentials were maintained to avoid cross contamination. Review of preventive maintenance and performance qualification records of the HVAC confirmed the suitability and functionality of the system.

8. Document Review

Generally, the documentation system was functioning satisfactorily and documents were prepared, checked and approved by authorized personnel. Some of the reviewed document included site master file, quality manual, organization chart , job descriptions and appointment letters, Standard Operating Procedures; Batch Manufacturing and Packaging Instructions and records; Validation Master Plans (VMP), Process Validation protocol and report, Analytical method validation protocol & report, Qualification reports for critical equipment (production and quality control); preventive maintenance schedule & records and environmental control test reports.

All documents scrutinized were well written, detailed, updated as per master SOP and were traceable hence provide evidence of conformity to GMP requirements.

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 of the inspection report, **Shanghai Dahua Pharmaceutical Co., Ltd situated at Changzheng Farm, Chongming County, Shanghai, China**, was considered to be operating at **an acceptable** level of compliance with EAC Compendium of Good manufacturing for the manufacturing of hormonal implant.

This TPIR will remain valid for 3 years from the date of approval for GMP compliance, provided that the outcome of any inspection conducted during the period is positive.

Part 4: References

1. EAC- *Good Manufacturing Practice Compendium, (2014), Technical Documents for Harmonization of Medicines Regulation in the East African Community*
2. TMDA *Good manufacturing practices inspection manual and SOPs*, Tanzania Medicines and Medical Devices Authority, Dar-es-Salaam, Tanzania.
3. Tanzania Medicines and Medical Devices Authority Act, Cap 219.
4. Site Master File - Shanghai Dahua Pharmaceutical Co., Ltd.