

WHO PUBLIC INSPECTION REPORT Finished Product Manufacturer
**WHO PUBLIC INSPECTION REPORT
(WHOPIR)**
Finished Product Manufacturer
Part 1: General information

Name of Manufacturer	Famy Care Ltd.
Unit number	Plot No. 20/21
Production Block	Hormone Tablets
Physical address	PHARMEZ, Pharmaceuticals Special Economic Zone, Sarkhej-Bavla, NH No. 8A, Near Village Matoda, Tal. Sanand, Dist. Ahmedabad, Gujarat – 382213, INDIA
Contact address	Mr Sushil Baukhandi, Vice President - Quality sbaukhandi@famycare.com
Date of inspection	3 to 6 September 2012
Type of inspection	Initial inspection
Dosage forms(s) included in the inspection	Tablets
WHO product categories covered by the inspection	Levonorgestrel 0.75mg and 1.5mg tablets
Summary of the activities performed by the manufacturer	Manufacturing, packaging, quality control and batch release of finished pharmaceutical products

Part 2: Summary

General information about the company and site

The manufacturing facility of **Famy Care Limited**, located at Plot No. 20/21, in PHARMEZ, **Pharmaceuticals Special Economic Zone**, Sarkhej-Bavla, NH No. 8A, Near Village Matoda, Tal. Sanand, District **Ahmedabad**, Gujarat – 382213, INDIA was inspected by WHO under its Prequalification of Medicines Programme on 3– 6 September 2012. According to the company’s Site Master File (SMF-A1-12-09, dated 28/5/2012) and the presentation by the site management at the start of the inspection, Famy Care Ltd. was incorporated in India in 1990 and currently has two manufacturing sites (Sarigam, District Valsad and Ahmedabad) in India.

Famy Care Ltd Ahmedabad was commissioned in December 2008 and is engaged in the manufacturing of medicinal products in oral solid dosage form (hormone and non-hormone tablets) and injectable formulations (sterile suspensions). The manufacturing site is about 42km away from Ahmedabad airport. The site being located within the Pharmaceuticals Special Economic Zone is surrounded by other manufacturing sites engaged in the manufacturing of Finished Pharmaceutical Products.

The first exhibit batch was produced in June 2009. At the time of inspection, the manufacturing site employed 140 staff.

History of WHO and/or regulatory agency inspections

This was the first inspection of the site by the WHO Prequalification of Medicines Programme. According to the company’s presentation, the site had been inspected by the following foreign regulatory authorities and they are:

- Ethiopia GMP Certificate: Feb 2011
- EU GMP Certificate: April 2011 (by The Netherlands Authority)
- Health Canada GMP certificate: June 2011 (based on paper evaluation through HC’s MRA with EU)
- Kenya GMP certificate: August 2011
- MCA Zimbabwe: Feb 2012

Focus of the inspection

The inspection focused on the production and control of Levonorgestrel 0.75mg and 1.5mg tablets. The inspection covered all the sections of the WHO GMP text, including premises, equipment, documentation, materials, validation, sanitation and hygiene, production, quality control and utilities.

Inspected Areas

- Quality assurance
- Good manufacturing practices for pharmaceutical products
- Sanitation and hygiene
- Qualification and validation
- Complaints
- Product recalls
- Contract production and analysis
- Self-inspection, quality audits and supplier's audits and approval
- Personnel
- Training
- Personal hygiene
- Premises
- Equipment
- Materials
- Documentation
- Good practices in production
- Good practices in quality control

2.1 QUALITY ASSURANCE

There were arrangements in place for evaluations and monitoring the implementation and compliance with GMP of the quality of the systems, procedures and products through self-inspection procedures and product quality reviews (PQR). There were procedures for equipment and systems qualification and validation of procedures and processes. There were written and approved procedures to investigate, assess the impact of and control changes, deviations and out-of-specification (OOS) incidents. Also, there was a system for quality risk management (QRM).

2.2 GOOD MANUFACTURING PRACTICES (GMPs) FOR PHARMACEUTICAL PRODUCTS

Famy Care Ltd, Ahmedabad had premises and equipment generally designed, constructed and maintained in acceptable condition and with adequate systems of controls in place to support the manufacture and control the quality of products under focus in compliance with good manufacturing practices.

It is to be noted that, there were not much manufacturing activity (only blending, primary and secondary packaging activities to produce the exhibit batches were seen) being carried out at the time of inspection.

2.3 SANITATION AND HYGIENE

Cleaning procedures for equipment and premises were in place to enhance hygiene on the site and to prevent cross-contamination in production.

In general, there were adequate controls on the entry of personnel to the respective modules/sections of the production areas. Personnel entering the production area were required to gown up with the appropriate attire for the area at the respective changing room following the procedures established for each of the area.

Manufacturing areas, corridors and change room were generally adequately spaced, well lighted, clean, orderly, well ventilated and laid out in a logical order corresponding to the sequence of the production process.

2.4 QUALIFICATION AND VALIDATION

There was a Validation Master Plan/VMP. It outlined the policy and approaches to be followed in qualification of equipment and validation of systems and processes. In addition, there was a separate protocol available on the cleaning validation.

2.5 COMPLAINTS

An SOP on the handling of complaints was in place which described how complaints related to design, appearance, identity, durability, safety, efficacy, quality, purity or performance of a product and/or its components shall be handled. The responsibility for handling of complaints and deciding the measures to be taken rest with the Regulatory Affairs and QA Department. The procedure provided a systematic approach from the start to end including documenting, classification of complaints (into critical, major & minor), investigating, and addressing the complaint in a timely manner including recall of a batch should it fails the agreed specifications or suspected to be defective. In general, the procedure was found acceptable.

2.6 PRODUCT RECALLS

The written procedure for batch recall and product withdrawal was reviewed. The Head QA and Recall Committee were responsible for the execution and coordination of recalls. Till the date of inspection there was no product recall carried out.

2.7 CONTRACT PRODUCTION AND ANALYSIS

It had been noted that no production operations were contracted out. Most of the quality control testing were carried in-house, with the exception of some analytical testing (e.g. where the company do not have the analytical instrument) were contracted out to external contract laboratories. The contract agreement drawn up with the external contract testing laboratory, Sitec Labs Private Limited, Mumbai was reviewed and generally contains the elements of GMP technical agreement.

2.8 SELF INSPECTION AND QUALITY AUDIT

A procedure for carrying out the self-inspection was reviewed.

2.9 PERSONNEL

Personnel met during inspection were generally found to be experienced, knowledgeable, trained and conscientious in their area of work.

At the time of the inspection the company employed a total of 140 staff, which included 27 in production, 30 in QA, 45 in QC, 6 in warehouse, 15 in engineering, 7 in HR, 2 each in purchasing & IT, 5 in accounts and 1 in commercial department.

2.10 TRAINING

Training procedure was reviewed and was found adequate in general.

2.11 PERSONAL HYGIENE

Personnel were trained in personal hygiene procedure and facilities were provided in form of change rooms, clean protective garments and disinfectants. In general, this area was found adequate.

2.12 PREMISES

The total plot area is about 24,315m² and the build-up area is about 7,288m². Manufacturing areas (Tablets and Injectables) were located on the ground floor of the building. All storage, production and testing areas were accessed through the primary changing rooms for each area. The gowning procedures for visitor and staff were pictorially displayed on the wall of each changing room. The toilet and washing facilities were located such that staff and visitors could use them before changing into factory clothing.

There were three modules or production lines housed within the facility, one for Tablet Manufacturing General (placebo and iron tablets), the second for Tablet Manufacturing Hormone (Oral Contraceptive Pills/OCP) and the third for Injection Manufacturing Hormone. The production module is generally designed and laid out in a logical order thereby allowing unidirectional sequence flow of activities (materials and personnel), from granulation, compression, coating, sorting, primary packaging to secondary packaging.

Each process area was fitted and ventilated with dedicated AHUs so as to provide complete segregation and avoid cross contamination of the different processes. Critical areas where there were product exposures to the environment were fitted with terminal HEPA filters at the air inlet and where there is hormone exposure, HEPA filters were provided at the inlet of the return air duct.

The water supply for the site is supplied by Zydus-SEZ which is of portable grade.

2.13 EQUIPMENT

Equipment used in the manufacturing, processing, packing or holding of a bulk product were appropriately designed, of adequate capacity, and suitably located to facilitate operations for their intended use including cleaning and maintenance. The manufacturing plant was adequately equipped for the production and testing of the products manufactured at the site. For tablet manufacturing of hormonal products, which was the focus of this inspection, these included RMG, Fluid Bed Processor, Rotary vacuum dryer & blender, Starch Paste Kettle, Vibro Sifter, Multi mill, IBC, IR dryers, Double cone blenders, Tablet Compression machines, digital metal detector, auto coater, tablets de-dusting unit, blister packing machine, inkjet printer, pouch sealing machine, carton packing machine etc. The product contact parts for all equipment were made up of SS316.

The QC laboratory were adequately equipped with the necessary lab ware and glassware for wet chemistry and other analytical instruments like HPLCs, GC with Head Space, FTIR and UV/VIS spectrophotometer, Particle counter and Auto-Titrators. In addition, the microbiology lab was equipped with LAF workstation, autoclaves, dry heat ovens, incubators and air sampler.

The laboratory equipment reviewed was well designed for the QC operation and they were regularly maintained, calibrated and qualified for their intended use. Balances were periodically calibrated and were verified daily using certified standard weights before use. Records of such verification were reviewed and found to be in order. There were procedures and records for equipment usage, cleaning and maintenance.

2.14 MATERIALS

There was a system for qualification of vendors for supply of Raw Materials (APIs and excipients) and Packaging Materials for production use. The system included site audits as well as assessment through questionnaire. An updated list of approved vendors was available.

There was a material checklist used for recording the findings/discrepancy (if any) following the physical inspection of the consignment before offloading into the warehouse. All starting and packaging materials were tested and subject to evaluation before they could be accepted and approved by QA for production use.

There was adequate storage space and generally materials were stored in an orderly manner, appropriately labelled and identified including the QC status labelling. Separate stores, sampling and dispensing areas were allocated for hormones and non-hormonal raw materials.

The monitoring and tracking of retest dates of raw materials was reviewed and was manually operated. However, the current practice to deface the label was found inappropriate as it did not permit the reading of the original information.

2.15 DOCUMENTATION

For Levonorgestrel 0.75mg and 1.5mg tablets, the specification of starting and packaging materials used, the formulation, the detail step wise production and packaging instructions, the batch manufacturing and packaging records, the finished product specifications including the testing procedures and corresponding results were established and available.

Each of the quality system documents (SOPs, Forms, Protocols, Layout plan etc) carried a unique document number which facilitate their documentation control by QA department, including document change control, distributing, tracing, filing/archiving, keeping (records) and retrieval.

2.16 GOOD PRACTICES IN PRODUCTION

Production activities

The general tablets area and the injection manufacturing area which were not covered in this inspection.

In the OCP area, hormones were geometrically mixed with lactose granules in a double cone blender and the premix was further blended with lactose granules and sifted lubricants in a double cone blender. The lubricated granules were then compressed and coated, as required. Operators in areas where the product was exposed wore pressurised suits supplied with filtered breathing air. Blend samples for QC testing were compacted into pellets for containment and easy transportation.

Packaging activities

At the time of inspection, there were primary packaging activities and secondary packaging activities in the respective areas. In general, the secondary packaging area was found satisfactory.

2.17 GOOD PRACTICES IN QUALITY CONTROL

There were quality control and quality assurance departments whose functions were independent of other units including production. The Quality assurance department was involved in approving new vendors for starting and packaging materials and equipment.

The quality control laboratory had adequate facilities in form of space, equipment, reagents and chemicals to test all starting material, packaging materials, intermediates and finished products before release for use or distribution.

The documentation and records maintained to support the different activities and routines are generally adequate to ensure the necessary traceability in their different perspectives.

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, **Famy Care Ltd. Ahmedabad** 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.