

Good Manufacturing Practices Assessment and Discussions on WHO Prequalification

Nairobi, Kenya

May 16-18, 2012

Trip Report

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Promoting the Quality of Medicines

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PROMOTING THE QUALITY OF MEDICINES

Executive Summary

Mr. Edwin Toledo visited Nairobi, Kenya to perform an assessment of Cosmos Limited's implementation of Good Manufacturing Practices (GMP). This assessment was performed using the World Health Organization (WHO) inspection procedures approach for auditing the manufacture of pharmaceuticals. The assessment revealed that the firm has the systems in place as well as the capabilities, facilities, infrastructure, knowledge, and skills necessary to manufacture zinc finished pharmaceutical products (FPP) compliant with WHO GMP. All the non-compliances and opportunities for improvement observed during the assessment are listed in a full confidential report for the manufacturer.

In addition to the assessment, a meeting was held with Sky Light Chemical to discuss the technical assistance that PQM can offer the firm in the process of obtaining WHO prequalification (PQ) for second-line tuberculosis (TB) medicines.

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About PQM

The Promoting the Quality of Medicines (PQM) program, funded by the U.S. Agency for International Development (USAID), is the successor of the Drug Quality and Information (DQI) program implemented by the United States Pharmacopeia (USP). PQM is USAID’s response to the growing challenge posed by the proliferation of counterfeit and substandard medicines. By providing technical assistance to developing countries, PQM helps build local capacity in medicine quality assurance systems, increase the supply of quality medicines to priority USAID health programs, and ensure the quality and safety of medicines globally. This document does not necessarily represent the views or opinions of USAID or the United States Government. It may be reproduced if credit is given to PQM and USP.

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- Mr. Vimal P. Patel, Director, Cosmos
- Mr. Jitendra Rishi, General Manager, Operations, Cosmos
- Dr. Meshack O. Odenyo, Quality Assurance Manager, Cosmos
- Mr. Abdiwahab Ahmed Nur, Chief Executive Officer, Sky Light Chemicals
- Dr. Weru M Douglas, Quality Assurance Manager, Sky Light Chemicals
- Mr. Anthony Boni, Dr. Maria Miralles, and Ms. Malia Boggs at USAID in Washington, D.C.
- PQM administrative staff and editors

ACRONYMS

API	Active Pharmaceutical Ingredient
CAPA	Corrective and Preventive Action
DQI	Drug Quality and Information Program
FPP	Finish Pharmaceutical Product
GMP	Good Manufacturing Practices
MCH	Maternal and Child Health
PQM	Promoting the Quality of Medicines Program
RA	Regulatory Affairs
SKL	Sky Light Limited
TA	Technical Assistance
TB	Tuberculosis
USAID	United States Agency for International Development
USP	United States Pharmacopeia
WHO	World Health Organization

Background

Since 2004, the Promoting the Quality of Medicines (PQM) program, and its predecessor, the Drug Quality and Information (DQI) program, have been involved in the efforts of the World Health Organization (WHO), United Nations Children’s Fund (UNICEF), and United States Agency for International Development (USAID) to roll out zinc products as a oral rehydration salt supplements in the management of children’s diarrhea, especially for those under the age of five.

In order to help ensure that quality zinc products can be procured in developing countries, PQM performs Good Manufacturing Practices (GMP) assessments of zinc manufacturers to ensure that their products are of high quality. In order to help manufacturers achieve WHO Prequalification (PQ) status, PQM provides recommendations to them to strengthen their quality assurance systems and GMP programs.

Purpose of Trip

The purpose of the trip was to:

- Conduct GMP assessment of zinc sulfate manufacturing activities at Cosmos Ltd. and provide technical assistance (TA) on GMP compliance
- Visit Sky Light Chemicals Ltd. to discuss future collaboration for products to be submitted to WHO PQ for second-line tuberculosis (TB) drugs.

Source of Funding

This trip was funded by USAID through Core Maternal and Child Health (MCH) and Core TB.

Overview of Activities

The following summarizes the pre-assessment of Cosmos’ manufacturing facility conducted by PQM. The assessment was conducted to assess the firm’s capabilities and future potential in terms of compliance with WHO current Good Manufacturing Practices (WHO cGMPs), main principles for pharmaceutical products. This pre-assessment was performed using the general scheme of the systems approach for auditing the manufacture of pharmaceuticals and included coverage of the areas listed in the table below.

Item	Description
Institution Evaluated	Cosmos Limited
Date	May 16-17, 2012
Specific Objectives	Assess overall compliance with WHO cGMP standards in the manufacturing activities of zinc sulfate tablets
Auditors/ Evaluators	Edwin Toledo
Key Personnel: Quality Assurance and Lab Management	<ul style="list-style-type: none">• Mr. Vimal P. Patel, Director• Mr. Jitendra Rishi, General Manager• Dr. Meshack O. Ondenyo, Manager, Quality Assurance

Agenda	See <i>Annex I</i> for a detailed audit agenda
Areas Evaluated	Utilities, Manufacturing areas, Warehouse, and Quality Control/ Microbiology Laboratories
Key Findings	PQM presented the findings of the visit on the final day to key Cosmos personnel. A complete confidential report of the visit observations, findings, and recommendations will be sent to the company separately.
Conclusion	Based on the areas inspected, Cosmos has the required systems to successfully participate in the WHO PQ Program for zinc sulfate tablets.
Next Steps	<ul style="list-style-type: none"> • Cosmos will compile the zinc sulfate dossier by September 2012 • PQM will support Cosmos on GMP corrective and preventive action plan implementation

Meeting with Sky Light Limited

Friday, May 18, 2012

Mr. Toledo met with Mr. Abdiwahab Ahmed Nur, Chief Executive Officer, and Dr. Weru M Douglas, Quality Assurance Manager, from Sky Light to discuss PQM technical assistance for second-line TB manufacturers.

Sky Light manufactures pharmaceutical liquid formulations and will expand to manufacture creams, ointments, tablets, and capsules in the next year. Sky Light management is very interested in receiving PQM technical assistance for second-line TB products next year, after the construction is complete and the new manufacturing facility is commissioned.

Conclusion

This baseline GMP assessment at Cosmos was successful, with Cosmos and PQM planning to work together to implement a CAPA plan and compile the zinc sulfate dossier for submission. Discussions regarding PQM TA for second-line TB medicines with Sky Light were also fruitful.

Agenda

Site	COSMOS LIMITED
Address	P.O. Box 41433-00100, Rangwe Road, off Lunga Lunga Road, Industrial Area, Nairobi, Kenya
Date	May 16-17, 2012
Product	zinc sulfate 20mg tablets

Time	Activity
Day 1	
09:30 AM	<u>Opening meeting with key personnel</u> <ul style="list-style-type: none"> • Introductions of all personnel • Cosmo Presentation • UNICEF CAPA plan status • Confirmation of proposed audit plan/schedule
10:30 AM	Tour of Utilities, Warehouse and Manufacturing area
12:00 PM	Lunch Break
1:00 PM	Tour of Utilities, Warehouse
2:15 PM	Tour Manufacturing Area
	<u>Quality Management System review:</u> <ul style="list-style-type: none"> • Personnel Policies: Organization charts, Job descriptions, Training, Health and Hygiene. • List of SOPs/SOP Index. • Deviations/Change control/OOS + related SOP • Finished product release procedure • Complaints handling system • Product recall system • Product Master Files, production flow diagrams and specifications <u>Quality Management System review:</u> <ul style="list-style-type: none"> • Personnel Policies: Organization charts, Job descriptions, Training, Health and Hygiene. • List of products/Production planning/Batch numbering system and batch register. • SOP and document preparation, review and control. • List of SOPs/SOP Index. • Deviations/Change control/OOS + related SOP • Reprocessing/Reworking policy + SOPs • Finished product release procedure • Self inspection (SOP, Plans, reports) • Complaints handling system • Product recall system

Time	Activity
	<ul style="list-style-type: none"> Product Master Files, production flow diagrams & specifications
Day 2	
9:30 AM	<p>Review of Plant Layout and Utilities (HVAC, Dust control, Water Purification and Compressed air systems):</p> <ul style="list-style-type: none"> Block layout, area classification, AHU distribution and material and personnel flow <p>HVAC and Dust Control system:</p> <ul style="list-style-type: none"> Qualification/Requalification/Monitoring the HVAC + Dust Control System Inspection of the HVAC + Dust extraction technical area <p>Water purification system:</p> <ul style="list-style-type: none"> PW system drawings and summary of specifications and capacities Qualification/Requalification/Monitoring the PW system (Sampling and trend analysis) Inspection of Water Generation and Purification System installations <p>Compressed air system</p> <ul style="list-style-type: none"> Qualification/Requalification/Monitoring the Compressed Air systems <p>Equipment qualification and preventive maintenance:</p> <ul style="list-style-type: none"> Equipment qualification/Requalification (DQ, IQ, OQ and PQ for major equipment) Calibration Preventive maintenance schedules and records <p>Validation</p> <ul style="list-style-type: none"> Validation Master Plan (including status and planned) Process validation and revalidation for the product in focus Cleaning validation <p>Review of BMRs</p> <ul style="list-style-type: none"> SOP on batch review and batch release Review of BMRs for selected batches
12:00 PM	Lunch break
1:00 PM	Discussion
4:00 PM	Summary of observations for the day and Closing meeting with company representatives