

**Good Manufacturing Practices Assessment of Lomus Chlorhexidine 7.1% Gel
Manufacturing Activities and Meetings with Deurali-Janta Pharmaceuticals Regarding
Levofloxacin Dossier**

Kathmandu, Nepal

August 26-29, 2013

Trip Report

Mr. Edwin Toledo, Senior GMP Specialist

Dr. Lawrence Evans III, Global Services and Standards Manager

Promoting the Quality of Medicines

Implemented by U.S. Pharmacopeia

12601 Twinbrook Parkway

Rockville, MD 20852 USA

Tel: (+1) 301-816-8165

Fax: (+1) 301-816-8374

Email: ert@usp.org or le@usp.org

Cooperative Agreement # GHS-A-00-09-00003-00

Funding Source: Core Maternal and Child Health (MCH) and TB

Grantee: Promoting the Quality of Medicines (PQM) Program

Author(s) Name: PQM staff

Language: English

Date of Publication: October 8, 2013



USAID
FROM THE AMERICAN PEOPLE



This report is made possible by the generous support of the American people through the United States Agency for International Development (USAID), under Cooperative Agreement No. GHS-A-00-09-00003-00. The contents are the responsibility of the Promoting the Quality of Medicines Program, implemented by the U. S. Pharmacopeia, and do not necessarily reflect the views of USAID, or the United States Government.

PROMOTING THE QUALITY OF MEDICINES

Executive Summary

Dr. Evans and Mr. Toledo traveled to Nepal to perform a follow-up assessment of Lomus Pharmaceutical, evaluate technical information required for the development of the chlorhexidine gel monograph, and discuss (in collaboration with PATH) the possibility of technology transfer to selected manufacturers in Nigeria.

The primary focus of the assessment was the Good Manufacturing Practices (GMP) corrective and preventive action plan that resulted from an earlier PQM assessment (performed in January 2013). The current PQM assessment revealed that Lomus has implemented recommendations for about 90% of the minor observations regarding GMP compliance found during the last visit. Lomus confirmed their willingness to engage in technology transfer for the manufacture of chlorhexidine gel, and to assist USP with monograph validation, Lomus provided 50 tubes of CHX gel.

In addition to the activities at Lomus, meetings were held with to follow up on the compilation of their dossier for levofloxacin, an anti-tuberculosis medicine. PQM was able to provide support in updating their levofloxacin dossier and with validation activities.

TABLE OF CONTENTS

<u>Acknowledgements</u>	4
<u>Acronyms</u>	5
<u>Background</u>	6
<u>Purpose of Trip</u>	6
<u>Source of Funding</u>	6
<u>Overview of Activities</u>	6
<u>Conclusion</u>	7

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.

ACKNOWLEDGEMENTS

We would like to thank:

- Mr. Prajwal Jung Pandey, Marketing Director, Lomus
- Mr. Pradeep Jung Pandey, Managing Director and Chairman, Lomus
- Mr. Hari Bhakta Sharma, Executive Director, Deurali-Janta
- Dr. Maria Miralles and Mr. Anthony Boni at USAID headquarters in Washington, D.C. for their support and advice
- PQM administrative and editorial staff for their support

Acronyms

CAPA	Corrective and Preventive Action
CHX	Chlorhexidine
DQI	Drug Quality and Information Program
DJPL	Deurali-Janta Pharmaceutical Limited
FPP	Finished Pharmaceutical Product
GMP	Good Manufacturing Practices
MCH	Maternal and Child Health
PATH	Program for Appropriate Technology in Health
PQM	Promoting the Quality of Medicines Program
TB	Tuberculosis
USAID	United States Agency for International Development
USP	United States Pharmacopeia
WHO	World Health Organization

Background

The United Nations Commission on Life-Saving Commodities for Women and Children was established to focus on 13 essential health commodities to assure the availability of medicines and other supplies needed to achieve the relevant Millennium Development Goals. In support of the UN Commission, PQM will provide technical assistance on Good Manufacturing Practices (GMP) and quality assurance to manufacturers of selected medicines such as chlorhexidine (CHX), oxytocin, misoprostol, and magnesium sulfate formulations, all of which are priority commodities for the UN Commission.

Lomus Pharmaceutical in Nepal has been a key supplier of CHX gel to many countries, including those in Africa. With a goal of establishing local CHX gel manufacturing in African countries, PQM, through its work on the UN Commission CHX working group, was requested to visit Lomus to determine its level of interest in technology transfer for CHX gel. In addition, PQM plans to evaluate Lomus's corrective and preventive action (CAPA) plan for manufacturing activities and obtain data to prepare a monograph.

Under the umbrella of its tuberculosis-related activities, PQM is also working in Nepal with Deurali-Janta Pharmaceutical Limited (DJPL) to develop its levofloxacin dossier for submission to the World Health Organization (WHO) Prequalification Program.

Purpose of Trip

The purpose of the trip was to:

- Evaluate Lomus Pharmaceutical's GMP CAPA (resulting from a PQM assessment conducted in January 2013) for the implementation of current CHX gel formulation manufacturing activities
- Obtain and review with Lomus the specifications, procedures, and supporting data needed to prepare the proposed monograph for CHX gel
- In collaboration with the Program for Appropriate Technology in Health (PATH), discuss with Lomus the CHX gel technology transfer to selected Nigerian pharmaceutical manufacturers
- Meet with DJPL to obtain an update of the manufacture of levofloxacin

Source of Funding

This trip was funded by USAID through Core Maternal and Child Health and Tuberculosis.

Overview of Activities

Manufacturer	Products	Status	Next Steps
Lomus	Chlorhexidine 7.1% Gel	Evaluation of the CAPA implementation was verified during a facility walkthrough. About 90% of the CAPA has been implemented and some critical equipment has been procured. The discussion with Lomus management regarding the	Lomus will finish the CAPA plan implementation by late October 2013. PQM will visit Nigerian manufacturers to evaluate CHX manufacturing capabilities in preparation for technology transfer by Lomus. Assessments will occur in September 2013.

		possibility of technology transfer to Nigerian manufacturers was very positive. Lomus is willing to provide technology transfer with PQM technical support.	
Deurali-Janta (DJPL)	Levofloxacin Finished Pharmaceutical Product	The company has started manufacturing new batches for stability and process validation and will update the dossier accordingly.	Validation batches with new active pharmaceutical ingredient to commence in mid September 2013. DJPL will continue compiling the dossier with submission to WHO scheduled by May 2014.

Highlights of meetings with Lomus

Technology Transfer Discussions

Mr. Toledo, Dr. Evans, and Ms. Mutsumi Metzler (PATH) met with Mr. Prajwal Jung Pandey, Marketing Director (Lomus) to discuss the transfer of CHX manufacturing technology to select Nigerian manufacturers.

- Lomus was given an overview of the UN Commission initiative and the CHX working group
- Lomus asked to join CHX working group
- Lomus agreed to a technology transfer to Nigerian manufacturers selected by PQM and PATH
- PQM will prepare a detailed plan for technology transfer and provide assistance where needed in the process, all of which is dependent upon Lomus and the prospective manufacturer agreeing on terms.

Chlorhexidine Gluconate Gel Monograph Discussions

Dr. Evans met senior staff from the QC department and manufacturing plant to review specifications, procedures, and data for developing the CHX gel monograph. The assay (content) procedure for the gel formulation is a modification of the current USP monograph for CHX topical solution that incorporates a sample preparation to accommodate the gel formulation. Lomus has performed the initial validation of the HPLC procedure to measure the content of CHX in the gel formulation, but additional validation is needed for acceptance into the USP Medicines Compendia. To assist USP with the validation, Lomus provided 50 tubes of CHX gel.

Conclusion

The assessment at Lomus revealed that the company has implemented about 90% of the minor observations PQM identified in the CAPA. Lomus confirmed their willingness to engage in technology transfer for the manufacture of chlorhexidine gel. In addition, the visit to DJPL was productive as PQM provided support in updating their levofloxacin dossier and with validation activities.

Additional Next Steps

- PQM will request the USP CHX reference standard for Lomus (by early October 2013)
- PQM lab staff will perform assay validation and development of monograph test procedures and specifications (estimated completion by mid-December 2013)