

# Quality System Assessment of Pavlodar Pharmaceutical Factory (Romat Pharmaceutical Company)

Pavlodar, Kazakhstan

October 16-17, 2013

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*Trip Report*

**Jennifer Derry**  
**Associate GMP Specialist**

**Michael Megargee**  
**Senior GMP Specialist**

**Kirill Burimski**  
**Program Manager**

## **Promoting the Quality of Medicines**

Implemented by U.S. Pharmacopeia  
12601 Twinbrook Parkway  
Rockville, MD 20852 USA  
Tel: (+1) 301-230-3275  
Fax: (+1) 301-816-8374  
Email: [jxd@usp.org](mailto:jxd@usp.org)

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**Author(s) Name:** Jennifer Derry

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## **Executive Summary**

Dr. Burimski, Mr. Megargee, and Ms. Derry traveled to Pavlodar, Kazakhstan to perform a Good Manufacturing Practices (GMP) assessment of the quality systems currently implemented at Pavlodar Pharmaceutical Factory (Romat Pharmaceutical Company). This assessment was performed using the World Health Organization (WHO) inspection procedures approach for auditing the manufacture of pharmaceuticals. A separate confidential report has been sent directly to the company.

While in-country, PQM also met with USAID/Central Asia Republics and the U.S. Centers for Disease Control and Prevention to summarize the assessment of Pavlodar Pharmaceutical Factory and discuss possible activities for the FY 14 workplan.

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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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## ACRONYMS

BE	Bioequivalence
CAR	Central Asia Republics
CDC	U.S. Centers for Disease Control and Prevention
DQI	Drug Quality and Information Program
GMP	Good Manufacturing Practices
HEO	Health and Education Office
MRA	Medicine Regulatory Authority
PQ	Prequalification
PQM	Promoting the Quality of Medicines Program
SOP	Standard Operating Procedure
TB	Tuberculosis
USAID	United States Agency for International Development
USP	United States Pharmacopeia
WHO	World Health Organization

## Background

Tuberculosis (TB) is a global concern, and PQM has actively contributed to the USAID strategic objective of “increased use of effective interventions to reduce the threat of infectious diseases, including tuberculosis” (P.E.1.2 -TB). PQM assists countries to implement medicine quality monitoring, and in 2008, began providing technical assistance related to Good Manufacturing Practices (GMP) to interested companies on the preparation of medicine dossiers they submit to the World Health Organization (WHO) with their "Expressions of Interest" for the WHO Prequalification (PQ) Program.

PQM began receiving funding from USAID/Central Asian Republics (USAID/CAR) in 2012 with the goal of improving the quality of anti-TB medicines produced by the major medicines manufacturers in Kazakhstan. In addition, PQM will collaborate with the national medicine regulatory authority to strengthen medicine regulatory requirements.

## Purpose of Trip

- Conduct a GMP assessment of the quality systems at the Pavlodar Pharmaceutical Factory facility in preparation for establishing a GMP compliant facility
- Meet with USAID/CAR staff in Almaty to summarize the results of the assessment and discuss activities for the FY 14 workplan

## Overview of Activities

Mr. Megargee, Ms. Derry, and Dr. Burimski toured the existing Pavlodar Pharmaceutical Factory manufacturing facility, reviewed the drawings for their new facility, and evaluated the Standard Operating Procedures (SOPs) currently in use by the Manufacturing, Metrology, and Quality departments. A detailed confidential report on the findings and observations has been sent directly to the company for review and follow-up. See *Annex 1* for the Assessment Plan.

Key Findings	Pavlodar Pharmaceutical Factory is in the process of building a new facility that will be GMP certified by the local regulatory agency. During this process, PQM will work with the staff from Pavlodar Pharmaceutical Factory to discuss the next steps in preparation for WHO Prequalification.
Next Steps	Pavlodar Pharmaceutical Factory will: <ul style="list-style-type: none"><li>• Implement a corrective action plan</li><li>• Provide corrective action plan to PQM for review</li></ul> PQM will: <ul style="list-style-type: none"><li>• Follow up in December/January on the progress of corrective actions</li></ul>

## Additional Meetings

PQM staff met with the staff of USAID/CAR and the U.S. Centers for Disease Control and Prevention (CDC) to provide an update on the visit to Pavlodar and to propose and discuss activities for the FY 14 workplan. The following is a list of PQM’s proposed activities:

- Provide technical assistance to manufacturers of anti-TB medicines to help achieve WHO PQ by conducting GMP assessments of the facility and quality system documents; provide support in compiling the Active Pharmaceutical Ingredient/Finished Pharmaceutical Product dossier per WHO guidelines; provide bioequivalence (BE) study support—review BE study protocol,

identify a contract research organization that meets WHO requirements, and provide input/comments on in-vitro dissolution study for bio-waiver products.

- Provide GMP training to regulatory staff as well as manufacturers in Kazakhstan—conduct one or two GMP trainings (one week each) in Almaty for the Kazakhstan regulatory agency staff and manufacturers.
- Conduct pharmacopeial education courses for local manufacturers of priority medicines as needed or requested.
- Collaborate with CDC and medicine regulatory authorities (MRAs) on establishing medicine quality monitoring programs as part of post-marketing surveillance—provide assistance with launch of Minilab<sup>®</sup> testing, appropriate training, and data collection and dissemination.
- Collaborate with MRAs, including conducting laboratory training courses for the staff of central and regional medicines quality control laboratories, and providing technical assistance to the laboratories in reaching WHO PQ and/or ISO 17025 accreditation based on assessments of their capacities.

### **Conclusion**

The WHO PQ preparation for Pavlodar Pharmaceutical Factory will continue in parallel with their new facility construction. Dossier compilation will start once a product has been confirmed by the company.

USAID/CAR will hold internal discussions on future activities, both in Kazakhstan and Uzbekistan, that they would like PQM to carry out for FY 14 and finalize the workplan.

### **Next Steps**

- PQM will continue communicating with Pavlodar Pharmaceutical Factory staff to provide technical assistance. Additional next steps will be determined upon review of the audit report by Pavlodar Pharmaceutical Factory staff.
- PQM will communicate with USAID/CAR to finalize the FY 14 workplan and submit for approval by the end of November.

## Assessment Plan

Item	Description
Institution Evaluated	Pavlodar Pharmaceutical Factory/Romat Corporation
Date	October 16-17, 2013
Specific Objectives	<ol style="list-style-type: none"> <li>1. Assess the quality systems in the manufacturing activities of second-line anti-TB medicines at Pavlodar Pharmaceutical Factory</li> <li>2. Discuss dossier queries, if available</li> </ol>
Scope	The assessment will focus on the quality systems documents relating to processes involved in Manufacturing, Process Control, Testing, Packaging, Storage and Distribution of the manufactured materials.
Documentation	<p>Documentation requested during the audit:</p> <ul style="list-style-type: none"> <li>• Site Master File (if available for new facility)</li> <li>• Copy of Organization Chart</li> <li>• Copy of SOP list</li> <li>• Validation Master Plan</li> <li>• Process and Cleaning Validation</li> <li>• Qualification and Maintenance plan</li> <li>• Product Quality Review (2011 and 2012)</li> <li>• List of changes, rejections, deviations, and complaints</li> <li>• Manufacturing batch record</li> <li>• Copy of Specification of material purchased</li> </ul>