

## **PQM Good Manufacturing Practices Assessment, Philippines**

**December 16-18, 2009**

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### ***Trip Report***

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### **Promoting the Quality of Medicines**

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PROMOTING THE QUALITY OF 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 leadership to developing countries, PQM is helping to 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 neither opinions of USAID or the United States Government nor that of USP. It may be reproduced if credit is given to PQM and USP.

## **Abstract**

PQM staff – Mr. Edwin Toledo, Dr. Souly Phanouvong, and Dr. Patrick Lukulay – traveled to the Philippines to visit United Laboratories, Inc. (UNILAB) subsidiaries Amherst Laboratories, Inc. and Amherst Parenterals, Inc., in Alabang, Philippines to discuss WHO prequalification requirements for levofloxacin tablets and amikacin sulfate injections and to perform baseline Good Manufacturing Practices (GMP) assessments of the facilities.

Based on the areas inspected, and the corrective actions programs in place as part of PQM's recommendations, Amherst Laboratories, Inc. and Amherst Parenterals, Inc. are operating at an acceptable level of GMP compliance as recognized by the national regulatory authority, the FDA. The companies are willing to submit an expression of interest for levofloxacin tablets and amikacin injections in response to the invitation to manufacturers of second-line TB medicines for product evaluation by the WHO Prequalification of Medicines Programme.

The PQM team also met with the Philippines FDA to discuss modifications to the Medicine Quality Monitoring program.

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## **Key Words**

UNILAB, Good Manufacturing Practices, Validation, Standard Operating Procedures, levofloxacin, amikacin injection, Dossier, Prequalification

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- Ms. Geraldine Guzman, Business Development Group of United Laboratories, for coordinating the PQM's team visit
- Mr. Nestor Felicio, Vice President; Mr. Limuel Razo, Division Vice President; Mrs. Glorina Villanueva, Director; and the staff from QA Department and Regulatory Affairs Division of United Laboratories for their support and cooperation during this assessment visit

## Acronyms

ACT	Artemisinin-based Combination Therapy
CAP	Corrective Action Plan
DMF	Drug Master File
DOTS	Directly-Observed Treatment, Short-course
EOI	Expression of Interest
FDA	Food and Drugs Administration
FDC	Fixed-Dose Combination
GDF	Global Drug Facility
GLC	Green Light Committee
GMP	Good Manufacturing Practices
MDR-TB	Multi-drug resistant tuberculosis
MQM	Medicine Quality Monitoring
QA	Quality Assurance
QC	Quality Control
RAS	Rapid Alert System
USAID	United States Agency for International Development
PQM	Promoting the Quality of Medicines Program
TB	Tuberculosis
USP	United States Pharmacopeia
WHO	World Health Organization
WPRO	Western Pacific Regional Office of WHO
XDR-TB	Extensively drug-resistant tuberculosis

## **Background**

Tuberculosis (TB), a global concern for many decades, is now compounded by the development of multidrug-resistant tuberculosis (MDR-TB) – strains of tuberculosis that are resistant to both isoniazid and rifampicin. The situation has been exacerbated by the emergence of extensively drug resistant tuberculosis (XDR-TB), which is described as resistance to isoniazid, rifampicin, and two or more of the six classes of second-line anti-tuberculosis (anti-TB) medicines.

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). For example, in 2001, at the request of USAID and WHO, USP developed pharmacopeial methods for testing a fixed-dose combination (FDC) tablet containing rifampicin, isoniazid, ethambutol, and pyrazinamide. This FDC is important in implementing the directly-observed treatment, short-course (DOTS), the internationally recognized strategy to control TB. PQM also assists countries in the Mekong Subregion to implement anti-TB drug quality monitoring and helped develop and deliver joint regional and national training courses on TB drug management for Central Asian countries and Russia. PQM also disseminated drug information on MDR-TB and TB/HIV co-infection to help improve drug selection and treatment.

## **Purpose of Trip**

The PQM team visited two manufacturing facilities of UNILAB’s subsidiaries; Amherst Laboratories, Inc. and Amherst Parenterals, Inc., in Alabang, Philippines to discuss World Health Organization (WHO) prequalification requirements for levofloxacin tablets and amikacin sulfate injections and to perform baseline GMP assessments of the facilities (see *Annex 1* for the visit agenda and *Annex 2* for the audit agenda).

Meetings were held with USAID/Philippines, the WHO/Western Pacific Regional Office (WPRO) Head Office, and Philippines FDA to debrief officials.

## **Source of Funding**

This trip was supported by USAID core funds for Tuberculosis, with some additional funding from the WHO/Bill and Melinda Gates Foundation grant.

## **Overview of Activities**

### ***Wednesday, December 16, 2009***

**Meeting with WHO/WPRO:** The PQM team met with Dr. Budiono Santoso, Regional Adviser, Pharmaceuticals, EDM and Dr. Eva-Marie Christophel, Medical Officer, Malaria Adviser to update WPRO on PQM’s regional activities. WHO asked if PQM could include antibiotics (ciprofloxacin, amoxicillin, cotrimoxazol) and medicines for some neglected diseases in the PQM-supported Medicine Quality Monitoring (MQM) program in the Philippines. PQM will pass the request to USAID and keep WHO informed on outcomes. WHO also asked if PQM could assist in providing technical assistance to Pacific countries (e.g. Papua New Guinea, Samoa) to train in establishing MQM. WHO/WPRO is planning to hold a meeting convening experts in medicines quality surveillance in Manila to discuss revitalizing the Rapid Alert System (RAS) to share information on counterfeit medicines to support regulatory actions in the region and would like to request PQM to be actively involved in the process. PQM agrees to

send one expert to attend the meeting and present PQM experience and provide expertise as appropriate.

WPRO Malaria requested technical assistance from PQM to address the quality of artemisinin-based combination therapies (ACTs) used in the containment zone in Cambodia. However, under the Bill and Melinda Gates Foundation grant for containment activities, there is no budget for medicines quality. PQM suggested that WHO, the leading organization in the containment zones, discuss with appropriate partners and make funds available so that PQM's involvement can be secured. PQM is using some funding from the USAID Regional Development Mission for Asia to cover malarial drug quality monitoring in Cambodia, but limited funding will constrain PQM's active involvement in ensuring the quality of ACTs used in the containment zones. WPRO agreed to take the issue up to the International Committee on Containment to discuss.

**Meeting with USAID/Philippines:** The PQM team met with Ms Ann Hirschey, Chief Office of Health; Dr. Corazon Manaloto, Development Assistance Specialist; Dr. Padma Shetty, Health Development Officer at USAID/Philippines; and Ms. Yvette Lopez, PQM Consultant to discuss the details of the trip. PQM proposed the following topics to the Mission, and all were in agreement:

- Approve the inclusion of antibiotics in the MQM program due to the increased quality problems reported from the Mekong region and as requested from WHO
- Strategically provide technical assistance to FDA in product registration – especially on dossier evaluation – and Quality Control lab capacity towards ISO 17025 accreditation
- Modify the MQM sampling strategy and techniques
  - Collect more samples from the public sector and include the informal sector also
  - Use “mystery shopper” technique, where applicable
  - Collect samples on a quarterly basis, instead of monthly
  - Hold a meeting to review outcomes, lessons learned, and challenges of the pilot phase of MQM in six sites on anti-TB medicines in the Philippines and define a new strategy for effective intervention
  - Send representatives to attend the regional medicines quality meeting, which PQM, in collaboration with the Laos Ministry of Health, will hold in Vientiane, Laos in March

***Thursday, December 17, 2009***

**Visit to Amherst Laboratories, Inc.:** The team visited Amherst Laboratories, Inc. to discuss WHO prequalification requirements for levofloxacin tablets and to perform baseline GMP assessments of the facilities. (see *Annex 3* for findings)

***Friday, December 18, 2009***

**Visit to Amherst Parenterals, Inc.:** The team conducted a baseline GMP assessment and discussed WHO Prequalification requirements with Amherst Parenterals, Inc., discussed WHO prequalification requirements for amikacin sulfate injections, and performed a baseline assessment (see *Annex 4* for findings).

Based on the areas inspected, and the corrective actions programs in place as part of PQM's recommendations, Amherst Laboratories, Inc. and Amherst Parenterals, Inc. are operating at an

acceptable level of GMP compliance as recognized by the national regulatory authority, the FDA. The companies are willing to submit an expression of interest for levofloxacin tablets and amikacin injections in response to the invitation to manufacturers of second-line TB medicines for product evaluation by the WHO Prequalification of Medicines Programme.

### Next Steps

- PQM will continue to support UNILAB on levifloxacin and amikacin dossier compilation.
- PQM will find out from WHO the stability temperature and humidity requirements for levoflocaxin and amikacin, as requested

**Meeting with Philippines FDA:** The PQM team and PQM consultant, Ms. Yvette Lopez, met with Ms. Maria Lourdes Santiago, Chief Regulatory Division, on behalf of the FDA Director to discuss PQM updates. Ms. Santiago gave the PQM team an update on activities related to Quality-basket Drugs, an initiative of the FDA – in collaboration with WHO and with technical support from PQM – to explore possibilities of making the MQM program sustainable by using local market leader products as reference/comparator products and utilizing the Minilab<sup>®</sup> testing methodology to reduce commodity costs.

The PQM team and Ms. Yvette Lopez also discussed and agreed on modifications to be incorporated in the MQM methodology and implementation:

1. TB medicines will now be collected/tested on a quarterly basis instead of each month on a rolling basis (5 per month is what is currently in operation). In other words, during one week or so of each quarter, 15 samples will be collected and tested at each of the six sites and then sent to the FDA central lab for confirmatory testing. This may be a more efficient method to obtain results. 15 samples per 6 sites per 4 quarters equals 360 samples collected/tested over the fiscal year, as stated in the approved work plan. Collecting/testing on quarterly basis would free up some time of the field staff to focus on their routine work. In the future, we may implement sample collection/testing on a six-month (bi-yearly) basis, as appropriate.
2. Efforts will be made to collect TB medicines from geographical areas that have not been previously sampled. In the future, we can look at expanding the number of sites as well.
3. “Sari-sari” stores and other informal outlets that are illegally selling TB medicines will now be included in sampling.
4. Sampling from wholesalers in Manila that are suspected to have quality problems per information from the FDA will be included.
5. The proportion of samples taken from the public sector will be increased; currently, most samples are from the private sector.
6. Staff needs to use people who are unrecognizable as “mystery shoppers”. It is believed that when staff members go into pharmacies to purchase TB medicines, they are recognized and sold medicines known to be of good quality. We will record from which outlets the mystery shoppers are able to obtain TB medicines without prescriptions.
7. PQM would like to begin sampling/testing amoxicillin, ciprofloxacin, and cotrimoxazole from the six sites in conjunction with the TB medicines. This idea is strongly supported by WHO/WPRO. These antibiotics are commonly used to treat co-infections with TB. In other countries where PQM works, we have consistently seen quality problems with

antibiotics (counterfeit and substandard). While we cannot be sure this is the case in the Philippines, we suggest collecting 5-10 samples of these antibiotics at each site per quarter (budget permitting).

8. Since the staff are already trained on basic testing techniques of TB medicines, PQM would only need to provide them with Minilab<sup>®</sup> monographs to test these antibiotics, secondary reference standards, and any additional reagents. This can likely be worked into the budget without needing additional funding.
9. Once the Quality Basket initiative is underway, staff from 16 regions will be testing 16 essential medicines including amoxicillin and ciprofloxacin (but not cotrimoxazole). As of January, one training for the Quality Basket has occurred for 8 out of the 16 regions, but it will take some time before collection/testing of the 16 selected essential medicines is carried out. PQM would like to take advantage of this opportunity to start testing these 3 antibiotics and get results before the end of the fiscal year.

### **Next Steps**

- PQM will follow up with the FDA and regularly update USAID/Philippines on the progress of methodology changes in the MQM program in the Philippines.

## Visit Agenda

When	With whom	Where	Discussion topics
Dec 16- 13:00-14:00	Dr. Eva Christophel, MD Medical Officer for Malaria Vectorborne and Other Parasitic Diseases, WHO Regional Office for the Western Pacific Mobile 09209037259 Office: 00632 5289723 –direct <a href="mailto:christophele@wpro.who.int">christophele@wpro.who.int</a>	United Nations Avenue WHO/WPRO Head Office	1. Update on MQM in the Mekong region 2. Malaria containment in Cambodia and Thailand – the MQ component
Dec 16- 3:00-4:00	Corazon Manaloto, M.D., D.T.M. & H. Development Assistance Specialist Office of Population, Health and Nutrition Tel : 632-552-9869 Fax : 632-552-9999 <a href="mailto:cmanaloto@usaid.gov">cmanaloto@usaid.gov</a>	US Agency for International Development 8/F, PNB Financial Center, Pres. Diosdado Macapagal Boulevard 1308 Pasay City, Philippines	1. Update on DQI/PQM's work in the region and the Philippines 2. Introduce PQM to the new Office of Health Director, Mrs. Ann G. Hirschey
Dec 17- 9:00 – 17:00	Geraldine  +63 917 859 5451 <a href="mailto:gcdeguzman@unilab.com.ph">gcdeguzman@unilab.com.ph</a>  Unilab assessment visit 1 <sup>st</sup> Facility	To be guided by Unilab	1. According to the proposed agenda submitted to Unilab
Dec 18- 9:00-15:30	As above Unilab assessment visit 2 <sup>nd</sup> Facility		As above
Dec 17 or 18 after 4PM	Tentative FDA Director and Regulatory Division	FDA Alanbang	Courtesy visit

## Audit Agenda

December 17–18, 2009

**Products:** Levofloxacin/ /Amikacin

### **DAY 1** (Oral Dosage Form Facility)

- I. Introduction**
  1. Introductions of all personnel
  2. Purpose of visit
  3. Discussion of PQM technical assistance for second-line TB products and World Health Organization (WHO) Prequalification Programme
  4. Finalization of visit agenda
  
- II. Tour of Utilities, Warehouse, Plant, and Laboratory**
  
- III. Review of Documents and Data**
  1. Site master file
  2. Air handling unit (AHU)
  3. Purified water system
  
- IV. Review of Documents and Data - continued**
  1. General manufacturing procedures
  2. Manufacturing equipment qualification
  3. Sanitation and hygiene
  4. Validation master plan
  5. Laboratory equipment cleaning, maintenance, and calibration
  6. Analytical method validation
  
- V. Quality Systems**
  1. Master batch record control and review
  2. Release process
  3. SOPs and documentation practices
  4. Records and sample retention (reserve sample program)
  5. Change control
  6. Training (GMP and job-specific)
  7. Complaint system
  8. Internal/external audit program
  9. Stability Program: Procedure, protocol, and summary of data
  10. Rejects: Investigation
  11. Product recall

**Day 2** (Sterile Products Facility)

**VI. Tour of Utilities, Warehouse, Plant, and Laboratory**

**VII. Review of Documents and Data**

1. Site master file
2. Air handling unit (AHU)
3. Purified water system

**VIII. Review of Documents and Data**

1. General manufacturing procedures
2. Manufacturing equipment qualification
3. Sanitation and sterilization
4. Validation master plan
5. Laboratory equipment cleaning, maintenance, and calibration
6. Analytical method validation

**IX. Review of Documents and Data**

1. General manufacturing procedures
2. Manufacturing equipment qualification
3. Sanitation and sterilization
4. Validation master plan
5. Laboratory equipment cleaning, maintenance, and calibration
6. Analytical method validation

**X. Closing Meeting**

1. Discussion of findings
2. Listing of items for UNILAB to complete with proposed timeframe
3. Next steps

## Amherst Laboratories, Inc. Audit Findings

The inspection involved the following key personnel from Amherst:

Division Vice President	Limuel Z. Razo
Director Corporate Compliance Office	Glorina N Villanueva
Director Office of Regulatory Affairs	Lourdes Sindico
Manager Office of Regulatory affairs	Lillibeth Escueta
Manger Business Development Group	Geraldine DE Guzman
Plant Head	Clauderia De Leon
Pharmacist in Charge	Kiven Marasigan
Team Leader QA/QC	Leadna Brigola
Group Leader Eng	Charesma Paul

General information for Amherst Laboratories:

Name of manufacturer	<b>Amherst Laboratories</b>
Physical and postal address	Alabang , Phillipines
Telephone number	049-512-4072
Fax number	632-858-1165
Summary of activities of manufacturer	Manufacturing of products in the following dosage forms: Tablets, Capsules
Scope of Assessment	Assessment of the manufacturing of levofloxacin tablets with special emphasis on dossier, validation/qualification of manufacturing process, equipment and utilities
Date of Assessment	December 17, 2009
Program	PE 3.1.2 TB

### Summary of Observations by PQM Team

Unilab is a regional healthcare company with a leading presence in Southeast Asia. It started operation in 1945 as a small drugstore, and by the end of the 1950s, Unilab had become the top pharmaceutical company in the Philippines. Unilab focuses on developing, manufacturing, and marketing a wide range of prescription and consumer health products – covering all major therapeutic categories – that are leading brand in the Philippines, Indonesia, Thailand, Malaysia, Singapore, Hong Kong, Vietnam, and Myanmar/Burma. Unilab has five manufacturing facilities in the Philippines and ten in the region. The PQM team visited Amherst Laboratories solid dosage and Amherst Parenterals manufacturing sites to evaluate GMP compliance in the manufacturing of levofloxacin tablets and amikacin injection in light of WHO requirements for their prequalification program and to discuss the products' dossier requirements.

In 2008, Amherst received GMP certification from Austria, a member of the European Medicines Agency. The Global Drug Facility also visited Amherst facilities.

The inspection covered all areas of activity related to the manufacture of the dosage forms:

Quality assurance; Facilities, i.e., HVAC, compressed air, water system, and electrical power back-up system; Storage areas; Sampling and dispensing areas; Filling, sealing, primary and secondary packaging; and Quality control and microbiological laboratories.

<b>Amherst Laboratories, Inc Solid dosage GMP Status based on observations during a base-line GMP Audit by PQM Team on Dec. 17, 2009</b>	
<b>Quality assurance</b>	A quality assurance system was implemented and maintained. The QA and QC units were independent from production. QA personnel were involved in all production and QC activities. A Quality Manual is available and contained all key components. Key SOPs were available and most seemed to be followed, however, for example, in Rejected Storage area, some rejected materials did not bear 'red label' or 'tag' on them which is required by the SOP. Another example was that all rejected materials should be disposed within one (1) month, but the mefenamic acid was kept in the rejected area for more than a month. An adequate internal inspection and SOP implementation follow up should be strengthened.
<b>Good manufacturing practices for pharmaceutical products</b>	Good manufacturing practices were implemented and maintained in accordance to national requirements. Manufacturing processes were clearly defined and reviewed. Manufacturing steps were recorded in Batch Manufacturing Documentation. Necessary resources were provided. Instructions and procedures were written in clear and unambiguous language.
<b>Sanitation and Hygiene</b>	The site's sanitation and hygiene program covered personnel, equipment, materials, and premises. The sanitation and hygiene measures in place at the time of the inspection were generally found to be sufficient to assure the prevention of contamination of the premises and product.
<b>Qualification and validation</b>	The key elements of a qualification and validation program were defined and documented in the Validation Master Plan. Generally, validations were considered to be appropriately performed. For cleaning validation, a matrix had been set up. This matrix was based on the assessment of the solubility and the toxicity of the active pharmaceutical ingredient in order to select some of the more toxic and the less soluble active substances as the worst case products (product chosen).
<b>Complaints</b>	Complaints and other information concerning potentially defective products were reviewed according to a written procedure and corrective/preventive actions were taken.
<b>Product Recalls</b>	Recalls were handled in accordance with a written procedure. The recall procedure was regularly reviewed and updated. Amherst had performed a Mock recall in collaboration with local authorities.
<b>Contract production and analysis</b>	No manufacturing was contracted out.
<b>Self-Inspection</b>	Self-inspection was performed in accordance with a written procedure. The procedure included questionnaires on GMP requirements and all essential GMP items were covered. After completion of each self inspection, a report was drawn up and necessary CAPAs were initiated.
<b>Personnel</b>	The personnel met during the audit were experienced, skillful and conscientious. An organization chart was available. Key personnel responsibilities were specified in job descriptions. The production and quality control responsibilities were independent and in line with GMP requirements.
<b>Training</b>	Training issues were covered in written SOPs. The company provides training at the time of recruitment, specific training relevant to area of deployment, and regular SOP training. Training comprehension was assessed by discussions and observation of performed activities. Training of personnel was properly recorded.

<b>Personal Hygiene</b>	Personnel were trained in personal hygiene procedures and facilities were provided in the form of changing rooms, protective garments, and disinfectants. The facilities were generally adequate and the procedures were quite well enforced, except for some improvement is necessary in the gowning room which requires adequate visual sign display to instruct personnel of the gowning procedure and placing their belongings (shoes and clothes) in the lockers provided.
<b>Premises</b>	Buildings and facilities used for manufacture and quality control were located, designed, and constructed to facilitate proper cleaning, maintenance, and production operations. Facilities were designed to minimize potential contamination; the production area had adequate space for the placement of equipment and materials to prevent mix-ups and contamination. There was also sufficient space for the movement of materials and personnel. There were separate personnel and material entrances. Temperature, relative humidity, and pressure differentials were regularly monitored and recorded. In general, the buildings were well-maintained and clean.
<b>Equipment</b>	Equipment calibration schedule was established on an annual basis and the calibration was performed by their respective supplier/vender accordingly.
<b>Materials</b>	The procedures describing the receipt, identification, quarantine, storage, handling, sampling, testing, and approval or rejection of materials was available. Incoming goods and finished products were quarantined until tested and released by QC. Amherst use SAP software for material management.
<b>Utilities</b>	Proper labeling with accurate date and time set on purified water should be implemented. Further, 'neutralizing water' should be properly daily recorded.
<b>Documentation</b>	There was a procedure for preparation, review, approval and authorization of SOPs. For products reviewed, there was a master formula, specification of starting and packaging materials, production and packaging instructions, batch processing and packaging records, finished product specifications, standard testing procedures and corresponding results.
<b>Good Practices in Production</b>	Production operations were carried out following clearly defined procedures. Operations on different products were not carried out simultaneously or consecutively in the same room. During processing, materials, bulk containers, major items of equipment, and the rooms and used packaging lines were labeled and indicated the products being processed, their strength and the batch number. Access to the production premises was restricted. All doors leading to the production areas were appropriately interlocked. An environmental monitoring program was established and followed.
<b>Good Practices in Quality Control</b>	In general, good practices in Quality Control were implemented and maintained. The quality control functions were independent of other departments. Adequate facilities, personnel and equipment, trained personnel and approved procedures were available for all relevant activities. Batches of products were released for sale or supply only after certification by the authorized person or designated persons. Sufficient samples of starting materials and products were retained to permit future examination of the product. Quality control personnel had access to production areas. Each "out of specification" (OOS) was appropriately evaluated and investigated in accordance with a written procedure. Some minor improvements needed to be implemented with respect to the following: <ul style="list-style-type: none"> <li>• Clear sign of QC lab should be at the entrance to the QC lab area</li> <li>• Equipment logbook and analytical note book dates should match (e.g., GC machine)</li> </ul>

## Amherst Parenterals, Inc. Audit Findings

The inspection involved the following key personnel from Amherst:

Division Vice president	Limuel Z. Razo
Director Corporate Compliance Office	Glorina N Villanueva
Director Office of Regulatory Affairs	Lourdes Sindico
Manager Office of Regulatory affairs	Lilibeth Escueta
Manger Business Development Group	Geraldine DE Guzman
Plant Head	Clauderia De Leon
Pharmacist in Charge	Kiven Marasigan
Team Leader QA/QC	Leadna Brigola
Group Leader Eng	Charesma Paul

### General information for Amherst Parenterals

Name of manufacturer	<b>Amherst Parenterals</b>
Physical and postal address	Alabang , Phillipines
Telephone number	049-512-4072
Fax number	632-858-1165
Summary of activities of manufacturer	Manufacturing of products in the following dosage forms: Injectables
Scope of Assessment	Assessment of the manufacturing of Amikacin Injections tablets with special emphasis on dossier, validation/qualification of manufacturing process, equipment and utilities
Date of Assessment	December 18, 2009
Program	PE 3.1.2 TB

### Amherst Parenterals GMP Status based on the observations during a baseline GMP Audit by PQM Team on Dec. 18, 2009

<b>Quality assurance</b>	A quality assurance system was implemented and maintained. A Quality Manual was available. The QA and QC units were independent from production and services were done by Unilab. QA personnel were involved in all production and QC activities. Key SOPs were available and seemed to be followed. However, some SOPs lacked signature and effective date. The manufacturing site had only one (1) coding machine which requires adequate SOP on coding/printing.
<b>Good manufacturing practices for pharmaceutical products</b>	Good manufacturing practices were implemented and maintained in accordance with the company's policy and local regulatory authority. Manufacturing processes were clearly defined and reviewed. Manufacturing steps were recorded in Batch Manufacturing Documentation.

<b>Sanitation and Hygiene</b>	The site's sanitation and hygiene program covered personnel, equipment, materials and premises. The sanitation and hygiene measures in place at the time of the inspection were generally found to be sufficient to assure the prevention of contamination of the premises and product. However, no adequate SOP on shoe washing and disinfecting. The current practice was that each employee took home every weekend his/her shoes, washed and disinfected and brought them back for use in the manufacturing plants. A proper mechanism to check/evaluate this current practice if it is adequate.
<b>Qualification and validation</b>	The key elements of a qualification and validation program were defined and documented in the Validation Master Plan. Generally, validations were considered to be appropriately performed. For cleaning validation, a matrix had been set up.
<b>Complaints</b>	Complaints and other information concerning potentially defective products were reviewed according to a written procedure and corrective/preventive actions were taken
<b>Product Recalls</b>	Recalls were handled in accordance with a written procedure. The recall procedure was regularly reviewed and updated. Amherst had performed a Mock recall in collaboration with local authorities.
<b>Contract production and analysis</b>	No manufacturing was contracted out.
<b>Self-Inspection</b>	Self-inspection was performed in accordance with a written procedure. The procedure included questionnaires on GMP requirements and all essential GMP items were covered. After completion of each self inspection, a report was drawn up and necessary CAPAs were initiated.
<b>Personnel</b>	The personnel met during the audit were experienced, skillful and conscientious. An organization chart was available. Key personnel responsibilities were specified in job descriptions. The production and quality control responsibilities were independent and in line with GMP requirements.
<b>Training</b>	Training issues were covered in written SOPs. The company provides training at the time of recruitment, specific training relevant to area of deployment, and regular SOP training. Training comprehension was assessed by discussions and observation of performed activities. Training of personnel was properly recorded.
<b>Personal Hygiene</b>	Personnel were trained in personal hygiene procedures and facilities were provided in the form of changing rooms, protective garments, and disinfectants. The facilities were generally adequate and the procedures were quite adequately enforced, except for some improvement is necessary in the gowning room which requires adequate visual sign display to instruct personnel of the gowning procedure and placing their belongings (shoes and clothes) in the lockers provided. Daily check of availability of disinfectant solution should be implemented.
<b>Premises</b>	Buildings and facilities used for manufacture and quality control were located, designed, and constructed to facilitate proper cleaning, maintenance, and production operations. Facilities were designed to minimize potential contamination; the production area had adequate space for the placement of equipment and materials to prevent mix-ups and contamination. There was also sufficient space for the movement of materials and personnel. There were separate personnel and material entrances. Temperature, relative humidity, and pressure differentials were regularly monitored and recorded. In general, the buildings were well-maintained and clean. However stability room Temperature and humidity parameters need to be monitored and controlled more effectively as was noticed during the inspection that the room was out of specification.
<b>Equipment</b>	Equipment calibration schedule was established on an annual basis and the calibration was performed by their respective supplier/vender accordingly.

<b>Utilities</b>	A separate air compressor unit provided air to each zone. Each air-compressor unit should have its own equipment logbook attached, and properly recorded, and calibrated as required by the manufacturers' specifications.
<b>Materials</b>	The procedures describing the receipt, identification, quarantine, storage, handling, sampling, testing, and approval or rejection of materials was available. Incoming goods and finished products were quarantined until tested and released by QC. Amherst use SAP software for material management.
<b>Documentation</b>	There was a procedure for preparation, review, approval and authorization of SOPs. For products reviewed, there was a master formula, specification of starting and packaging materials, production and packaging instructions, batch processing and packaging records, finished product specifications, standard testing procedures and corresponding results.
<b>Good Practices in Production</b>	Production operations were carried out following clearly defined procedures. Operations on different products were not carried out simultaneously or consecutively in the same room. During processing, materials, bulk containers, major items of equipment, and the rooms and used packaging lines were labeled and indicated the products being processed, their strength and the batch numbers. Access to the production premises was restricted. All doors leading to the production areas were appropriately interlocked. An environmental monitoring program was established and followed.
<b>Good Practices in Quality Control</b>	<p>In general, good practices in Quality Control were implemented and maintained. The quality control functions were independent of other departments. Adequate facilities, trained personnel and approved procedures were available for all relevant activities. Batches of products were released for sale or supply only after certification by the authorized person or designated persons. Sufficient samples of starting materials and products were retained to permit future examination of the product. Quality control personnel had access to production areas. Each "out of specification" (OOS) was appropriately evaluated and investigated in accordance with a written procedure.</p> <p>In the CoA , the applicable specifications, e.g., USP, JP, or EP the tests performed should be indicated in the CoAs.</p>