Medicine Quality Monitoring Program

Philippines Report
Medicine Quality Monitoring Program 2 Year Report
Philippines
2008-2010

Supported by: USAID through USP DQI/PQM

Rosario Dalangin
Gwendolyn Bardos
Yvette Martha Lopez

March 2010
# CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACKNOWLEDGEMENTS</td>
<td>3</td>
</tr>
<tr>
<td>LIST OF ACRONYMS</td>
<td>4</td>
</tr>
<tr>
<td>PROJECT SUMMARY</td>
<td>5</td>
</tr>
<tr>
<td>BACKGROUND</td>
<td>7</td>
</tr>
<tr>
<td>MAIN OBJECTIVE</td>
<td>8</td>
</tr>
<tr>
<td>SPECIFIC OBJECTIVES</td>
<td>8</td>
</tr>
<tr>
<td>METHODS</td>
<td>9</td>
</tr>
<tr>
<td>RESULTS AND DISCUSSION</td>
<td>14</td>
</tr>
<tr>
<td>CONCLUSION</td>
<td>17</td>
</tr>
<tr>
<td>NEXT STEPS</td>
<td>18</td>
</tr>
<tr>
<td>ANNEX A: Minilab Results</td>
<td>22</td>
</tr>
<tr>
<td>ANNEX B: Specific Active Pharmaceutical Ingredients of Interest of Philippines</td>
<td>25</td>
</tr>
<tr>
<td>ANNEX C: List of Essential Medicines for the FDA in a Suitcase (Quality Basket)</td>
<td>27</td>
</tr>
<tr>
<td>ANNEX D: Map of sentinel site locations in the Philippines</td>
<td>28</td>
</tr>
</tbody>
</table>
ACKNOWLEDGEMENTS

Deep gratitude is expressed by the authors of this Report to the United States Agency for International Aid and Development (USAID) for its sponsorship of the activities of United States Pharmacopeia Promoting the Quality of Medicine (USP PQM) in the Philippines.

For the mutual interest and efforts in participating in the activities of the Project Quality Monitoring of Anti-Tuberculosis drugs, we extend our sincere gratitude to Dr. Cora Manaloto and Dr. Padmaja Shetty.

For the provision and arrangement of all the logistics of the Minilab Project in the Philippines, words could never be enough in extending our appreciation to Laura Krech, Program Manager, Southeast Asia USP PQM. Worth mentioning as well are the unselfish advice and sharing of technical knowledge to Philippine FDA by Christopher Raymond, Dr. Mustapha Hajjou, Dr. Daniel Bempong, Dr. Lawrence Evance and Sanford Bradby.

Our FDA Director Nazarita T. Tacandong, thanks a lot for your valuable support. For the extensive advice, assistance and guidance throughout the entire course of the Project, Ms. Maria Lourdes Santiago, our sincerest appreciation for everything you have done. Maria Victoria Calub and Teresa Malabanan, and to other FDA employees who in one way or the other are contributory to the improvement and sustainability of the Project, thanks a lot.

We cordially acknowledge Dr. Yolanda Oliveros and Dr. Lyn Vianzon of the Department of Health National Center for Disease Prevention and Control (DOH-NCDPC) for their help in the implementation of the Project by means of monitoring the quality of medicines and in providing statistical data on cases of Tuberculosis in the country.

For their dedication and hardwork in carrying out the agreement, recognition is given to the six (6) sentinel sites and the Center for Health Development (CHD) of Regions 1, 3, 6, 7, 9, 11, and the Heads of the Local Government Units (LGUs) of Malolos City, Iloilo City and Zamboanga City; namely: Dir. Eduardo Janairo, Ryan Lewis, Veronica Obille, Joselyn Guzman, Dir. Rio Magpantay, Alicia Montano, Dir. Ariel Valencia, Gemma Tabiano, Dir. Susana Madrieta, Sarah Oriol, Grace Cardona, Monina Coyoca, Dir. Aristides Tan, Sharon Garcia, Dir. Teogenes Baluma, Gwendolyn Bardos, Eva Maghuyop, Estille Tutor, Danilo Domingo, Dr. Victor Batanes, Dr. Eric Villano, Jerry Trenas, Barabara Hortillo, Mirasol Gupiteo, Celso Lobregat, Maria Iryn Fortin, and Dr. Pascualito Concepcion.
<table>
<thead>
<tr>
<th>Acronym</th>
<th>Full Form</th>
</tr>
</thead>
<tbody>
<tr>
<td>API</td>
<td>Active Pharmaceutical Ingredient</td>
</tr>
<tr>
<td>ATB</td>
<td>Anti-Tuberculosis</td>
</tr>
<tr>
<td>BFAD</td>
<td>Bureau of Food and Drugs</td>
</tr>
<tr>
<td>BIHC</td>
<td>Bureau of International Health Cooperation</td>
</tr>
<tr>
<td>BP</td>
<td>British Pharmacopeia</td>
</tr>
<tr>
<td>CHD</td>
<td>Center for Health Development</td>
</tr>
<tr>
<td>DOH</td>
<td>Department of Health</td>
</tr>
<tr>
<td>DOTS</td>
<td>Directly Observe Therapy Short-course</td>
</tr>
<tr>
<td>FDA</td>
<td>Food and Drug Administration</td>
</tr>
<tr>
<td>FDC</td>
<td>Fixed Dose Combination</td>
</tr>
<tr>
<td>FDRO</td>
<td>Food and Drug Regulation Officer</td>
</tr>
<tr>
<td>GPHF</td>
<td>Global Pharma Health Fund</td>
</tr>
<tr>
<td>LGU</td>
<td>Local Government Unit</td>
</tr>
<tr>
<td>MQM</td>
<td>Medicine Quality Monitoring</td>
</tr>
<tr>
<td>NCDPC</td>
<td>National Center for Disease Prevention and Control</td>
</tr>
<tr>
<td>NTP</td>
<td>National Tuberculosis Control Program</td>
</tr>
<tr>
<td>PMS</td>
<td>Post Marketing Surveillance</td>
</tr>
<tr>
<td>PQM</td>
<td>Promoting the Quality of Medicine</td>
</tr>
<tr>
<td>TB</td>
<td>Tuberculosis</td>
</tr>
<tr>
<td>USAID</td>
<td>United States Agency for International Development</td>
</tr>
<tr>
<td>USP</td>
<td>United States Pharmacopeia</td>
</tr>
<tr>
<td>USP/NF</td>
<td>United States Pharmacopeia / National Formulary</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
</tr>
</tbody>
</table>
PROJECT SUMMARY

The Government of the Philippines has been involved in different programs concerning health issues more particularly in terms of the strategic detection, prevention and elimination of tuberculosis cases. Through the Department of Health (DOH), it has set its goal to implement a program that would help the nation’s dilemma on tuberculosis. Over the past years, the Directly Observed Therapy Short-course (DOTS) program has been in action to help Filipinos battle the disease. One of the five (5) important components of DOTS is the effective quality drug supply. Quality Anti-Tuberculosis (ATB) drugs being provided by the government is a key to the success of this program.

The United States Pharmacopeia Promoting the Quality of Medicine (USP PQM), through the support of United States Agency for International Development (USAID) Philippines, recognizes the need for the conception and implementation of a program that would monitor the quality of TB drugs available in the country. In close collaboration with the DOH and the Food and Drug Administration (FDA), it has been agreed upon to establish such program that would strengthen the national quality drug assurance system.

The project was designed to be implemented in six (6) pilot sentinel sites. Each sentinel site would collect ATB drug products to be tested for quality using Minilabs®. Samples that fail basic tests would be sent to the national laboratory for confirmatory testing. Minilab® testing does not replace pharmacopeial or legally accepted test methods. Instead, it identifies products requiring further investigation. No regulatory action can be initiated on the basis of the test results, and all samples considered to be potentially counterfeit or substandard are referred for testing so as to verify and confirm the findings of the initial screenings.

In May 2008, PQM conducted a training course in performing basic screening test on TB medicines. Fixed dose combination (FDC) of Isoniazid, Rifampicin, Ethambutol, and Pyrazinamide were identified using the Global Pharma Health Funds (GPHF) Minilab® with members of FDA, Center for Health Development (CHD) and Local Government Units (LGUs) as participants.

Signed as agreements between the DOH, FDA, CHDs and LGUs were written Department Order and Memorandum of Understanding. These formal agreements cover the guidelines and procedures on the pilot implementation of quality monitoring of anti-TB drugs that will be localized on the six sentinel sites chosen. The signing of this legal document took some time and caused the delay of the project’s commencement.
To assess the implemented monitoring program on TB medicines, the PQM team went to the Philippines in September 2008 and May 2009 to conduct visits in a sentinel site. One of its objectives is to observe how the Food and Drug Regulation Officer (FDRO) conducts sampling collection and to provide technical assistance, if needed.

In line with the monitoring program, a training to provide technical assistance with focus on the analysis of the four (4) fixed dose combination (FDC) TB medicines was held last September 28 to October 2, 2009 conducted by USP. The training is on Good Laboratory Practices and Pharmaceutical Analysis. Analysts from FDA were trained using HPLC and Dissolution techniques in accordance to the USP-NF specifications.

Field data results for TB medicines were obtained within the six-month analysis period which was initially performed on the six (6) sentinel sites. A total of three hundred twenty (320) samples were collected and tested from May to September of 2009. Sixty-six (66) samples were submitted to the FDA laboratory for confirmatory testing. Among the submitted samples, only one Rifampicin suspension was declared violative for not conforming with the BP Specification on pH test. However, it conformed on the assay. Eight (8) samples are still undergoing confirmatory testing at FDA.

Among the challenges encountered by the sentinel sites were (a) the lack of human resources, (b) time consumed to achieve targets on the sample collection and testing, and (c) other work-related priorities that need to be accomplished as part of their daily activities.
Comprised of 7,107 islands and consisting of seventeen (17) regions with Manila as its capital, the Republic of the Philippines is a country in Southeast Asia. The regions are geographically combined into three (3) major islands: Luzon, Visayas, and Mindanao. The projected population of the Philippines by the year 2010\(^1\) is 94,013,200.

Ranking ninth (9\(^{th}\)) in the roster of the twenty-two (22) countries stricken by Tuberculosis (TB),\(^2\) the Philippines bears much of the world’s TB-burden. With one hundred seven (107) Filipinos dying of TB every day, it is the country’s sixth leading cause of death and illness. The majority of TB cases are found between the age range of 15–54 year-old.\(^3\) Among the seventeen (17) regions, the highest number of new smear positive cases detected based on the NTP accomplishment report for 2009 is in Region 6, the Western Visayas. It was followed by the National Capital Region (NCR). Over the past years, the National Tuberculosis Control Program (NTP) serves as the country’s prime mover in its commitment to address the TB problem. The NTP which is being implemented nationwide through all government health centers has been in focused to reach its objective of detecting at least seventy percent (70\%) of active TB cases. This program has a success rate of at least eighty-five percent (85\%).

The main reason hindering the achievement of this target is drug resistance. Though considered as a natural response, it is also aggravated by several other factors such as rational drug use, poor patient compliance, poverty, and quality of available drugs in the market. The quality of these drugs, however, is affected and linked to storage condition and proper handling. These situations are mostly common in the informal sectors\(^{a}\). Substandard and counterfeit drugs have been proliferating around the country for years which is a serious health risk for the populace. Concerned primarily by the quality of medicines available, the PQM, as supported by the USAID, and through closed collaboration with the local government units, planned and created a project that would monitor the quality of TB medicines.

\(^1\) Philippines National Statistic Office. URL: \texttt{www.census.gov.ph/data/sector\_data/datapopproj.html}
\(^3\) USAID Philippines. Program. Health. Tuberculosis, URL: \texttt{http://philippines.usaid.gov/he_health_areas_tb.html}
\(^a\) Informal Sectors – Establishments that sell medicines without a valid license to operate.
The Regulation Division 1 of the FDA Philippines, through the support of the World Health Organization (WHO) has also proposed and conducted a training entitled “FDA/BFAD in a Suitcase” which aims to detect suspected counterfeits on fifteen (15) essential medicines (List see Annex C). In coordination with other organizations, it is setting forth a project in relation to monitoring the quality of medicines in local level within the sixteen (16) chosen regions. All the supplies that will be used shall be locally procured but the equipment in use is similar to the Minilab®. Commencement and sustainability of the project is still an ongoing subject matter. Once started, the initiative will be implemented in conjunction with the results of the PQM Program.

**MAIN OBJECTIVE**

- Strengthen the National Drug Quality Assurance System.

**SPECIFIC OBJECTIVES**

- Obtain evidence-based data from the field on the quality of selected ATB medicines
- Reduce the number of substandard ATB medicines circulating in the Philippines
- Expand the scope of sample collection on or outside the geographical areas of the selected sentinel sites.
- Increase public awareness on the dangers of substandard and counterfeit drugs.
- Provide training to enhance the capacity of the laboratory
METHODS

Six (6) sentinel sites were chosen based on the prevalence of TB cases and the presence of analysts and inspectors in the Center for Health Development (CHDs). Another factor in the selection process was the possibility of the project to succeed in such areas. In the end, the pilot sites (map at Annex D) composed of CHDs and Local Government Units (LGUs) which represent the three (3) major islands of the Philippines are as follows:

<table>
<thead>
<tr>
<th>MAJOR ISLAND</th>
<th>CHD</th>
<th>SENTINEL SITE</th>
<th>LGU</th>
<th>COORDINATING CHD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Luzon</td>
<td>Region 1</td>
<td>Ilocos</td>
<td>Malolos City</td>
<td>Region 3 – Central Luzon</td>
</tr>
<tr>
<td>Visayas</td>
<td>Region 7</td>
<td>Cebu City</td>
<td>Iloilo City</td>
<td>Region 6 – Western Visayas</td>
</tr>
<tr>
<td>Mindanao</td>
<td>Region 11</td>
<td>Davao City</td>
<td>Zamboanga City</td>
<td>Region 9 – Zamboanga Peninsula</td>
</tr>
</tbody>
</table>

Three (3) personnel in each of the six (6) sentinel sites were involved in implementing and performing the sample collection and sample testing using the Global Pharma Health Fund (GPHF) Minilab® Kits.

The following are the guidelines for the pilot implementation of the Project on the quality monitoring of anti-TB drug products, particularly Rifampicin, Isoniazid, Ethambutol, and Pyrazinamide using the Minilab® kits:

1. The Food and Drug Administration (FDA), in collaboration with the National Center for Disease Prevention and Control (NCPDC), is authorized to:
   a. Coordinate with CHDs, LGUs, and other stakeholders in the implementation of the Project;
   b. Design testing protocol and reporting system to ensure the success of the Project; and
   c. Facilitate the training to be conducted by the technical officers of the USP PQM Program.

2. The FDA shall prepare the Final Report and endorse it to the DOH’s National Center for Disease Prevention and Control (NCDPC). The FDA shall provide copies to the following:
   a. DOH’s Bureau of International Health Cooperation (DOH–BIHC);
   b. United States Pharmacopeia Promoting the Quality of Medicine (USP PQM) through the DOH-BIHC;
c. United States Agency for International Development (USAID) through the DOH-BIHC; and

d. CHDs and LGUs of Pilot Sentinel Sites

3. The NCDPC shall associate with the FDA in the monitoring of the Project and evaluate the Final Report for recommendation to the National TB Control Program.

I. SPECIFIC GUIDELINES:

1. Roles and Responsibilities:

1.1. The FDA shall:
   • In collaboration with NCDPC, PQM, and USAID, oversee the implementation of the entire Project;
   • Jointly monitor with the NCDPC the conduct of the Project in the pilot sentinel sites, in a quarterly basis or as the need arises;
   • Provide one (1) unit of Minilab® kit to each of the six (6) Pilot Sentinel Sites;
   • Provide the necessary and additional technical assistance in the use of the minilab kits;
   • Shall verify and confirm all of the non-conforming test results and the ten percent (10%) of the conforming test results generated from the Minilab®;
   • Determine which of the conforming test results will be further verified by the national FDA laboratory;
   • Shall prepare the Final Report of the Project;
   • Through a Memorandum of Understanding with the Local Chief Executives, shall request the LGU Technical Officers of Malolos City, Iloilo City, and Zamboanga City, to:
     ▶ Conduct random sampling of TB drug products in the market with the assistance of the CHD Partner Overseers;
     ▶ Conduct simple test procedures using the Minilab® kits on the products collected;
     ▶ Properly document all of the sample collections and testing conducted;
     ▶ Forward all products and original copies of the test results and other reports to the CHD Partner Overseers; and
     ▶ Submit monthly reports to the FDA Laboratory Services Division, through the DOH-CHD Partner Overseers. For this purpose, monthly reports shall include all products collected, the corresponding minilab test results, complete analytical data, and photocopy of the TLC plates. Non-conforming products and the minilab test results, however, shall be submitted immediately for appropriate FDA action.
1.2. The Food Drug Regulatory Officers (FDROs) of the respective CHD Partner Overseers 3, 6, and 9 shall:
   - Supervise the LGU Pilot Sentinel Site in the implementation of the Project;
   - Assist the LGU Pilot Sentinel Site in its conduct of random sampling of TB drug products in the market; and
   - Receive all products and original copies of the test results and other reports from the LGU Pilot Sentinel Site and immediately endorse these to the FDA Laboratory Service Division.

1.3. The Food Drug Regulatory Officers (FDROs) of CHDs 1, 7, and 11 shall:
   - Incorporate in its conduct of routine post-market surveillance the use of the Minilab® kits to perform simple test procedures on collected TB drug products in the market;
   - Properly document all sample collections and testing conducted;
   - Submit monthly reports to the FDA Laboratory Services Division, through the DOH-CHD Partner Overseers. For this purpose, monthly reports shall include:
     ✓ all products collected
     ✓ the corresponding Minilab® test results
     ✓ complete analytical data; and
     ✓ photocopy of the TLC plates.

   Non-conforming products and the Minilab® test results, however, shall be submitted immediately for appropriate FDA action.

1.4. The Project, through the PQM and USAID, shall support the implementation of the Minilab® testing initiatives including training, implementors’ travel costs and sample collection, data management, reporting, and monitoring including the hiring of a Project Secretariat.

1.5. The Project Secretariat (Ms. Yvette Lopez) assigned to the Project shall:
   - Report to FDA;
   - Consolidate all the laboratory reports and other relevant information and prepare the Final Technical Report;
   - Handle the procurement of supplies and materials for the Project;
   - Send to PQM an itemized list of the supplies, materials, and reagents; and
   - Respond promptly to any of the requests from PQM on the status of the Project in order to complete reports to be submitted to the USAID and the USP.

2. Ownership and utilization of and procurement of supplies for the minilab kits and technical data generated:
2.1. Minilab® Kit Ownership and Utilization

The FDA shall officially turnover the ownership of the Minilab® kits and will issue the corresponding Memorandum of Understanding and Invoice Receipt to the Directors of CHDs 1, 7, and 11. The respective CHDs shall be responsible for the full utilization and maintenance of the Minilab® kits after the Project.

The FDA shall provide the Minilab® kits to each of the LGU Pilot Sentinel Sites in Malolos City, Iloilo City, and Zamboanga City for the expressed purpose of the completion of the project. After the Project, the FDA shall officially turnover the ownership of the Minilab® kits to the LGU Pilot Sentinel Site, and will issue the corresponding Invoice Receipt through its Mayor.

2.2. Supplies/Consumables

The Project shall purchase the additional laboratory supplies needed in the utilization of the Minilab® kits.

The CHD Pilot Sentinel Site shall request for supplies through the Project Secretariat. The LGU Pilot Sentinel Site shall request for supplies through the CHD Partner Overseer. CHD Partner Overseer will communicate with the Project Secretariat about the reagents/supplies/materials that need to be ordered.

2.3. Technical Data Generated from the Minilab® Kit

All information generated from the Minilab® kits during the Project, shall be officially submitted to the FDA.

3. Sampling and Product Coding:

3.1. Samples will be collected from FDA licensed establishments only.

3.1.1. Public: hospitals, health clinics, dispensaries, drug stores, LGU warehouse

3.1.2. Private: hospitals, health clinics, drug outlets, drug traders, drug distributors

3.2. Quantity of samples to be collected is set at ten (10) per month, or 30 samples per quarter.

3.3. Sample is defined as follows:
3.3.1. Six (6) bottles for liquid dosage forms
3.3.2. Eighty (80) to one hundred (100) units for solid dosage forms
3.3.3. One (1) bottle X 80-100 tablets/capsules

3.4. Samples should be collected with their secondary packaging.

3.5. Product Coding shall be as follows:

<table>
<thead>
<tr>
<th>Pilot Sentinel Site</th>
<th>Coding</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHD 1: Ilocos</td>
<td>YY-CHD1-####</td>
</tr>
<tr>
<td>CHD 7: Central Visayas</td>
<td>YY-CHD7-####</td>
</tr>
<tr>
<td>CHD 11: Davao</td>
<td>YY-CHD11-####</td>
</tr>
<tr>
<td>LGU: Malolos City</td>
<td>YY-LGUM-####</td>
</tr>
<tr>
<td>LGU: Iloilo City</td>
<td>YY-LGUI-####</td>
</tr>
<tr>
<td>LGU: Zamboanga City</td>
<td>YY-LGUZ-####</td>
</tr>
</tbody>
</table>

4. Reports and Forms

The following reports shall be directly submitted to FDA on a monthly basis or 10 days after the end of each month, by the CHD Pilot Sentinel Sites and thru the CHD Partner Overseer by the LGU Pilot Sentinel Sites:

4.1. The Sentinel Site Sample Collection Form which provides the detailed information of the sample and the results obtained in basic test conducted.

4.2. Log sheet of all the products collected and the status of the quality monitoring from collection to issuance of the reports.

4.3. The Request for Analysis which officially endorses to FDA all products tested thru the minilab by the pilot sentinel sites. This is where FDA verifies the minilab tests results.
RESULTS AND DISCUSSION

Collection and testing of ATB drugs started in the second quarter of 2009. The method performed by the FDROs in each sentinel site is through random sampling on private and public drug establishments. The reporting system was designed to be done on a monthly basis, collecting and testing once a month followed by the submission of results to FDA Central Laboratory. The strategic area assigned to the FDROs was the location where they collect and buy samples. The aim of this strategy is to cover the entire region in monitoring ATB drug products.

Most of the sentinel sites have performed satisfactorily and achieved the required number of samples that need to be collected and tested in their area of responsibility. However, two (2) of the sentinel sites did not accomplish the required target, both of which were from the Local Government Units (LGUs). This can be associated with the lack of dedicated personnel to focus on the project. Another factor that hinders the success of the project on the LGU side is associated with the upcoming national election making them busy with different activities. Sentinel sites are composed of CHDs and LGUs, these are the two modes of approaches used in the pilot testing to determine the possibility of the success of the project. Initial data shows that CHDs performed better than the LGUs.

Evidence of data collection on the tested samples were gathered and examined. There were 320 ATB drug products collected and tested within the six-(6) month period of initial data collection. An analysis of the Project’s accomplishment within six (6) months of initial sampling had showed fifty (50) samples with unsatisfactory results in the basic test (see Annex A). The number of samples reflected in the report of the sentinel sites with unsatisfactory results may be due to proficiency of the staff to do basic testing. These samples were usually declared “doubtful” by the staff of the sentinel site. Some of the non-confirming results however were not submitted to FDA for confirmatory testing. One of the reasons for non-submission is the insufficient number of sample bought at the sentinel sites which are only adequate for conducting basic test procedure but not sufficient for confirmatory testing. The allowable minimum number of samples to be collected as approved by PQM was thirty (30) samples. When these samples were found to be of doubtful quality, FDROs would go back to the pharmacy of origin and search for the specific lot or batch number, In those situations, however, the particular lot/batch number happened to be no longer available in the pharmacy.
Out of the 320 samples, 66 were submitted to FDA Central Laboratory for confirmatory testing. Confirmatory test results showed that all samples conformed to the specifications of the tests conducted following USP32/NF27 and BP 2008. There is however one sample of Rifampicin 200mg/5ml suspension that did not conform to the specification for the pH test in BP 2008 which is pH 4.2-4.8 and the test result is pH 5.61. The results were forwarded to the Legal Information and Compliance Division for proper action. There were still eight (8) samples from the 66 submitted yet to be tested at the FDA central laboratory.

ATB drug samples that FDA routinely monitors and subjects to testing have not been a great concern to be among the list of counterfeit drugs that infiltrate the Philippine market. As shown in (Annex A), five-year data analysis, a very minimal percentage was seen for the ATB drugs to fail official procedures in the laboratory. This process is through performing Post Marketing Surveillance (PMS). One of the factors that may affect the quality of the product is the storage condition.

In 2009, the staff of PQM and FDA visited the six sentinel sites to assess the implementation of the Project and to provide technical assistance on how to perform the basic tests.

Factors that challenge the monitoring program are the following:

1. Lack of dedicated personnel to focus on the project
   - No new staff to do the basic test other than the participants who attended the May 2008 training
   - Some FDROs are taking leave of absence for personal reasons and there are no replacements

2. Lack of time to perform the Minilab® tests
   - FDROs have other responsibilities given to them by their supervisors

3. Problems in performing the confirmatory tests using the USP compendial method (ie. fixed dose combination difficulty in the analysis of ethambutol)
   - This problem was addressed during the Good Laboratory Practice (GLP) training in Sept/Oct 2009

4. Problems with the reporting system (data are not being reported properly)
   - Sentinel site sample collection and report form were not completely or properly filled out
   - Place where the samples were bought and sometimes the registration number are not indicated in the report form
   - Delays in submission of monthly reports
5. Lack of samples collected at the sentinel site
   • 19 samples were not submitted to FDA for confirmatory testing due to limited number of samples collected.

6. Frequent sampling collection and testing
   • For 2010, the number of samples to be collected per month per site has been reduced to five. Based on the data, it has been observed that the samples being collected were just the same as in the previous collection. They were just doing it to comply with what was stated in the protocol. To eliminate this practice, it has been proposed to reduced the number of samples collected per month.

We are proposing to hold an internal meeting with all the involved stakeholders to discuss these challenges and come up with a solution to ensure the success of the Project.
The project on quality monitoring of ATB drugs in the Philippines is functioning for more than a year now. It commenced in 2008 with the training for FDA, CHD, and LGU staff regarding the utilization of the Minilab®. Sampling and testing began at the six sentinel sites by the second quarter of 2009. Among the ATB drug products collected and observed within six (6) months of initial data collection, only one did not meet the specification in pH test.

The USAID support the Philippines by extending the medicine quality monitoring program of PQM for another year is really of advantage.

Having identified the challenges affecting the Project, we have proposed the following solutions to obtain better results and ensure participation by everyone:

1. The reporting system should be on a quarterly basis instead of monthly. The number of samples to be collected per month should be five (5). To allow the field staff focus on their routine work, only fifteen (15) samples per site per quarter are to be accomplished. In the near future, sample collection/testing may be implemented on a six-month (bi-annual) basis.

2. Extensive efforts should be exerted to collect ATB samples on geographical areas that have not been previously sampled.

3. Even if the quantity of drugs available are not sufficient, informal outlets commonly known as “sari-sari (variety) stores” and other informal sectors are to be subjected to sample collection of ATB drugs.

4. Wholesalers in Manila area should be included in the collection of ATB samples that are suspected to have quality problems, though it was already a part of the routine sampling by Regulation Division I.

5. Other ways, such as “Mystery Shopper Technique,” should be implemented.
6. Drug products that will be monitored for basic tests should be increased to include antibiotics and some essential drugs.

The quality of ATB drug products in the Philippines has not been evidently the main reason for the high incidence of TB cases. The high rate of TB cases in the country may be due to drug resistance and irrational drug use which is a serious health issue. Currently, it is an alarming incidence in the country. This reason for drug resistance may be exacerbated by several other factors, including abuse, underuse or misuse of antimicrobials, poverty, and poor patient compliance.

NEXT STEPS

As products of public health importance needed to maintain and promote better health for the majority of the population, essential drugs can address many of the leading causes of morbidity and mortality in the country. However, the persistent burden of preventable diseases like TB, malaria, and pneumonia, as well as, the increasing trend in morbidity from complications of chronic diseases, seems to indicate that access to these health products, along with other factors, is not being met adequately.

In looking for means to meet this inadequacy, the government needs to further improve its approaches in ensuring access to essential drugs, particularly for the poor sector and other vulnerable groups. The lack of information by patients on the nature of their disease or physical condition and the corresponding treatment thereof makes them vulnerable to the hazards and costs of self medication and irrational treatment.

As multinational companies dominate the pharmaceutical market, access to safe, effective and cheap drugs have been among the major problems affecting the health sector. Through parallel drug importation, efforts have been made to provide access to cheaper medicines. The poor and the disadvantaged segment of the populace still have limited access to cheap and quality medicines.

This situation seems to be among the reasons for an international movement to be espoused by countries and international agencies. Hence, the Millenium Development Goals came into being to ensure sustainability and assure universal primary education.

In the Philippines, initiated by the Department of Health is the FOURmula One (F1) for Health which seeks to enhance the performance of the health sector by improving the provision and financing of health services with the expansion of the national and local public health programs, increasing access to personal health services provided by public
and private providers especially among the poor, and reducing the burden on individual families through universal coverage of the national health insurance program. With four major components such as (1) health financing, (2) governance, (3) health regulations, and (4) service delivery, this initiative was adopted as the implementation framework for health sector reforms for the medium term period through Administrative Order No. 2005-0023 dated August 30, 2005. It is designed to implement critical health interventions supported by effective management infrastructure and financing arrangements. Its implementation is geared towards achieving health systems goals of the World Health Organization, the Millennium Development Goals (MDGs), and the Medium-Term Philippine Development Plan (MTPDP) for (a) better health outcomes, (b) more responsive health system, and (c) more equitable health financing.

The major function of the government that ensures access to quality products, devices, facilities and services for the improvement and well being of the population, particularly the poor is Health Regulation. Inclusive of the setting up and monitoring of systems, standards, rules, and regulations and compliance, health regulation also involves harmonizing, licensing, accreditation and certification of health products and services (DOH, 2005b, 2005c).

The Food and Drug Administration has the following priority plans to address in the next 2-3 years to ensure the safety, efficacy and quality of imported and locally produced medicines.

1. Good Manufacturing Practice (GMP) compliance for manufacturers

   GMP is the part of quality assurance that ensures that medicines are consistently produced and controlled according to the quality standards of their intended use and product specifications.

   - Provide national legislation and regulations for controlling pharmaceutical production.
   - Align the existing Good manufacturing practice guidelines with that of the international guidance such as PICS.
   - Promote compliance with current GMP guidelines for medicines production by regulation.
   - Enforce compliance with current GMP guidelines by all medicines manufacturers.

2. Adoption of ASEAN Common Technical Dossier (ACTD)

   ACTD is the part of marketing authorization that is common to all ASEAN member countries. It is based on the agreed upon common format for the preparation of well structured CTD applications that will be submitted to ASEAN Drug Regulatory Agencies (DRAs) for the pharmaceuticals for human use. FDA has the following objectives:
To have a common format for both administrative and technical documentation which will significantly reduce the time and resources needed to compile applications for registration, and/or will ease the preparation of electronic submissions.

To facilitate regulatory assessment and correspondence with the applicant by having a standard document of common elements.

To simplify the exchange of regulatory information between DRAs.

3. Implementation of Bioequivalence (BE) to certain drugs to ensure interchangeability

To confirm that the pharmaceutical products being registered, procured, or used can produce the expected therapeutic result, FDA must request BE studies for multisource or generic pharmaceutical products data. There are two institutions in the Philippines conducting BA/BE studies, the University of Santo Tomas Center for Drug Research and Evaluation Studies (UST CeDRES) and La Salle University.

4. Expansion of quality monitoring projects such as the implementation of “FDA in a Suitcase” in all regions

To speed up detection of the active ingredients of the suspected counterfeit drugs, FDA expanded the quality monitoring program. One of this is the “FDA in a Suitcase”, containing simple apparatus, laboratory reagents, and rapid test procedures. This course of action will be more helpful for the FDROs in their field inspection and monitoring. The FDROs will conduct basic test such as visual inspection, disintegration and TLC test for products which are suspicious based on the physical appearance. Those drugs found negative for active ingredients will be prioritised for quantitative analysis at FDA Laboratory Services Division, thereby, expediting the release of official results of analyses.

In lieu of the increasing responsibilities of FDA in the field and its compliance with its mandate, there is then a greater need to enhance the capacities and capabilities of its FDROs for the effective and efficient accomplishment of their local task of quality monitoring of drugs; and ensuring that these are safe, pure, and effective.

FDA has the following outline or summary of strategies to be implemented in the next five years to improve the quality of essential medicines.

1. Train other government staff from CHD / LGU to learn how to perform basic testing.

2. Expand the scope of drug samples to be tested.

3. Choose and evaluate potential sentinel sites in addition to the existing sites.
4. Set a small laboratory area in the regional offices to conduct the basic test.

5. All consumables will be procured locally.

6. Provide a reporting system that would be easily followed.

5. Capacity building for all technical personnel to address fast and emerging issues confronting the food and drug regulation system.
ANNEX A

Table 1: Minilab® result and a five year data of FDA on the ATB drugs routinely collected in public sectors and tested in the laboratory.

<table>
<thead>
<tr>
<th>Year</th>
<th>Total No. of samples tested of all medicines (TB Medicines)</th>
<th>No. of samples that passed testing (basic testing and confirmatory testing)</th>
<th>No. of samples that failed confirmatory testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>2005</td>
<td>81</td>
<td>81</td>
<td>0 / 0%</td>
</tr>
<tr>
<td>2006</td>
<td>128</td>
<td>124</td>
<td>4 / 3.125%</td>
</tr>
<tr>
<td>2007</td>
<td>62</td>
<td>62</td>
<td>0 / 0%</td>
</tr>
<tr>
<td>2008</td>
<td>51</td>
<td>51</td>
<td>0 / 0%</td>
</tr>
<tr>
<td>2009</td>
<td>194</td>
<td>189</td>
<td>5 / 2.58%</td>
</tr>
<tr>
<td>Minilab® 6 Mos. Sampling May-Sept 09</td>
<td>320</td>
<td>319</td>
<td>1 / 0.32%</td>
</tr>
</tbody>
</table>

The numbers shows a minimal percentage of non conforming results. Reasons for such failure are due to the administrative requirement of the FDA on batch certification and non compliance to pH requirements.

Table 2: Number of results using the minilab kit per sentinel site for 2009 (Satisfactory vs. Not Satisfactory)

<table>
<thead>
<tr>
<th>TEST RESULT</th>
<th>LUZON CHD1</th>
<th>LUZON LGU Malolos City</th>
<th>VISAYAS CHD 7</th>
<th>VISAYAS LGU Iloilo City</th>
<th>MINDANAO CHD 11 Davao City</th>
<th>MINDANA O LGU Zamboanga City</th>
</tr>
</thead>
<tbody>
<tr>
<td>MINILAB KIT TEST RESULT SATISFACTORY</td>
<td>43</td>
<td>20</td>
<td>60</td>
<td>51</td>
<td>62</td>
<td>34</td>
</tr>
<tr>
<td>MINILAB KIT TEST RESULT NOT SATISFACTORY</td>
<td>22</td>
<td>9</td>
<td>0</td>
<td>9</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>TOTAL</td>
<td>65</td>
<td>29</td>
<td>60</td>
<td>60</td>
<td>66</td>
<td>40</td>
</tr>
</tbody>
</table>
A total of 50 samples against 320 collected and tested were found to be of unsatisfactory result through the use of the minilabs®. The number of samples reflected in CHD 1 with unsatisfactory result may be due to proficiency to do basic testing. These samples were usually declared “doubtful” by the staff of the sentinel site. Some of these samples were not submitted to the FDA because the samples collected were insufficient to conduct confirmatory testing.

**Graph 1:** Overall Failure vs. Passed Rate 2009
(Based on confirmatory testing at FDA)

**Graph 2:** Total Number of samples tested per round*

*Round is the no. of time the sentinel sites collect and test TB samples using the Minilab® in a year.

**Graph 3:** Summary of private and public outlets to where TB samples were collected
Most of the samples collected at the sentinel sites were from the private drug establishments and currently some sentinel sites were focus to collect within the cities only.

**Graph 4:** Overall test result by each Active Pharmaceutical Ingredient (API)
The three graphs (3-5) below shows the Active Pharmaceutical Ingredients (API) that usually being reported as counterfeits in Philippines.

**Graph 3:** Shows the 5 year trend of Amoxicillin (as trihydrate)

![Graph 3: Amoxicillin Trend](image)

**Graph 4:** Shows the 5 year trend of Cloxacillin (as sodium)

![Graph 4: Cloxacillin Trend](image)
The three API presented above were usually collected from public drug establishments by the FDA inspectors. Through Post Marketing Surveillance (PMS), they were able to detect quality problems in the available products in the market. The graph shows a variable values from year 2005 to 2009. The numbers detected does not decrease through the years. Compare to the 5 year data result of ATB drugs collected in Table 1, it showed that these three drugs have a higher failure rate than the ATB drug products.
## List of 15 Essential Medicines

<table>
<thead>
<tr>
<th></th>
<th>Medicine</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Amoxicillin</td>
</tr>
<tr>
<td>2</td>
<td>Ampicillin</td>
</tr>
<tr>
<td>3</td>
<td>Aspirin</td>
</tr>
<tr>
<td>4</td>
<td>Cephalexin</td>
</tr>
<tr>
<td>5</td>
<td>Chloramphenicol</td>
</tr>
<tr>
<td>6</td>
<td>Ciprofloxacin</td>
</tr>
<tr>
<td>7</td>
<td>Cloxacillin</td>
</tr>
<tr>
<td>8</td>
<td>Erythromycin</td>
</tr>
<tr>
<td>9</td>
<td>Furosemide</td>
</tr>
<tr>
<td>10</td>
<td>Glibenclamide</td>
</tr>
<tr>
<td>11</td>
<td>Paracetamol</td>
</tr>
<tr>
<td>12</td>
<td>Phenoxyymethylpenicillin</td>
</tr>
<tr>
<td>13</td>
<td>Prednisone</td>
</tr>
<tr>
<td>14</td>
<td>Quinine SO₄</td>
</tr>
<tr>
<td>15</td>
<td>Salbutamol</td>
</tr>
</tbody>
</table>
ANNEX D

Location of Sentinel Sites

San Fernando City
Iloilo City
Zamboanga City
Cebu City
Davao City
Figure 1 FDA Central Laboratory staff headed by Ms. Maria Lourdes C. Santiago