RPM Plus National Training Course on Pharmaceutical Management for Malaria, Phnom Penh, Cambodia, December 4-8, 2006

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About RPM Plus

RPM Plus works in more than 20 developing and transitional countries to provide technical assistance to strengthen drug and health commodity management systems. The program offers technical guidance and assists in strategy development and program implementation both in improving the availability of health commodities—pharmaceuticals, vaccines, supplies, and basic medical equipment—of assured quality for maternal and child health, HIV/AIDS, infectious diseases, and family planning and in promoting the appropriate use of health commodities in the public and private sectors.

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ACRONYMS

ACT	artemisinin-based combination therapy
ACTMalaria	Asia Collaborative Training Network for Malaria
A+M	artesunate and mefloquine
ARI	acute respiratory infection
CNM	National Center for Entomology, Parasitology and Malaria Control
GFATM	Global Fund to Fight AIDS, Tuberculosis and Malaria
GMP	good manufacturing practices
MSH	Management Sciences for Health
RDT	rapid diagnostic test
RPM Plus	Rational Pharmaceutical Management Plus (Program)
STG	standard treatment guidelines
USAID	U.S. Agency for International Development
WHO	World Health Organization

EXECUTIVE SUMMARY

The national training course on Pharmaceutical Management for Malaria was held in Phnom Penh, Cambodia, December 4-8, 2006. As a complementary activity to promote the management and rational use of medicines in public health facilities, RPM Plus conducted this pharmaceutical management training course to strengthen the capacity of national malaria program personnel as well as staff from provincial and district medical stores and the national quality control laboratory. By strengthening capacity to better manage antimalarials, it is anticipated that health care staff will be able to transfer their pharmaceutical management skills to better manage other essential medicines.

All participants were Ministry of Health employees. In attendance were 22 participants from six U.S. Agency for International Development (USAID) priority provinces and 12 from the central level, including the national malaria control program, procurement unit, planning unit, central medical stores, and national laboratory. The course provided information and hands-on practice to facilitate national program managers' understanding and implementation of basic pharmaceutical management concepts and methods as well as the monitoring the implementation process in the context of pharmaceutical management.

The course was funded through the Regional Development Management Office of Asia (RDM/A) and organized by the RPM Plus Program of Management Sciences for Health (MSH) in collaboration with the National Entomology, Parasitology and Malaria Control Program. This is the first time an RPM Plus Pharmaceutical Management for Malaria training course was offered in the region. It is anticipated that the Asia Collaborative Training Network for Malaria (ACTMalaria) will sponsor future such training courses in the sub-Mekong region[1].

The overall goal of the Pharmaceutical Management for Malaria course was to build national capacity and increase knowledge and awareness of the elements of pharmaceutical management that affect access to and rational use of antimalarial medicines. Workshop materials focused on pharmaceutical management for malaria, particularly the selection and quantification of antimalarials, procurement, distribution, quality assurance, rational use, and monitoring and evaluation. Participants learned practical approaches for applying key concepts in monitoring the pharmaceutical management cycle. By the end of the course, participants were able to understand basic pharmaceutical management theories, establish mechanisms for managing antimalarials and related supplies, and also identify key performance indicators for monitoring implementation of malaria case management programs.

The workshop consisted of presentations, discussions, and group exercises. The design was highly participatory, and the exchange of skills and experience among participants added valuable depth to the learning process. The workshop was conducted predominantly in English with simultaneous Khmer translation, and course materials were made available in English and Khmer. Course materials were developed by the Rational Pharmaceutical Management (RPM) Plus Program.

[1] A representative from ACTMalaria from Manila, Phillipines attended the course

BACKGROUND

With an incidence rate of 7.5 per 1,000 and 382 deaths in 2004, malaria in Cambodia is currently the third most common cause of outpatient visits, the fifth main health problem among inpatients and the second most common cause of hospital mortality, despite the limited areas of transmission in the country (forested hilly areas)[2]. Also, malaria treatment and control is hampered by the spread of resistance to common antimalarial medicines, especially along the Cambodian-Thailand border where multi-drug resistant malaria is prevalent. Another compounding problem has been the high prevalence of counterfeit and substandard antimalarial medicines sold across the country.

Since 2001, the Rational Pharmaceutical Management (RPM Plus) program has worked with the Ministry of Health and other partners in Cambodia to determine the strengths and weaknesses of the pharmaceutical management system at the central and community levels to support access to essential medicines, especially in relation to child health and malaria services. RPM Plus experience in working with malaria and child survival issues indicate that lack of access to quality medicines and pharmaceutical services is a serious problem in rural and urban areas and likely contributes to Cambodia's high level of childhood morbidity and mortality.

A key finding in many drug management surveys conducted by Management Science for Health include the low availability of essential medicines and supplies in public health facilities especially those used in the treatment of malaria. Blister packs of Artesunate and Mefloquine intended for children, were found to be available at 57% of public health facilities (n=269) while choloquine was found to be available at 21% of the same facilities[3].

In an effort to address this issue, as well as the other identified gaps in pharmaceutical management, the Mission and RPM Plus discussed the notion of strengthening supervision at district level medical stores to ensure better drug availability in USAID priority geographic areas. As a complementary activity to promote the management and rational use of medicines in public health facilities, RPM Plus conducted the Pharmaceutical Management of Malaria (PMM) course to strengthen the capacity of national malaria program personnel as well as staff from provincial and district medical stores. By strengthening capacity to better manage antimalarials, it is anticipated that health care staff will be able to transfer their pharmaceutical management skills to better manage other essential medicines.

RPM Plus in partnership with the National Center for Parasitology, Entomology and Malaria Control (CNM) conducted a national training course on Pharmaceutical Management for Malaria (PMM) from December 4-8, 2006 in Phnom Penh, Cambodia. The PMM workshop focused on developing capacity at all levels to manage medicines and supplies for the national malaria control program. The workshop targeted individuals involved in the pharmaceutical

[2] National Health Statistics Report. 2003. Cambodia.

[3] Lynders, M., J. Briggs, C. Theary, C. Ketsana. 2006. *Community Drug Management for Childhood Illness: Cambodia Assessment, December 2004.* Submitted to the U.S. Agency for International Development by the Rational Pharmaceutical Management Plus Program. Arlington, VA: Management Sciences for Health.

management of malaria, as well as those responsible for the process of procurement and estimating needs of antimalarials and related commodities.

Purpose of the Course

This course provides information and develops skills that are useful in managing medicines and supplies for national malaria programs.

General Objectives

By the end of the course, participants will be able to identify—

1. Appropriate criteria for the selection of first- and second-line medicines and supplies for the national program, taking into consideration the World Health Organization (WHO) recommendations

2. Assumptions and basis for quantification, select an appropriate method for quantification, and identify appropriate sources of data

3. Good procurement practices for antimalarial medicines and other commodities

4. Technical specifications and appropriate mechanisms of supply to ensure the quality of medications and commodities are procured and used in the national malaria program

5. Appropriate mechanisms to guarantee that medicines and supplies are stored and distributed to health care providers at the right moment and in adequate quantities

6. Appropriate mechanisms for ensuring rational use of antimalarial medicines

7. Effective monitoring mechanisms to assure availability and use of antimalarial medicines and related commodities

METHODOLOGY

The national training course on Pharmaceutical Management for Malaria in Cambodia was a five-day course designed to be highly participatory to provide an opportunity for the exchange of skills and experience among participants as an added dimension of the learning process.

The workshop sessions used a combination of the following methods—

- Presentations
- Discussions
- Group exercises
- A field activity

The training course consisted of nine sessions—

Course Overview and Objectives
Session 1: Introduction
Section 2: Monitoring and Evaluation
Session 3: Selection
Session 4: Quantification
Session 5: Procurement
Session 6: Storage, Distribution, and Inventory Management
Session 7: Quality Assurance
Session 8: Rational Medicine Use
Session 9: Field work

RPM Plus staff members facilitated the workshop, using training course materials developed by RPM Plus. The workshop was conducted primarily in English with Khmer interpretation. Materials were available in both languages, and presentations were projected simultaneously in both Khmer and English. Simultaneous interpretation to and from English was provided during presentations, discussions, group exercises, and the field activity.

Participants made presentations to share experiences on particular aspects of implementation within the context of their program. Field visits were organized on the last day of the workshop to the central medical stores, the National Quality Control Laboratory, two health centers and the Phnom Penh Municipality hospital. Participants took the opportunity to apply the knowledge gained during the course to develop and apply indicators for monitoring and evaluation of various aspects of pharmaceutical management for malaria during the fieldwork.

WORKSHOP PROCEEDINGS

Welcome and Introductions

Ms. Lynders welcomed the course participants and invited guests of honor, and provided a brief rationale for the training course. Opening remarks were made by Jonathan Ross, USAID; Dr. Michael O' Leary, WHO; Dr. Doung Socheat, Director of CNM; and Dr. Lon Chanthap, Vice Director of CNM.

Plenary Presentations

Course overview and objectives

Presenter: Marion Lynders

The objectives of this workshop were designed so that participants will be able to identify—

1. Appropriate criteria for the selection of first- and second-line medicines and supplies for the national program, taking into consideration the World Health Organization (WHO) recommendations

2. Assumptions and basis for quantification, select an appropriate method for quantification, and identify appropriate sources of data

3. Good procurement practices for antimalarial medicines and other commodities

4. Technical specifications and appropriate mechanisms of supply to ensure the quality of medications and commodities are procured and used in the national malaria program

5. Appropriate mechanisms to guarantee that medicines and supplies are distributed to health care providers at the right moment and in adequate quantities

6. Appropriate mechanisms for ensuring rational use of antimalarial medicines

7. Effective monitoring mechanisms to assure availability and use of antimalarial medicines and related commodities

The course outline and methodologies to be used in this workshop were described.

Plenary Discussions on Course Objectives and Expectations

Participants were given the opportunity to express their expectations of the training course. The following was a summary of participant expectations and needs—

- Mastery of quantification methods

- Availability of artemisinin-based combination therapies (ACTs) and rapid diagnostic tests (RDTs)
- Quality assurance
- Private sector experience

Session 1. Introduction

Presenter: Marion Lynders

This session introduced the general concept of pharmaceutical management and the management of malaria medicines and supplies in particular, with an emphasis on the differences in the management of malarial commodities compared to other pharmaceuticals.

The pharmaceutical management cycle was used to graphically illustrate the interdependent relationships among various activities—selection, procurement, distribution, and use of malaria medicines within the existing policy and legal framework. Careful management and coordination of those activities are necessary for the cycle to function optimally. By understanding the elements of pharmaceutical management and the challenges presented by antimalarial medicines and current approaches to treatment, managers will be able to improve the efficiency of their programs, aim for the most rational use of medicines, and develop beneficial relationships with the private sector, thus ensuring availability of malaria medicines to the public.

Upon completion of this session, the participants were able to—

- Define each of the components of the pharmaceutical management cycle and its relationship to the other components
- Discuss the importance of pharmaceutical management for the success of malaria programs
- Discuss the challenges to effective antimalarial commodity management
- Discuss how the management of antimalarials differs from that of other pharmaceuticals
- Identify the effect of pharmaceutical management practices on availability and quality of malaria medicines

Group Activity

The session was followed by a group activity where the participants evaluated and identified the main pharmaceutical management problems and weaknesses experiences in their provinces and districts. Using the pharmaceutical management cycle, participants identified the following problems associated with each element.

Policy and Legal Framework:

- Large number of substandard medicines and fake drugs circulating in the market
- Laws exist but are not enforced. Local authorities have little power to enforce the laws. Provincial governors need to be involved in law enforcement.
- Need better collaboration among stakeholders, organizations, and across public and private sectors
- Private sector remains largely unregulated
- Lack of skilled human resources
    - Inadequate number of trained pharmacists
    - Not enough inspectors to monitor/inspect commodities

Management Support:

- No mechanisms exist to create linkages between public and private sectors
- Low motivation of staff especially at district level
- Need more technical and human resources support from national level
- Staff at warehouses/depots have poor drug management skills

Procurement:

- Delays in supplies are frequent.
- Tenders are carried out at the national level with no feedback to district level
- Due to regular stock outs, supplement supplies of antimalarials and commodities are purchased locally of unknown quality. Participants reported that in select provinces, an NGO purchased an emergency supply of Quinine from a local source which was dispensed to patients
- Short expiry dates of medicines
- Program staff are largely unaware of the procurement procedures at MOH and within different agencies
- Program staff are largely unaware of how drug estimates/quantification are determined
- Greater need for transparency
- Often tender documents are ready but the Ministry of Finance does not make funds readily available which creates further delays

Distribution:

- Some medicines are supplied to district medical stores but are not requested or needed
- Medical stores receive medicines not in response to need
- Waiting for procurements to arrive results in delays in distribution
- There are no control measures to ensure timely and sufficient supplies are delivered to the operational district level
- There are no quality control measures placed on NGOs that supply certain medicines. Some NGOs purchase medicines such as chloroquine and malarine from private sources

Rational Use:

- Need more support to reach populations in high risk forested areas

- Repeat stock outs of antimalarials and Rapid Diagnostic Tests (RDTs)
- RDTs are expensive
- RDTs detect P. *falciparum* only
- Patients use private sector more as they perceive service is better
- Providers are not following standard treatment guidelines (STG), contributing to increased drug resistance. Last training was provided in 2000-2001 with no follow up or refresher training since
- Patients do not adhere to treatment protocols
- Many patients self treat
- Some providers do not administer artesunate suppositories correctly
- Refrigeration required to store suppositories is inadequate at some facilities
- Monotherapy use is widespread

Session 2. Monitoring and Evaluation

Presenter: Rima Shretta

This session described how, when, and why to monitor the performance of the pharmaceutical management system for malaria. The session briefly covered assessment or diagnosis of pharmaceutical management systems and also provided an overview of methodologies used to evaluate the effect of interventions and the effectiveness of their implementation. The main focus was on monitoring and improving performance through indicator-based methods, supportive supervision, on-the-job training, and capacity building.

After completing this session, participants were able to—

- Differentiate between monitoring and evaluation
- Describe performance monitoring
- Describe the performance improvement process
- Provide information on methods to monitor performance and evaluate the effect of pharmaceutical management interventions
- Identify key performance indicators for monitoring management of malaria medicines and pharmaceutical supplies
- Elaborate on the use of monitoring systems in improving performance of the malaria pharmaceutical management system and evaluate the effect of pharmaceutical management interventions
- Evaluate the quality of the data
- Have an opportunity to become familiar with the concepts of performance monitoring and evaluation through group exercises and fieldwork

Session 3. Selection

Presenter: Rima Shretta

This session focused on the process of evidence-based selection of first-line treatment policies for malaria, taking into consideration factors such as parasitic resistance to the various medicines being considered, efficacy, cost, quality, adverse effects, acceptability, and the system's management and distribution capabilities. Program managers were reminded to carefully balance need against resources and ease of implementation. In addition, recommendations from international experts such as WHO need to play a part in the treatment selected.

Upon completion of this session, participants were able to—

- Discuss the basic principles of selection of appropriate essential antimalarial medicines
- Define the WHO's recommendations for treatment of *Plasmodium falciparum* and *P. vivax* malaria
- Discuss the process of selection of first- and second-line treatments for malaria
- Discuss the challenges for selection of first- and second-line antimalarial treatments
- Define essential medicines lists and standard treatment guidelines (STGs) and their relationship to each other

Session 4. Quantification

Presenter: Rima Shretta

This session outlined the rationale for quantification of antimalarials and identified the methods commonly used for quantification and the data needed. It also looked at the particular issues related to malaria medicine quantification. The four commonly used quantification methods—morbidity, consumption, adjusted consumption, and service-level extrapolation—were described in detail, with discussions on the principles underlying the choice and use of the various methods. When treatment policies are changed, policy makers must take into consideration essential data sources for each quantification method and the weaknesses of the various types of data together with the challenges to the quantification of antimalarials in the context of selecting a new treatment policy, including the assumptions that need to be made in the practical execution of the quantification process.

Participants practiced the morbidity and consumption methods using examples until they grasped concepts.

By the end of the session, participants were able to—

- Outline the rationale for quantification of antimalarials

- Identify four methods commonly used in the pharmaceutical quantification process and describe their uses, strengths, and limitations
- Recognize data needed to conduct the quantification
- Discuss particular issues related to malaria medicine quantification, including the assumptions that must be made
- Outline the steps for using the consumption and morbidity methods
- Practice the morbidity and consumption-based methods

Plenary Discussions on Quantification

Quantification remains a challenge for district and provincial level personnel. Challenges were centered around the capacity to do quantification. In Cambodia quantification is carried out by the provincial level and lower levels are often not involved. There was some discussion about triangulating morbidity and consumption data in certain districts.

Session 5. Procurement

Presenter: Kathy Webb

This session reviewed the standard methods of the procurement process and the resources (organizational components) that a supply system must have to procure medicines and supplies at the lowest possible total cost. The session outlined some procurement processes and requirements of theGlobal Fund to Fight AIDS, Tuberculosis and Malaria (GFATM), particularly in relation to how they affect national-level procurement of ACTs and other related antimalarials (procured using GFATM resources).

By the end of the session, participants were able to—

- Identify and describe the steps in the procurement cycle
- Compare the advantages and disadvantages of the four alternatives for purchasing medicines: open tender, restricted tender, competitive negotiation, and direct procurement
- Recognize the characteristics of a good pharmaceutical procurement system
- Understand the necessary components of a procurement plan and maintain an efficient procurement timetable with minimal lead time
- Recognize the importance of price comparison as an indicator of procurement efficiency

- Discuss GFATM procurement requirements in relation to procurement of first-line antimalarials

Plenary Discussions on Procurement

Participants asked about the shelf life of ACTs and the effect of the long procurement process on shelf life. Ms. Webb explained that according to WHO, ACTs that arrive in country should have at least 18 months' shelf life remaining before expiry; however, because of this short shelf life, all the elements of the distribution cycle must be well prepared before the ACTs arrive in country.

Participants were informed that although the production of ACTs has been increased to meet growing demand, the importance of taking delivery lead time into consideration when ordering ACTs is paramount.

Presentation on: Availability of ACTs and Related Procurement Issues

Dr. Yim Yann, President of the Pharmacist Association of Cambodia (PAC) gave a presentation on "Counterfeit Drugs and Drug Accessibility in Cambodia." (see Annex 2) Dr. Yann spoke primarily about the key issues surrounding counterfeit drugs in Cambodia; lack of awareness of the public and decision makers about the problem, lack of legislation and political will, lack of collaboration and cooperation between different regulatory agencies at the national level and between countries, and the issues of poverty and low purchasing power.

Dr. Yann cited several examples of quality tests performed by MOH, MSH and USP/DQI, indicating that most counterfeit antimalarials failed quality testing because of no active ingredient. He reported that 50% of medicines in Cambodia are currently not registered. He further explained that 25% of artesunate tablets failed quality testing because of no active ingredient in 2003. According to Dr. Yann, the main obstacles to finding solutions to the problems associated with counterfeit and substandard medicines are corruption, lack of cooperation among drug regulatory agencies across borders, weak law enforcement, weak penalties for offenders, and a weak post marketing surveillance system.

In his suggestions to tackle the growing problem of counterfeit medicines in Cambodia, Dr. Yann discussed the procedure for the Rapid Alert System which was proposed by the MOH in 2005, but has yet to be implemented to its fullest extent. He further proposed developing the following potential strategies to address the issues related to counterfeit medicines in Cambodia:

- A multi-level performance-based network of pharmacies, franchised rural health care and private clinics
- A group purchasing cooperative for network and perhaps non-network facilities
- An innovative community based health insurance schemes
- A comprehensive government controlled drug quality assurance program
- Community based care programs including public participation in all facets of drug management, planning, education and evaluation

Session 6. Storage, Distribution, and Inventory Management

Presenter: Kathy Webb

This session discussed the elements in a distribution system—including its design (centralized or decentralized), the information system, the storage conditions, the delivery mechanism, and inventory management—and analyzed each of those elements while discussing a variety of options for improving the efficiency of the entire system.

By the end of the session participants were able to—

- Discuss the various components of the distribution cycle
- Discuss the principles of good storage, distribution, and inventory management
- Identify the inefficiencies in participants' distribution, storage, and inventory management systems
- Discuss mechanisms to improve the efficiency of storage, distribution, and inventory management systems
- Calculate and discuss inconsistencies between physical inventory and recorded quantities

Plenary Discussions on Storage, Distribution, and Inventory Management

Participants were referred to *Managing Drug Supply*,[1] and copies were distributed to participants who are directly involved in drug management in each province as well those at national level.

The director of the Battambang provincial health department, Dr. Ngek Bun Chhup, gave a brief presentation of pharmaceutical inventory practices at the provincial and district level drug stores.

Session 7. Quality Assurance (see Annex 3)

Presenter: Abdelkrim Smine

In this session, quality assurance and the different approaches to it were clarified. The session expanded the participants' awareness of global concerns regarding the use of substandard pharmaceuticals and the cause of their proliferation as well as the determinants of pharmaceutical quality. It emphasized both the technical and managerial actions that can be used to ensure pharmaceutical quality.

After completing this session, participants are able to—

[1] Management Sciences for Health and World Health Organization. 1997. *Managing Drug Supply*. 2nd ed. West Hartford, CT: Kumarian Press.

- Specify what is meant by quality assurance and quality control in managing the supply of antimalarials and identify the factors that affect their quality

- Describe the components of a comprehensive quality assurance program and practical framework at different levels of responsibility

- Identify practical technical and managerial approaches and procedures to ensure pharmaceutical quality in daily activities

Plenary Discussions on Quality Assurance

Participants raised the issue of the need to continue testing to ensure quality antimalarials are available at the peripheral levels. Mr. Smine responded that Cambodia is procuring ACTs using GFATM funds and GFATM has a formal policy for procurement of limited or single-source pharmaceuticals, requiring that manufacturers must be WHO pre-qualified or internationally recognized as adhering to good manufacturing practices (GMP).

Mr. Smine also described the current surveillance system set up in Cambodia. He explained that teams travel the country performing quality tests on medicines and samples that are suspected of being substandard are sent to the national quality control lab for confirmation.

One participant asked about quality control measures that could be performed at the health facility level. Mr. Smine described how visual checks alone could help reduce the likelihood of dispensing fake or counterfeit medicines. He further talked about the need for providers to check the package, including the label, expiry date and manufacturing information.

Group Activity

At the end of the presentation, participants worked in small groups to identify practical quality control measures they could implement to improve the quality of antimalarials in their respective positions. Participants identified the following quality measures:

1) Management

    a) Review forecasting and quantification methodology to ensure sufficient supplies of antimalarials and related commodities procured through the Global Fund are always available at all health care levels
    b) Educate health facility staff regarding appropriate storage conditions for antimalarials and RDTs
    c) Review treatment guidelines with health care providers to improve diagnosis and treatment of malaria
    d) Monitor prescribing practices
    e) Strengthen outreach health services to better reach remote populations

2) Regulation

    a) Advocate for stronger law enforcement

b) Create a working group tasked to educate drug vendors on the national treatment guidelines and to monitor prescribing practices

3) Information/Education/Communication

a) Providers
   i) Take existing supplies of educational materials as well as standard treatment guidelines stored at the central level and distribute to all health facilities
   ii) Strive to improve provider-patient relationship; provide providers the knowledge for good counseling practices

b) Patients/Consumers
   i) Develop new public health messages about the prevalence and dangers of fake medicines
   ii) Continue to support the expansion of the volunteer malaria work programs
   iii) Attempt to improve the image of public health facilities by strengthening the delivery of quality health services
   iv) Promote the use of Long Lasting Insecticide Treated Nets

"Dealers in Death"

The regular use of substandard or counterfeit medicines can lead to therapeutic failure or drug resistance, and in some cases it can lead to death. A study conducted in WHO's South-East Asia Region in 2001 revealed that 38% of 104 antimalarial drugs on sale in pharmacies did not contain any active ingredients. In 1999, at least 30 people died in Cambodia after taking counterfeit antimalarials prepared with sulphadoxine-pyrimethamine (an older, less effective antimalarial) which were sold as Artusenate[5].

Because of a lack of regulation and enforcement, the quality, safety and efficacy of both imported and locally manufactured medicines in Cambodia cannot be guaranteed. The WHO sponsored documentary *"Dealers in Death"* was shown to participants. This documentary conducted in Khmer, highlights the consequences of substandard and counterfeit medicines on patients. Copies of the DVD were distributed to participants from each province.

Session 8. Rational Medicine Use

Presenter: Marion Lynders

This session covered how appropriate mechanisms for ensuring rational antimalarial medicine use can be established. It described the medicine use processes from diagnosis to prescribing, dispensing, and patient use and the problems experienced with antimalarials at each level. It also described the factors influencing antimalarial use and discussed appropriate interventions to improve antimalarial medicine use.
After completing this session, participants were able to—

[5] http://www.who.int/mediacentre/factsheets/fs275/en/print.html. Accessed: January 25, 2007.

- Define rational use
- Discuss the factors affecting use of antimalarials
- Discuss and apply methods to identify these problems
- Identify effective strategies to promote rational use of antimalarials

Plenary Discussions on Rational Medicine Use

Discussion focused on lack of treatment adherence and the effect of different variables within the health system on adherence. Participants described some issues related to the large number of untrained and unregulated medicine sellers dispensing medicines, such as poor case management and non-adherence to standard treatment guidelines.

Group Activity

Considering five different strategies to improve antimalarial medicines use; communication, managerial, economic, product related and regulatory practices, the participants broke into smaller groups to discuss appropriate interventions to improve rational use of medicines. Each group then provided outcomes from their discussion.

Private Sector Involvement

Mr. Mean Samol from Population Services International (PSI) gave a presentation on the topic of public private partnership in malaria control (see Annex 4. The presentation included background information on PSI as an organization, their products and associated price, the distribution mechanism and the monitoring and evaluation framework. Mr. Mean Samol, explained some of the causes and possible solutions to problems his program encountered:

1) Inflated price of Malarine

    a) Possible causes
        i) Shortage of product
        ii) Lack of consumer's awareness of appropriate price
        iii) Some providers are unaware of appropriate use of malarine

    b) Possible solutions
        i) Strengthen supply security through improved procurement processes
        ii) Increase funding
        iii) Increase consumer awareness of price through communication
        iv) Improve training curriculum for providers

2) Splitting co-blistered products to sell as part of "cocktail" packets of medicines

    a) Possible causes
        i) Behavior motivated by profit
        ii) Price is too high
        iii) Lack of confidence in the product

iv) Limited understanding of compliance

b) Possible solutions

i) Improve profit margins for the medicine seller
ii) Increase consumers knowledge
iii) Improve provider's knowledge of treatment guidelines
iv) Strengthen monitoring of providers behavior

3) Low use of Rapid Diagnostic Tests (RDTs) relative to Malarine uptake

a) Possible Causes
i) Competition from cheaper laboratory diagnostic methods
ii) Mobile population – patients buy malarine prior to testing
iii) Lack of knowledge

b) Possible Solutions
i) Improve profit margins to encourage providers to promote RDTs
ii) Promote product more and provide incentives to increase usage
iii) Increase consumers awareness of RDTs and ACT

Next Steps:

1. Mobilize additional resources
2. Revise products so that dosages are in line with new treatment guidelines
3. Develop an ACT for under age 5 age group
4. Improve field monitoring of product quality
5. Promote RDT usage and provide additional training to providers
6. Revise print media as a way to improve compliance
7. Revise RDT pricing and incentives to trade
8. Improve forecasting and procurement procedures

Presentation on: Community Drug Management of Child hood Illnesses Survey: Cambodia 2004.

Ms. Lynders presented results from the Community Drug Management for Childhood Illness (C-DMCI) assessment in 2004 (see Annex 1). The Reproductive and Child Health Alliance (RACHA), with the participation of RPM Plus conducted this survey in 10 operational districts in five provinces (Phnom Penh, Siem Reap, Pursat, Kratie, Koh Kong) to identify potential household and provider drug management problems that may affect the treatment of childhood illness.

In both urban and rural communities, 3,000 households and 1,379 providers from the public and private sectors were surveyed. Children included in the sample had recently recovered from malaria, acute respiratory infection (ARI) pneumonia, ARI non-pneumonia, or diarrhea. However, for the purpose of this workshop, only malaria data was presented.

Information was gathered from the caregivers on the timeliness of their care-seeking, the places they went for care and medicines, which medicines they obtained, and how they used them. The providers gave information on their prescribing or selling practices, the availability and prices of medicines, their most commonly sold or dispensed medicines for certain conditions, and their dispensing practices.

Key results from the household survey show –

1. Caregivers report only nine of the 2,574 children with fever received a blood test to diagnose malaria;
2. Of the 2,574 children with symptoms of fever, only 8 received antimalarials;
3. 51% of caregivers say they obtain antimalarial medicines from general shops and markets, and obtain antibiotics equally from licensed and unlicensed providers in the private sector;
4. 25% of respondents state their child received an injection as a form of treatment regardless of condition.

Key Results from providers survey show–

1. Only 53% of providers at public health facilities report they recommend artesunate/mefloquine combination (A+M) the first-line treatment for malaria and even fewer private sector providers mentioned recommending the first line treatment-artesunate/mefloquine combination;

Proposed recommendations from the survey included–

1. Increase availability of essential medicines
2. Promote rational use of medicines including good dispensing practices to promote adherence
3. Engage the private sector more to meet public health goals
4. Communicate messages to caregivers on the danger signs, appropriate sources of care and management for symptoms of fever, convulsions, diarrhea and use of ORS, and fast breathing, through media, community, and provider sources
5. Encourage caregivers to request instructions from providers on how to administer medicines

Session 9: Field Exercise:

Participants conducted a field exercise during which they selected indicators, prepared instruments, and collected data. This exercise was to challenge participants to think critically about the performance of pharmaceutical management systems and the data that can be collected to make decisions regarding selection, procurement, distribution, availability, and use of antimalarial medicines. Field visits were organized to the Central Medical Stores (CMS), the National Quality Control Laboratory, Phnom Penh Municipal Hospital as well as the Pochentong and Don Penh health centers.

Procurement at Central Medical Stores

The focus of the visit to the CMS was to review procurement and distribution procedures and inventory control measures. During the visit, the group assessed the antimalarials availability at CMS. Throughout the physical stock check, no expired medicines were found. The average procurement time for antimalarials to be received at CMS is three to four months. According to the team, the quantification method based on average consumption may be a wrong method since stock outs are frequent at district levels.

Quality Assurance at the National Quality Control Laboratory

The group that visited the National Quality Control Laboratory was not able to collect data for the indicators they had identified. Unfortunately, the staff at the laboratory did not prepare as expected to receive the participants. However, the group did tour the facility and gain a better understanding of the work performed at the laboratory. The friability test on the artesunate and mefolquine sample was performed and the sample was confirmed to be of good quality.

Field Visits to Ponchentong and Don Penh Health Centers

The teams visiting the Ponchentong and Don Penh health centers focused on antimalarial availability, inventory management and providers prescribing practices. As Phnom Penh is not a malarious area, antimalarials are not available at all health centers. Artesunate and mefloquine are available at the municipal hospital and so all malaria cases are referred to this facility. However, to facilitate the learning process for this exercise, participants were asked to consider instead a list of antibiotics as the process for collecting information on availability and use is the same regardless of the medicine. Collectively, the teams found the following:

- Based on observation, all patients received counseling for taking medicines
- 90 percent of patients understood the instructions for taking their medicines appropriately by repeating the dispenser's instructions accurately (n=32)
- In both health centers, actual stock levels (physical count) of amoxicillin and co-trimoxazole were not consistent with stock levels listed on the stock cards
- No expired medicines were found

Assessment of Pharmaceutical Management for Malaria at Phnom Penh Municipal Hospital

During this field visit, participants met with pharmacists who reviewed the inventory management system used at this facility. Three pharmacists are employed at the municipal hospital. The Phnom Penh Municipal Hospital sees about 150 sick children every day, most of which are cases of diarrhea and typhoid fever requiring medicine. Participants had the opportunity to observe storage conditions, count and compare actual physical stock with stock records in the storeroom. The team found the following:

- Despite being a referral level hospital, there were no first or second line antimalarials available at the hospital at the time of the visit
- No malaria cases were reported to or treated at this facility in 2006
- All medicines are arranged by alphabet; however, no bin cards were available
- Stock levels are manually recorded in a registry book and all records conformed to physical stock levels

Recommendations

1) Organize future courses

    a) Collaborate with the Asian Collaborative Training Network for Malaria organization to replicate the Pharmaceutical Management Training courses targeted at regional level

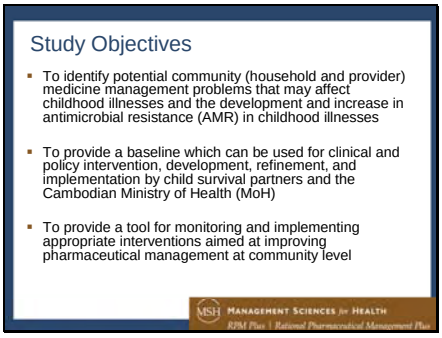
2) Improve management of drug supply

    a) Problems related to quantification, recording keeping and stock outs were identified at the health facilities visited by the participants RPM Plus can provide technical assistance to strengthen the quantification, inventory management and distribution systems to reduce the problem of stock outs

3) Revise packet of course materials

    a) Without compromising the objectives, shorten the content of some sessions
    b) Allow more time for discussion and hands on practice for quantification exercises
    c) Modify the training materials to be more visually stimulating
    d) In preparation for field site visits, develop a check list of tasks for clinical staff at facility level to ensure optimal learning experiences for participants

ANNEX 1. PRESENTATION ON THE ASSESSMENT OF COMMUNITY DRUG MANAGEMENT FOR CHILDHOOD ILLNESSES: CAMBODIA, 2004



Data Collection and Analysis

5 provinces
- Phnom Penh
- Siem Reap
- Pursat
- Kratie
- Koh Kong

10 operational districts
- Choeung, Tbong
- Kralanh, Siem Reap
- Bakan, Sampov Meas
- Chhlong, Kratie
- Smach Meanchay, Sre Ambel

- Data cleaning and analysis by Reproductive and Child Health Alliance (RACHA) IT team

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Conditions Studied

- Malaria and severe malaria (fever and convulsions)
- Acute respiratory infection (ARI) pneumonia (fast breathing)
- ARI nonpneumonia (cough without fast breathing)
- Mild and bloody diarrhea

- This presentation will focus on the number of children with symptoms of fever (malaria) and convulsions (severe malaria) sampled in the survey

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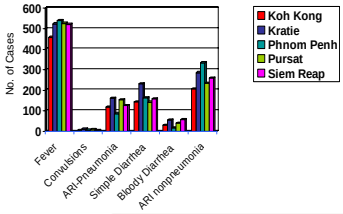
Distribution of Symptoms



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Sampling

- Households: 3,000
  - 2,574 cases of fever
  - 33 cases of convulsions
- Providers: 1,379
  - Public and nonprofit health facilities—health centers, nongovernmental hospitals
  - Licensed drug outlets—pharmacies, drug depots A&B
  - Licensed for-profit providers—doctors, nurses
  - Unlicensed drug outlets—general shops, market sellers, traditional healers

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Appropriate Drug Management at Community Level

- Caregiver makes a timely decision to start treatment according to the child's signs and symptoms
- Appropriate medicines are available and accessible
- Appropriate medicines are obtained or purchased
- Medicines are used according to standard treatment guidelines

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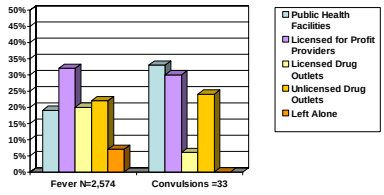
Respondents Going Outside the Home as the First Source of Care



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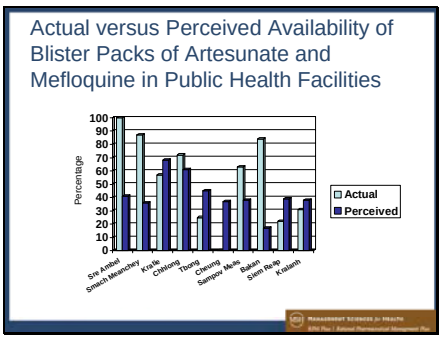
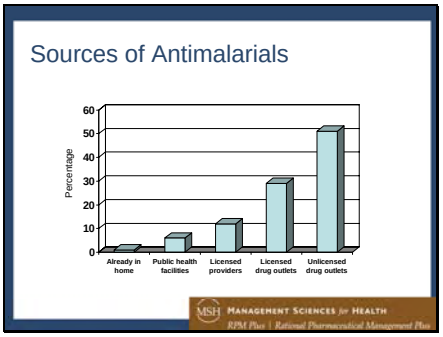

Actual versus Perceived Availability of Blister Packs of Artesunate and Mefloquine in Public Health Facilities
Percentage
100
90
80
70
60
50
40
30
20
10
0
Sre Ambel
Smach Meanchey
Kratie
Chhloung
Thong
Chkoung
Sampov Meas
Balam
Siem Reap
Kralanh
Actual
Perceived


Sources of Antimalarials
Percentage
60
50
40
30
20
10
0
Already in home
Public health facilities
Licensed providers
Licensed drug outlets
Unlicensed drug outlets
MSH
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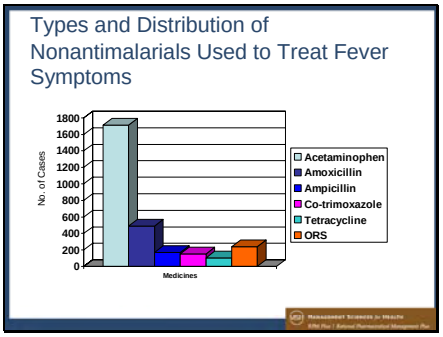
Types and Distribution of Nonantimalarials Used to Treat Fever Symptoms
No. of Cases
1800
1600
1400
1200
1000
800
600
400
200
0
Medicines
Acetaminophen
Amoxicillin
Ampicillin
Co-trimoxazole
Tetracycline
ORS

Biological Diagnosis: Caregivers Report

- 2,574 fever cases ⇨ 9 children received a blood test prior to starting antimalaria treatment
  - 5 received antimalarial on first day
  - 2 received antimalarial on second day
  - 2 unknown
- 33 convulsion cases ⇨ 1 child received a blood test
  - 3 received first-line antimalarials
  - 21 received nonantimalarial medicines
  - 9 unknown

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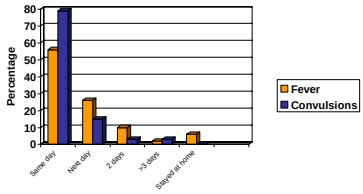
Timeliness of Treatment



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Treatment of Children with Symptoms of Fever

Treatment	*N*	%
Received first-line antimalarials	8	0.3
Received medicines besides antimalarials	1,868	73
Received traditional medicines	40	1.5
Did not know name of medicine	5	0.2
Could not obtain medicine name	653	25
Total	**2,574**	**100**

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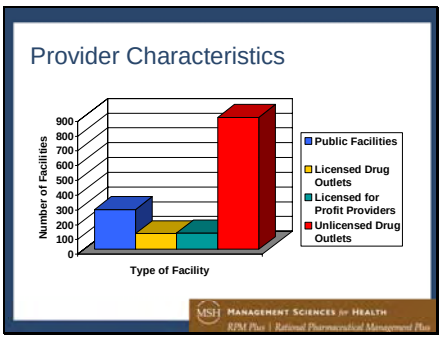
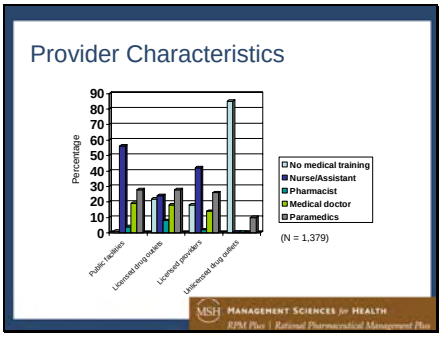
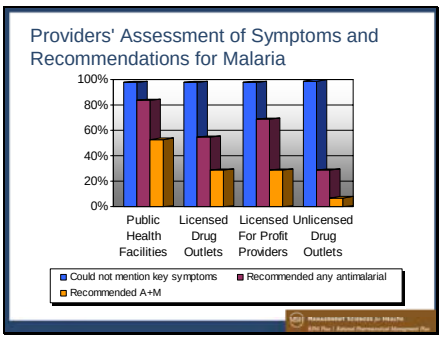
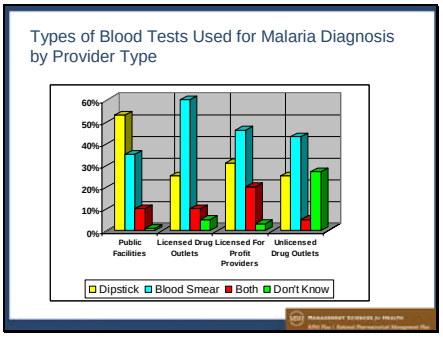




Overall Availability of Specific Medicines at All Drug Outlets

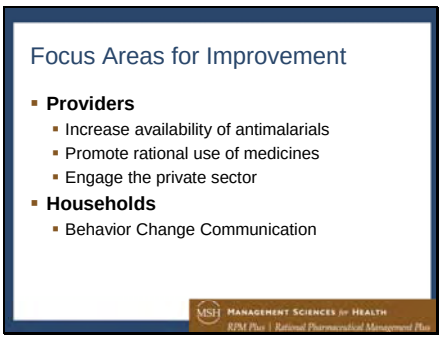
Type of Medicine	Tracer Medicine	Public Facilities (*N* = 289)	Licensed Drug Outlets (*N* = 106)	Licensed For Profit Providers (*N* = 111)	Unlicensed Drug Outlets (*N* = 893)
First-line	Blister packs of A&M, %	57	46	41	10
	Artesunate tablet, %	26	42	42	14
	Mefloquine, %	35	18	28	8
	Chloroquine, %	21	25	23	8
	Malarine (private sector), %	9	44	33	9
Second-line	Quinine sulfate tablet, %	54	36	40	17





Dispensing Practices of Providers

	Type of Provider			
Practices Reported by Provider	**Public Facilities (*N* = 269)**	**Licensed Drug Outlets (*N* = 106)**	**Licensed For Profit Providers (*N* = 111)**	**Unlicensed Drug Outlets (*N* = 893)**
Identifies correct verbal instruction—name of medicine, what it treats, when and how to take it, side effects, %	7	1	1	0
Provides correct labeling—name of medicine, how to take it, duration, %	43	6	4	1
Dispensed medicines outside of original packaging, %	18	38	10	3
Mixed different pills in same container, %	6	26	7	3
Dispensed loose tablets in inappropriate packaging, %	18	36	10	3


Focus Areas for Improvement
Providers
Increase availability of antimalarials
Promote rational use of medicines
Engage the private sector
Households
Behavior Change Communication
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ANNEX 2. PRESENTATION ON COUNTERFEIT DRUGS

 វិសមភ្លែងក្លាយ និង

អាស្រ័យភាពវិសម នៅ កម្ពុជា

Counterfeit Drugs &
Drugs Accessibility in Cambodia

National Training Course on
Pharmaceutical Management for Malaria
CNM , December 4-8, 2006

Yim Yann

President of Pharmacist Association of Cambodia

Counterfeit Drugs (CD) definitions

WHO : Drugs which have been deliberately & fraudulently mislabelled with respect to identity & or source.

Could be products :

- with correct ingredients
- wrong ingredients
- without active ingredient
- with incorrect quantity of active ingredient
- fake packaging
- applies to both branded or generic products.

CD definitions (cont)

USA: Unauthorised imitation/copying of trademark, trade name, identifying mark,an imprint.

Philipines (has a broader definition):

- a drug deliberately & fraudulently mislabelled with respect to identity & or source;
- unregistered imported products
- Products containing less than 80%of the labelled amount;

CD definitions (cont)

Cambodia : Drugs , which is :

- produced deliberately with incorrect quantity of or wrong active ingredients.
- produced without active ingredients or unregistered product, which amounts of active ingredients are deliberately outside the defined pharmacopoeias or accepted standard.
- produced deliberately & fraudulently mislabeled with respect to identity, source or with fake packaging .
- repacked or produced by unauthorized person.

Substandard drugs (SD)

Drugs which do not meet specifications set for them. They are outside the limits or standards.

- Quality standards (monographs, pharmacopeias)
- Regulatory standards-shelf-life, labeling, information, GMP, etc

SD & CD / **similarities & differences**

- Both are public health problem
- Both undermine confidence in health care system-health professionals, industries, distributors & DRAs
- Both could prolong treatment period & lead to development of resistance to drugs-antibiotics ,anti-malarial, etc
- Both have economic consequences to the patient, government, industry, distributors.

SD & CD / **similarities & differences (cont)**

- Not all SD are CD
- All CD are SD
- **There are no good quality CD**
- SD are not the result of criminal action
  - They are regulated drugs & problem could be due to
    - Poor GMP compliance
    - Pour storage & distribution
- CD are the result of criminal action
  - They are intentionally made .

Main factors / constraints

1. Lack of awareness of the public and decision-makers about problem of CD
2. Economics-supply and demand, issue of poverty or low purchasing power, **high price of drugs**, desire for high profit
3. Lack of legislation and political commitment

Main factors / constraints (cont..)

4. Corruption
5. Lack of collaboration & cooperation between different regulatory agencies at national level & between countries & lack of communication internationally& externally
6. Weak enforcement, weak penalty, weak post-marketing surveillance
7. Weak DRA- lack of human & other resources
.

Where & by whom are CD produced ?

- Hard to know where & who produces CD
- Could be produced any where by criminals, but the chances are high in countries where drug regulation is very weak & government commitment is lacking
- Are found in both developed & developing countries, but problem is more serious in developing countries
- Undercover investigation is essential to know where & who is producing.

Pharmaceutical sector

Pharmaceutical expenditure for 2000 were 31.46 Million USD

- **Households : 57%**
- **Donors : 25%**
- **MoH : 18%**

Quality of Product (2001)

- MoH cambodian drug market study found overall failure rate of **13.5%**
- 50% of drug are not registered
- Failure rate :
  - Registered : 5.2%
  - Unregistered : 22.3%

Quality of Product cont.
(malaria medicine 2003)

- 44% quinine samples collected failed quality testing- no AI
- 25% artesunate samples collected failed quality testing- no AI.

Quality of Product (MSH 2001)

- Samples were collected from public facilities, NGO/ Mission and private retail outlets
- Samples were submitted to University Pharmaceutical of Maryland, Inc., located in Baltimore, Maryland, USA for tests of the labeled strength.

Quality of Product (MSH 2001)-cont-

- # of different drugs tested 14
- # of sample tested 132
- Samples were found to be substandard 5 of 14
- Failure rate 12.4%

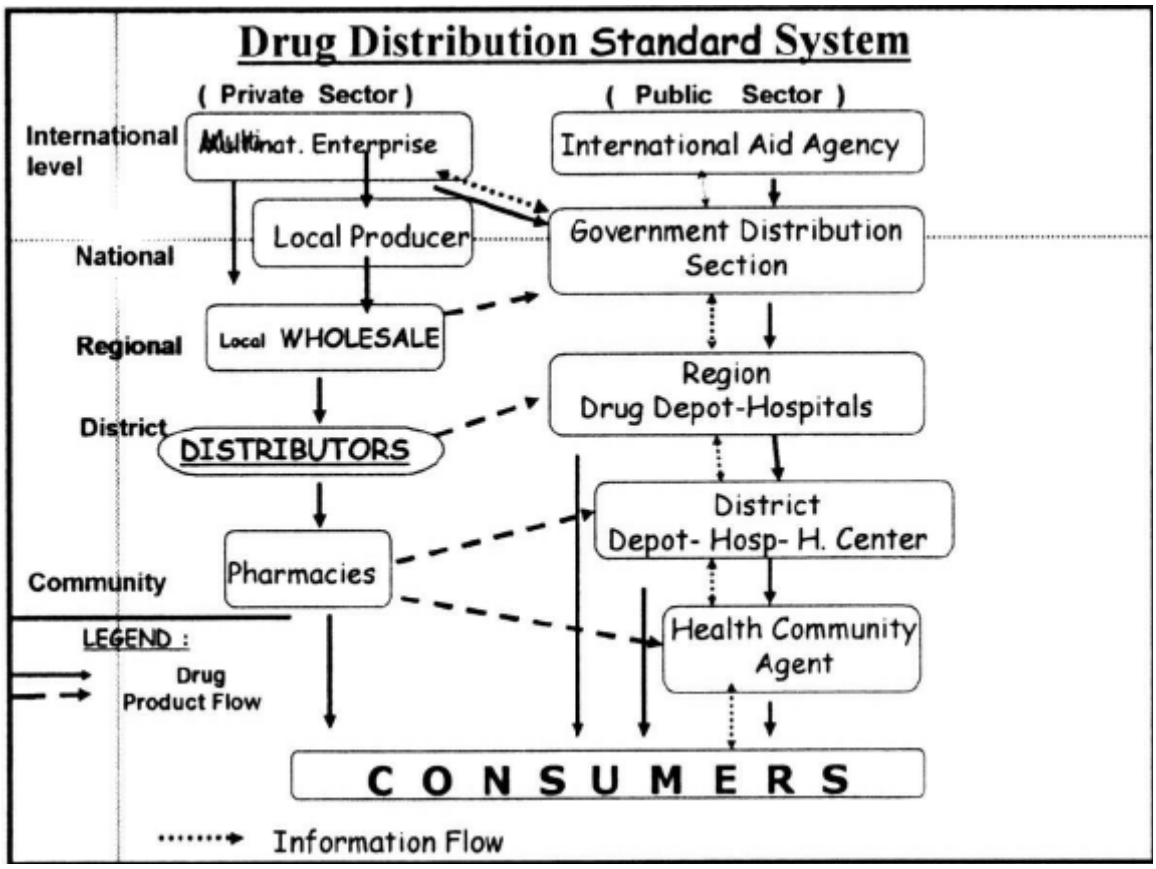
Result of TLC project USP-DQI 2005 (Q1/2005)

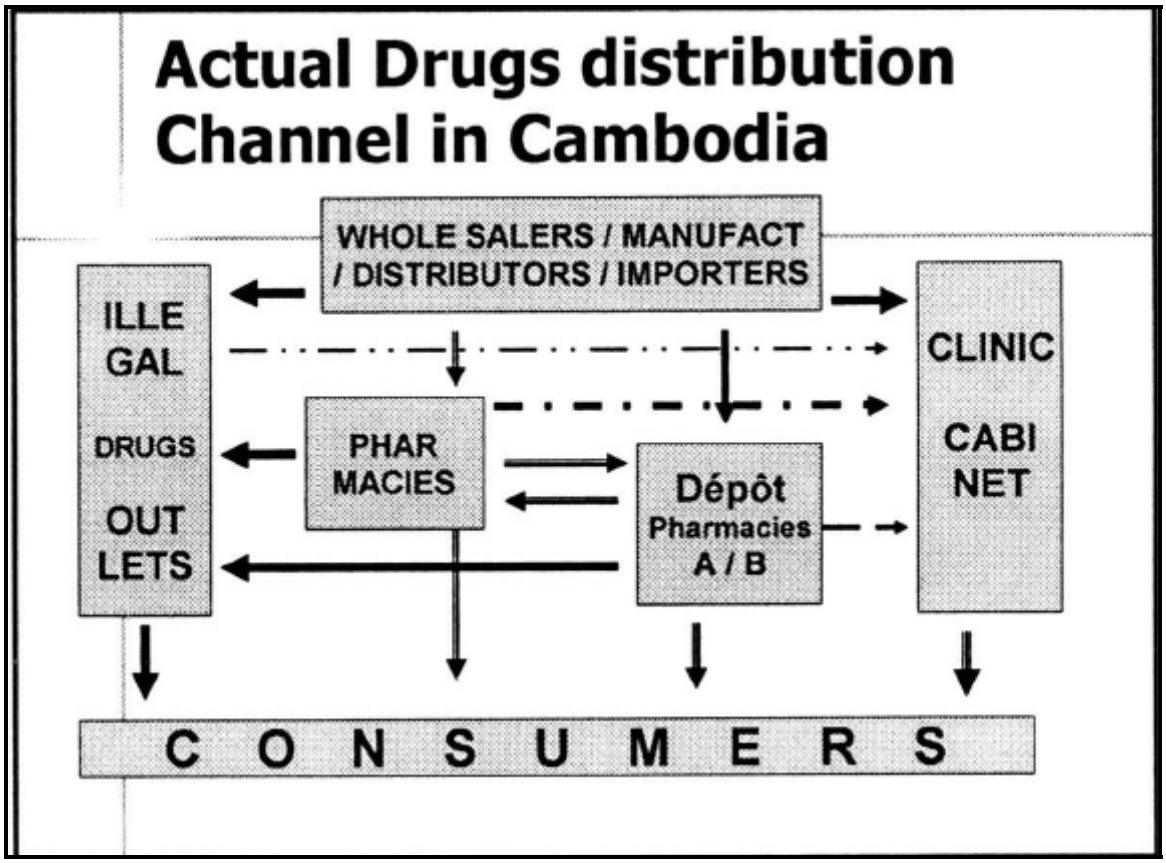
- After TLC test at sentinel site & **confirming test** at NLDQC, we found amount 185 samples,
  - 18 samples are **Failed**, Of this :
    - 12 samples : 0%- 0.08% of AI
    - 6 samples : 12% – 16% of AI

(**TLC** : Thin Layer Chromatography, **USP-DQI** : US Pharmacopoeia for Drug Quality Insurance, **NLDQC** : National Lab for Drug Quality Control, **AI** : active ingredient)

Quality of services (2000)

- In retail drug shops, antibiotic were inappropriately recommended : **72%** of the time (ARI / no pneumonia)
- **50%** actually purchased antibiotic .



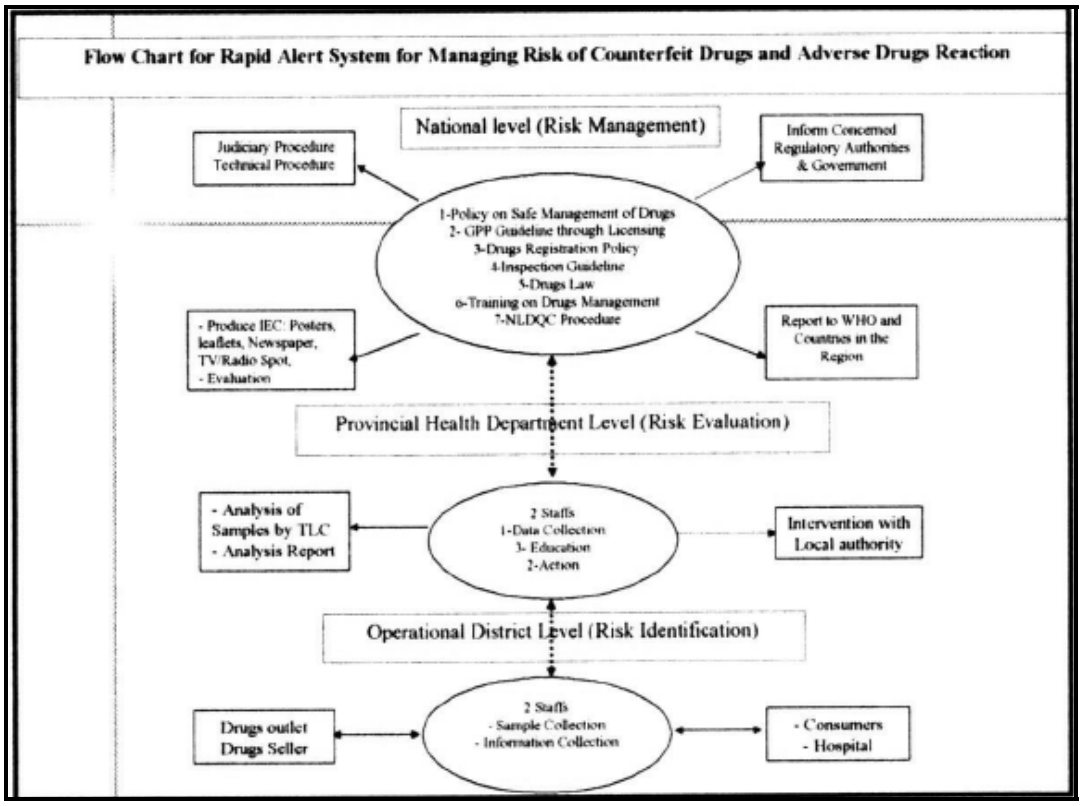


Pharmaies & Dépôt of Pharmacies (MoH 2005)

	PHARM	D. A&B	TOTAL	ILLEGAL
P.PENH	290	192	482	**111**
PROVINCES	135	426	561	**2113**
TOTAL COUNTRY	**425**	**618**	**1043**	**2224**

How to solve ??

RAPID ALERT SYSTEM
on Counterfeit Drugs
MoH 2005



Procedure for the Rapid Alert System

Data Collection:

-Gather all information related to Suspected Drugs

-Sent the sample to NLDQC for confirming the result

Data Validation:

- DDF and Partners validate data
- NLDQC confirm the test is needed

IEC Alert to Consumers:

- Write the letter to MoH for Special Right in order to disseminate the finding. There are 2 ways for implement these activities:

  * Special Authorization to disseminate the information of Counterfeit Drugs to the public through Rapid Alert System. The Director of Drugs and Food Department has to ask the Minister

  * Ask the Minister to allow DDF to disseminate the Counterfeit issue within 1 day. The DDF Director has to ask the Minister

- The dissemination should be done through:

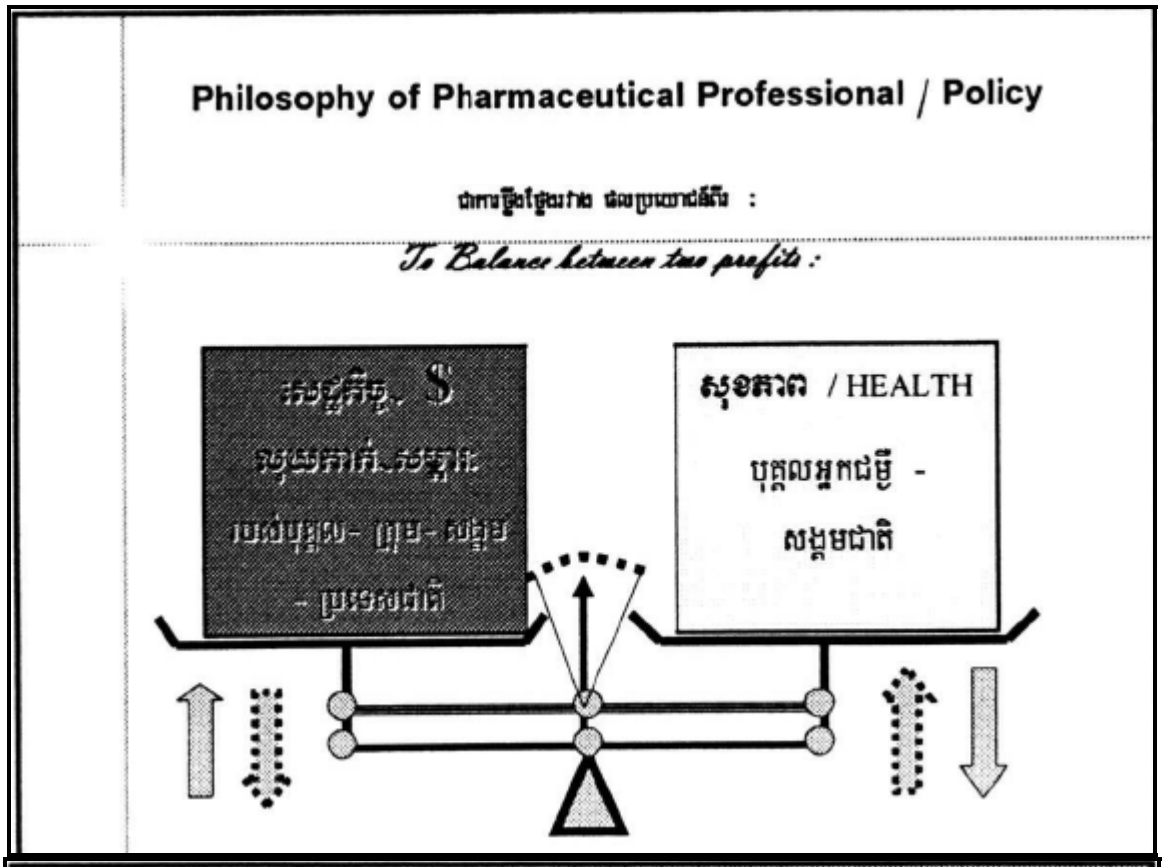
  * TV news or Radio news
  * Daily Newspaper
  * News letter of CPA

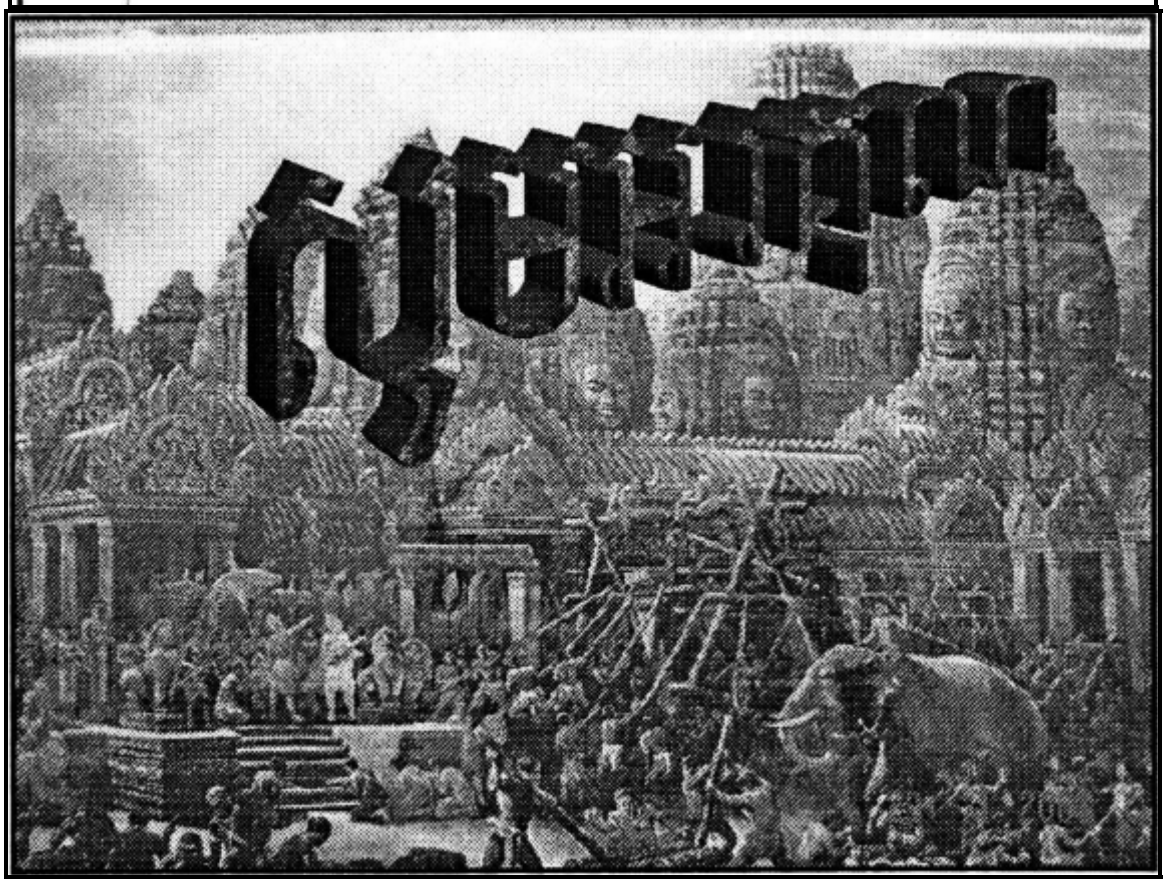
Potential Country Strategy (a)

- Development of a multi-level, performance-based network of pharmacies, franchised rural health care & private clinics .
- Development of a group purchasing cooperative for network & perhaps, non-network facilities.

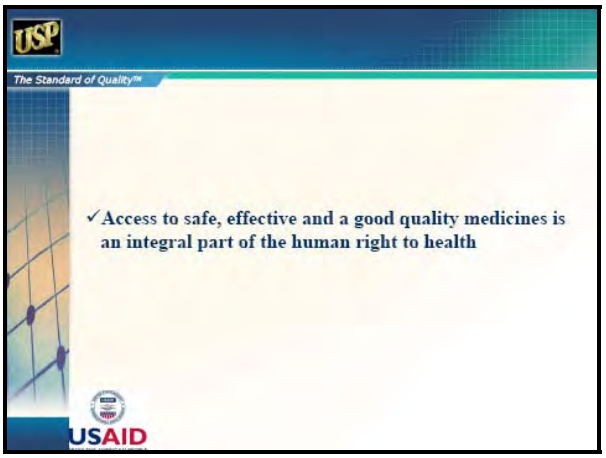
Potential Country Strategy (b)

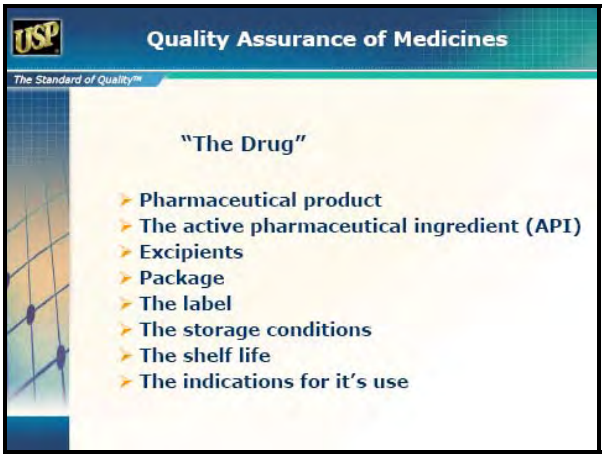
- Development of innovative community based health insurance schemes (Output Based Aid) .
- Development of a comprehensive government controlled drug quality assurance program.
- Implementation of community-based care programs include public participation in all facets of drug management planning, education, & evaluation.

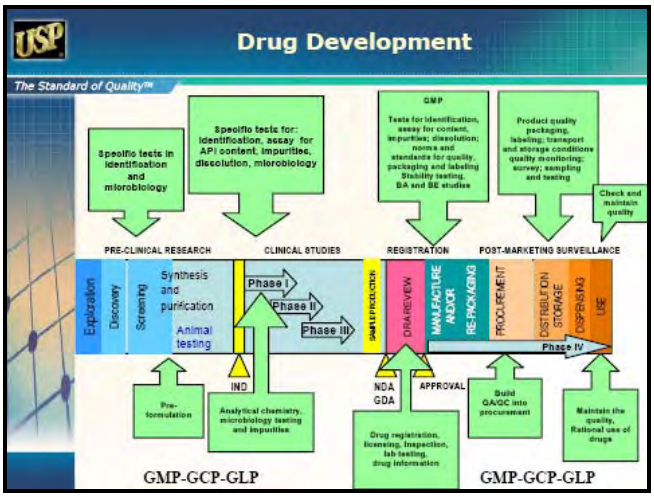

Philosophy of Pharmaceutical Professional / Policy
To Balance between two profits :
$
សុខភាព / HEALTH
បុគ្គលអ្នកជម្ងឺ -
សង្គមជាតិ



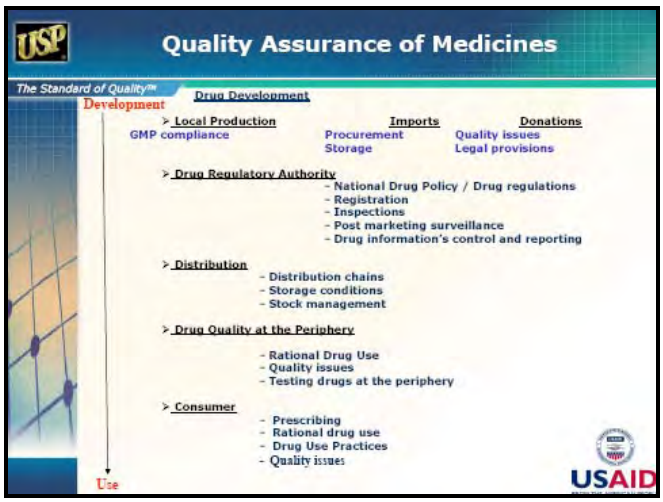
ANNEX 3. PRESENTATION ON QUALITY ASSURANCE

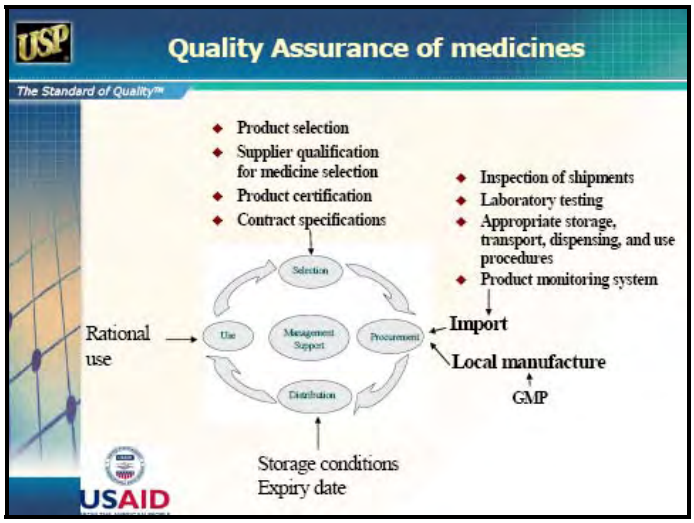




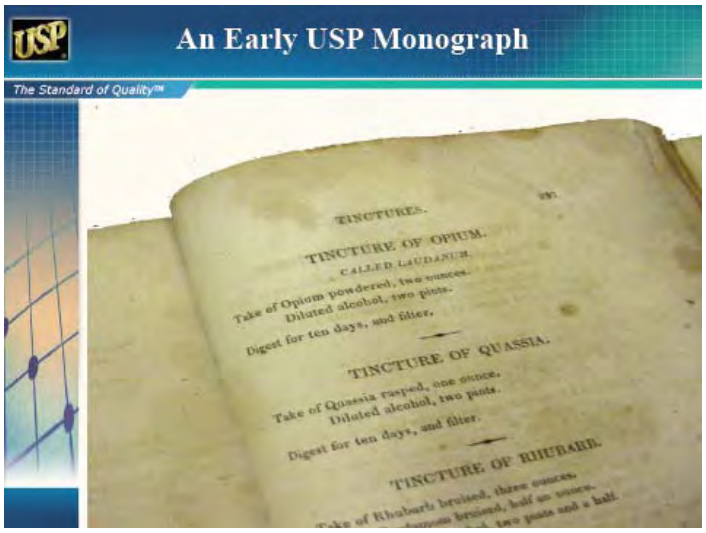

Drug Development
The Standard of Quality™
Specific tests in identification and microbiology
Specific tests for: identification, assay for API content, impurities, dissolution, microbiology
GMP
Tests for identification, assay for content, impurities; dissolution; norms and standards for quality, packaging and labeling Stability testing, BA and BE studies
Product quality packaging, labeling; transport and storage conditions quality monitoring; survey; sampling and testing
Check and maintain quality
PRE-CLINICAL RESEARCH
CLINICAL STUDIES
REGISTRATION
POST-MARKETING SURVEILLANCE
Exploration
Discovery
Screening
Synthesis and purification
Animal testing
Phase I
Phase II
Phase III
SAMPLE PRODUCTION
DRA/REVIEW
MANUFACTURE AND/OR RE-PACKAGING
PROCUREMENT
DISTRIBUTION STORAGE
DISPENSING
USE
Phase IV
IND
NDA GDA
APPROVAL
Pre-formulation
Analytical chemistry, microbiology testing and impurities
Drug registration, licensing, inspection, lab testing, drug information
Build QA/QC into procurement
Maintain the quality, Rational use of drugs
GMP-GCP-GLP
GMP-GCP-GLP

Quality Assurance of Medicines
The Standard of Quality™
Quality Assurance of drugs, are all measures taken to assure the quality of the drug from its development to its use by the patient.
In other words: QA = make sure that the pharmaceutical products are FIT FOR THEIR INTENDED USE…
Efficacy, Quality, Strength, Purity, Packaging and labeling, storage and appropriate use.
USAID


Quality Assurance of Medicines
The Standard of Quality™
Development
Drug Development
Local Production
GMP compliance
Imports
Procurement
Storage
Donations
Quality issues
Legal provisions
Drug Regulatory Authority
- National Drug Policy / Drug regulations
- Registration
- Inspections
- Post marketing surveillance
- Drug information's control and reporting
Distribution
- Distribution chains
- Storage conditions
- Stock management
Drug Quality at the Periphery
- Rational Drug Use
- Quality issues
- Testing drugs at the periphery
Consumer
- Prescribing
- Rational drug use
- Drug Use Practices
- Quality issues
Use
USAID


Quality Assurance of medicines
The Standard of Quality™
Product selection
Supplier qualification for medicine selection
Product certification
Contract specifications
Inspection of shipments
Laboratory testing
Appropriate storage, transport, dispensing, and use procedures
Product monitoring system
Selection
Use
Management Support
Procurement
Distribution
Rational use
Import
Local manufacture
GMP
Storage conditions
Expiry date
USAID

Quality Control – Quality Standards
The Standard of Quality™
Drugs should be conform to the Standards
Internationally recognized pharmacopoeias
- IP, USP, BP, JP, and EP
Official national pharmacopoeias
Standards and analytical methods developed by the manufacturer (when monographs are not available)
USAID


An Early USP Monograph
The Standard of Quality™
TINCTURES.
TINCTURE OF OPIUM.
CALLED LAUDANUM.
Take of Opium powdered, two ounces.
Diluted alcohol, two pints.
Digest for ten days, and filter.
TINCTURE OF QUASSIA.
Take of Quassia rasped, one ounce.
Diluted alcohol, two pints.
Digest for ten days, and filter.
TINCTURE OF RHUBARB.

Isoniazid monograph

The Standa

$C_6H_7N_3O$ 137.14
4-Pyridinecarboxylic acid, hydrazide.
Isonicotinic acid hydrazide [54-85-3].

» Isoniazid contains not less than 98.0 percent and not more than 102.0 percent of $C_6H_7N_3O$, calculated on the dried basis.

Packaging and storage— Preserve in tight, light-resistant containers.

USP Reference standards ⟨11⟩ — *USP Isoniazid RS*

Identification—

A: *Infrared Absorption* ⟨197K⟩.

B: Transfer about 50 mg of it to a 500-mL volumetric flask, add water to volume, and mix. Transfer 10.0 mL of the resulting solution to a 100-mL volumetric flask, add 2.0 mL of 0.1 N hydrochloric acid, dilute with water to volume, and mix to obtain a 1 in 100,000 solution: the ultraviolet absorption spectrum of the solution so obtained exhibits maxima and minima only at the same wavelengths as that of a similar solution of *USP Isoniazid RS*, concomitantly measured.

Melting range ⟨741⟩: between 170° and 173°.

pH ⟨791⟩: between 6.0 and 7.5, in a solution (1 in 10).

Loss on drying ⟨731⟩ — Dry it at 105° for 4 hours: it loses not more than 1.0% of its weight.

Residue on ignition ⟨281⟩: not more than 0.2%.

Heavy metals, *Method II* ⟨231⟩: 0.002%.

Organic volatile impurities, *Method I* ⟨467⟩: meets the requirements.

Assay—

Mobile phase— Dissolve 4.4 g of docusate sodium in 600 mL of methanol, add 400 mL of water, adjust with 2 N sulfuric acid to a pH of 2.5, and mix. Make adjustments if necessary (see *System Suitability*

Quality Control – Quality Standards

The Standard of Quality™

Critical Attributes for Testing Dosage Forms

Identity, Purity, quality, strength, packaging and labeling

- Identity
- Assay (dosage = amount of active ingredient)
- Disintegration (prerequisite for bioavailability)
- Dissolution (higher level of assurance of bioavailability)
- Impurities (generally related to active pharmaceutical ingredient, similar toxicities)
- Uniformity
- Sterility

USAID

Quality Control – Quality Standards

The Standard of Quality™

Definition: Good quality medicines meet official standards for identity, strength, purity, quality, packaging, and labeling.

✓**Identity** – Same active pharmaceutical ingredient (API) that is on the label

✓**Strength** – The amount of the API claimed on the label

✓**Purity** – The relative absence of unlabeled ingredients

✓**Quality** – Characteristics that allow the API to deliver the intended therapeutic effect

Quality Control – Quality Standards

The Standard of Quality™

- **Packaging** – the container that holds the article does not interact physically or chemically with the article so as to alter the strength, quality, or purity.
- **Labeling** – all labels must present information as required by the governmental regulatory body in addition to pharmacopeial requirements per article.

USAID

Quality Control – Quality Standards

The Standard of Quality™

- **Fake/counterfeit** – Deliberately mislabeled for identity and/or source. (No active ingredient or a different active ingredient than on the label)
- **Substandard** – Legal branded or generic product, but does not meet official standards for identity, quality, purity, strength, packaging and labeling.

USAID

Specifications

The Standard of Quality™

Definition:

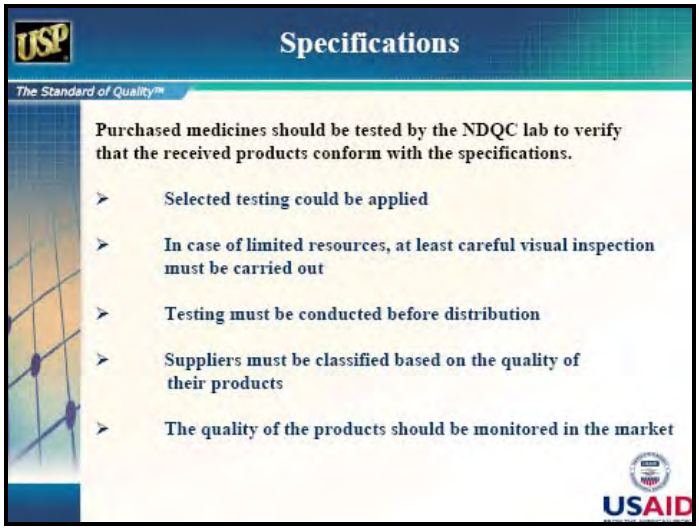
Specification is a list of detailed requirements with which the products or materials used or obtained during manufacture have to conform. They serve as a basis for quality evaluation.

For medicines the specifications concern;

- The package
- The label
- Identity, strength purity and quality
- Expiry date
- Storage conditions
- Information/indications about the drug use

All these specifications should be defined during the selection and the Procurement.

USP
Specifications
The Standard of Quality™
During the procurement, the adequate dosage form and strength should be selected.
The adequate primary and secondary package
Shelf life at reception of drugs
Storage temperature according to real conditions of use
Procurement services should ask for clear specification and determine the monograph to which the product should conform
Procurement services should request complete certificate of analysis together with drug samples to be quality tested.
USAID


USP
Specifications
The Standard of Quality™
Purchased medicines should be tested by the NDQC lab to verify that the received products conform with the specifications.
Selected testing could be applied
In case of limited resources, at least careful visual inspection must be carried out
Testing must be conducted before distribution
Suppliers must be classified based on the quality of their products
The quality of the products should be monitored in the market
USAID

USP
Selection of suppliers
The Standard of Quality™
Manufacturers prequalified by WHO
Suppliers of UN agencies
Suppliers with track record of quality products
Manufacturers assessed by local DRA
The selection of suppliers should not be based only on the cost of the product. The quality of the drug must always be the priority.
USAID

Maintaining the quality of medicines

The Standard of Quality™

- Storage of medicines should comply with manufacturer's conditions.
- Good Storage and Distribution Practices should be followed
- The quality of medicines must be monitored in the market
- The quality of medicines should be maintained throughout their shelf life
- DRA and health programs should promote the rational use of medicines

USAID

Why do we need quality assurance?

The Standard of Quality™

Because counterfeit and substandard drugs are widely available and are:

- A constant threat to public health worldwide
- Most affecting people living in countries with limited regulatory capacity and resources
- FDA estimated that up to 10% of drugs worldwide are counterfeit, and in some countries more than 30% of the drug supply is made up of counterfeit drugs
- Costing over 22 billion USD per year, representing about 7- 10 % of world-wide pharmaceutical sales. This market is supposed to reach 75 billion USD by 2010. *(www.who.int/mediacentre/factsheets/fs275/)*

Causes of proliferation of poor quality drugs

The Standard of Quality™

- Poor health systems in developing countries
- Lack of legislation
- Weak or absent drug regulatory/control (1/3 of African countries)
- Weak law enforcement and penal sanctions
- High drug demands with short supplies
- Imports via Free Trade Zones
- Corruption and conflict of interests
- High cost of drugs-lucrative business

USAID

Consequences of using fake and substandard drugs

The Standard of Quality™

- Diminished trust in the health care systems
- Waste of financial resources
- Health at risk
- Prolonged illness, treatment failure, and increase drug resistance
- Death

USAID

Extend of the Problem - Facts

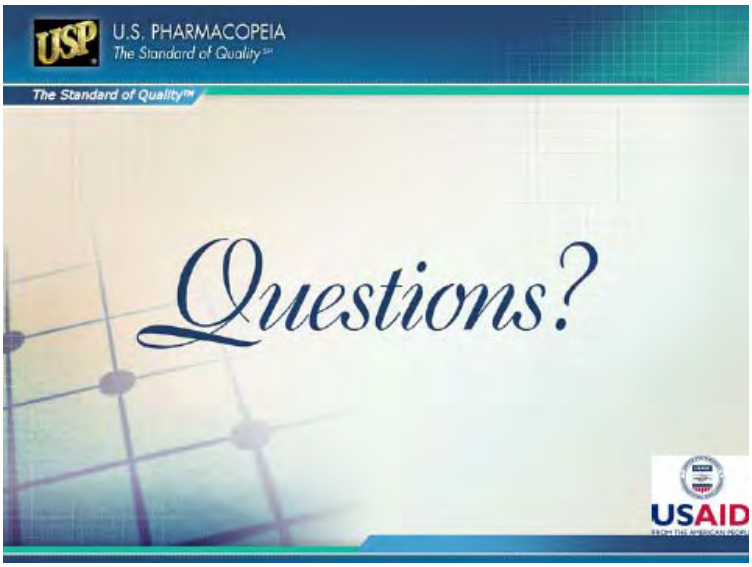
The Standard of Quality™

- Few weeks ago in Panama, a Diethylene glycol (DEG) poisoning killed 30 people. In this case a material labeled as glycerin purportedly contained a mixture of 1% glycerol, 25% DEG and 75% unknown material…
- Same DEG contaminated syrup killed 30 children in India in 1998
- Same problem occurred in Haiti, 1995
  Because of DEG contaminated acetaminophen, 109 children had renal failure 89 of them died.
- In Niger in 1995, 50,000 were inoculated with fake vaccine
  2500 died.
- In 2006, fake Tamiflu (oseltamivir) was found in USA (FDA alert, 2006)
  in Netherlands Tamiflu capsules were found to contain lactose and vitamin C,
  in UK officials seized 5000 packets of counterfeit Tamiflu in early 2006,
  estimated to be worth £500 000

Conclusion

The Standard of Quality™

- Substandard and counterfeit drugs is an increasing problem posing a serious impact to public health.
- All those involved in public health should control the quality of medicines used in their programs
- The quality of medicines must be assured by proper selection, good procurement, quality control, good storage and distribution
- Counterfeit and substandard drugs is a growing market worldwide
- USAID has been supporting drug quality and drug management programs in many countries through regional and bilateral initiatives. (USP DQI – RPM Plus)


U.S. PHARMACOPEIA
The Standard of Quality
The Standard of Quality
Questions?
USAID

U.S. PHARMACOPEIA
The Standard of Quality
The Standard of Quality
Thank You
Abdelkrim Smine, Ph.D.
Manager, Drug Quality & Training
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 number HRN-A-00-00-00017-00. The contents are the responsibility of the U. S. Pharmacopeia Drug Quality and Information Program and do not necessarily reflect the views of the United States Government.
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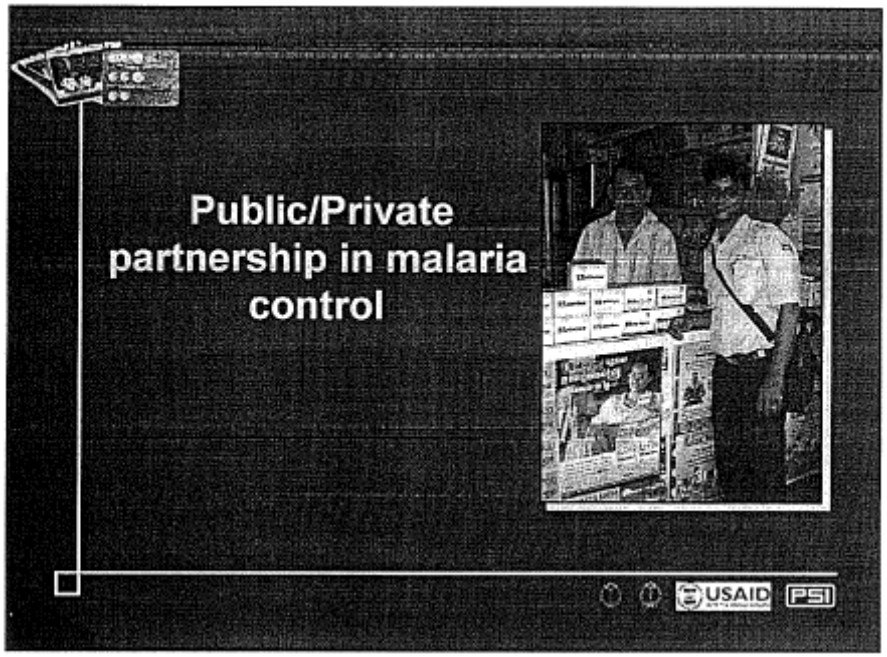
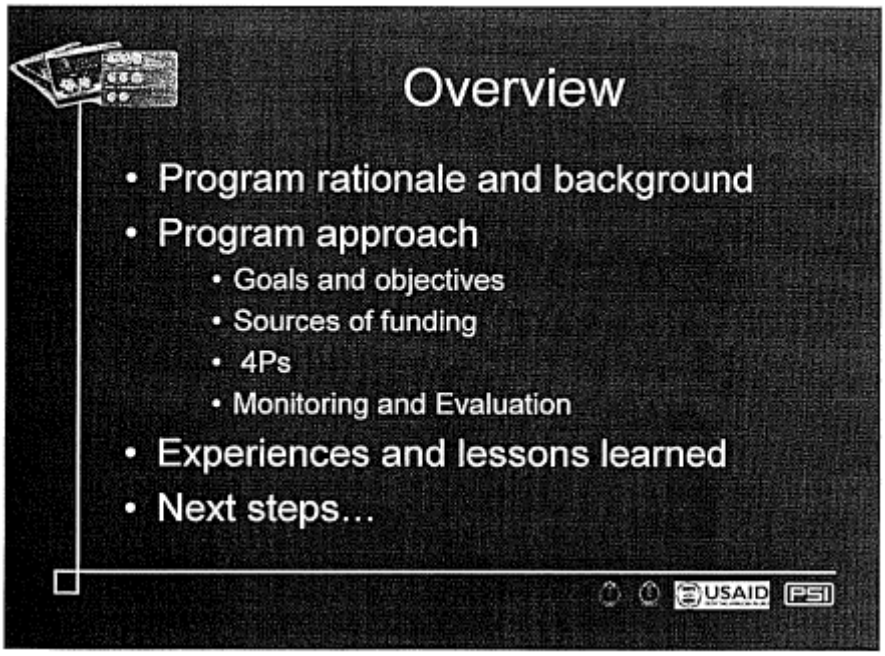
ANNEX 4. PRESENTATION ON PUBLIC AND PRIVATE PARTNERSHIPS IN MALARIA CONTROL





Program Rationale

- EC - Cambodia Malaria Control Project Baseline (1998) suggests:
  - Up to 90% of malaria patients in remote malaria areas seek 1st line treatment through private providers
  - Treatment received did not usually conform to national guidelines
- Market Research Survey combined with laboratory tests from three independent int'l labs showed:
  - Many of the more popular anti-malarial drugs were counterfeit
  - Up to 85% of retail outlets stocked these counterfeit drugs

USAID PSI

Program Background

- CNM (MoH)/EU/WHO Pilot phase from Sept. 2000
  - Two districts of Cambodia
  - To assess Accessibility, Acceptability, Affordability and Compliance of ACT and RDTs
- Study Review (May 2001); Main conclusions:
  - Subsidy on products needed to be increased
    - Malarine retailed for $2.25 – 3.75
    - Malacheck retailed for $0.60 – 1.20
  - Communication needed to be increased
- CNM and PSI sign an MOU for PSI to expand social marketing of Malarine and Malacheck as part of national case management strategy (Feb 2003 to present)

USAID PSI

Program Approach

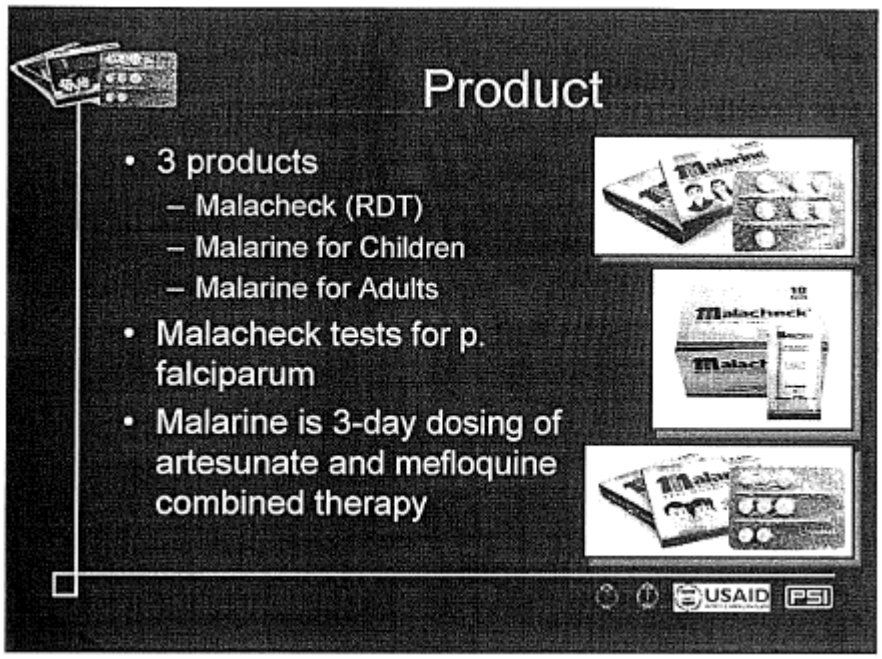
- Goal
  - To provide complementary services for malaria treatment to the target population who do not use or have access to public health system
- Objectives
  - To make Malarine® (pre-packaged malaria treatment) & Malacheck® (rapid diagnostic test kits) accessible through private sector
  - Increase behavior change communication regarding malaria prevention and treatment

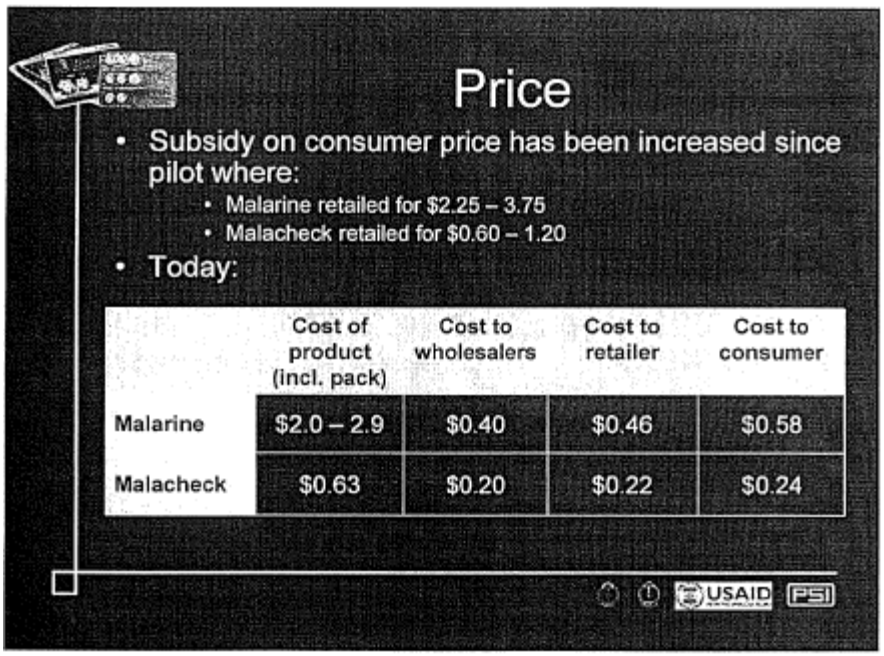
USAID PSI

Sources of funding

- GFATM Round 2:
  - Commodity & Packaging
  - Communication and Implementation
  - Training of Private Provider
  - Monitoring and Evaluation
- USAID:
  - Communication – IEC/BCC
  - Packaging
- PSI private funds and program income –
  - Commodity and Packaging
- CIDA
  - MVU Capacity building
  - MVU Materials
- GFATM Round 6 (anticipated 2008):

USAID PSI


Product
• 3 products
– Malacheck (RDT)
– Malarine for Children
– Malarine for Adults
• Malacheck tests for p. falciparum
• Malarine is 3-day dosing of artesunate and mefloquine combined therapy
USAID
PSI

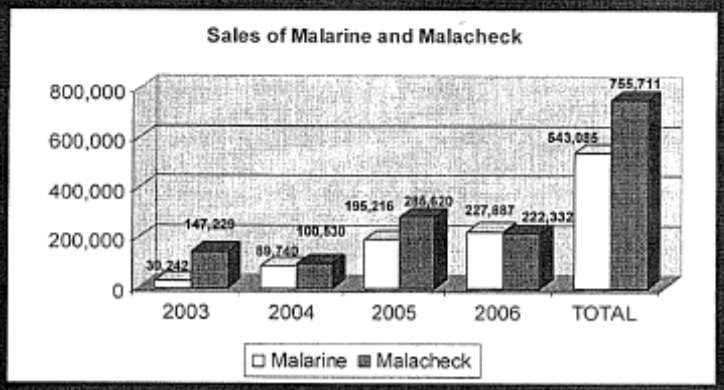

Price
• Subsidy on consumer price has been increased since pilot where:
• Malarine retailed for $2.25 – 3.75
• Malacheck retailed for $0.60 – 1.20
• Today:
Cost of product (incl. pack)
Cost to wholesalers
Cost to retailer
Cost to consumer
Malarine
$2.0 – 2.9
$0.40
$0.46
$0.58
Malacheck
$0.63
$0.20
$0.22
$0.24
USAID
PSI

Place (Distribution)

- Target 17 provinces with malaria risk
- Outlets types
  - Clinics and Hospitals
  - Pharmacies
  - Clinical Pharmacies
  - Drug Stores
  - Sun Quality Clinics and UHN partners

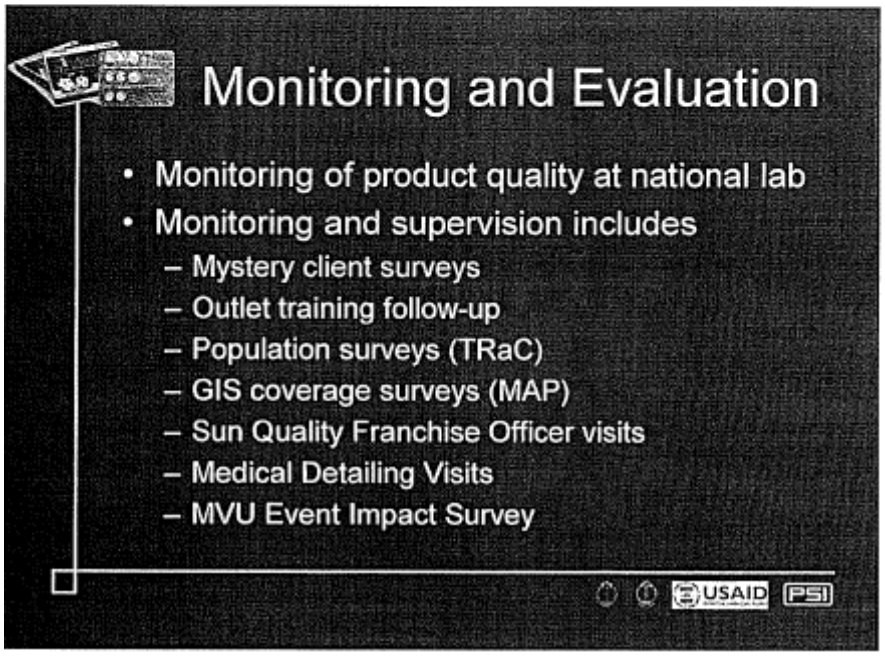
USAID PSI

Distribution



USAID PSI

Promotion (and Training)
• Extensive communication
– Seriousness of malaria
– Need for diagnosis / how to do it
– How to treat malaria
– Need to refer severe malaria cases
• Use of mass media
– TVCs and Radio spots
• Mobile Video Units in rural areas
• Point-of-sale materials
• Medical Detailing Program
• Multi-level provider training
– Including Sun Quality and UHN
USAID
PSI


Monitoring and Evaluation
• Monitoring of product quality at national lab
• Monitoring and supervision includes
– Mystery client surveys
– Outlet training follow-up
– Population surveys (TRaC)
– GIS coverage surveys (MAP)
– Sun Quality Franchise Officer visits
– Medical Detailing Visits
– MVU Event Impact Survey
USAID
PSI

Experiences and Lessons Learned I

- Price inflation of Malarine to the consumer
  - Possible cause
    - Shortage of product
    - Need for increased consumer price awareness
    - Need for increased training of provider
  - Possible solutions
    - Ensure supply security through improved procurement processes and increased funding
    - Increase awareness of consumer price through communication and packaging display
    - Improvement of training curriculum

USAID PSI

Experiences and Lessons Learned II

- Splitting up of co-blistered products to sell as part of "cocktails"
  - Possible Causes
    - Profit seeking behavior of the outlet
    - Price is too high
    - Lack of confidence in the product
    - Limited understanding of compliance
  - Possible Solutions
    - Improved margins for the outlet
    - Increase knowledge and promotion to consumer
    - Improved provider training
    - Better monitoring of provider behavior

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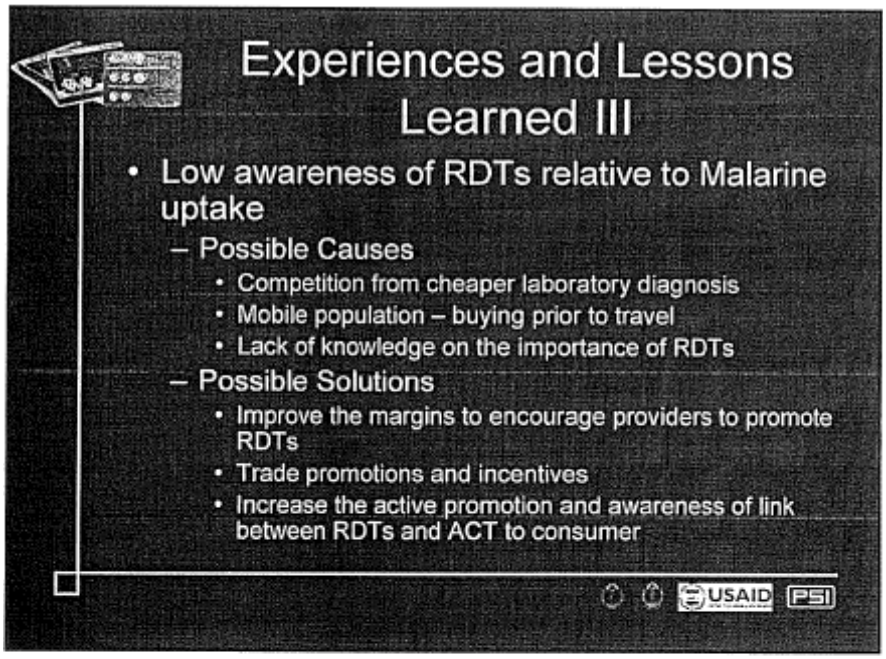
Experiences and Lessons Learned III
• Low awareness of RDTs relative to Malarine uptake
– Possible Causes
• Competition from cheaper laboratory diagnosis
• Mobile population – buying prior to travel
• Lack of knowledge on the importance of RDTs
– Possible Solutions
• Improve the margins to encourage providers to promote RDTs
• Trade promotions and incentives
• Increase the active promotion and awareness of link between RDTs and ACT to consumer
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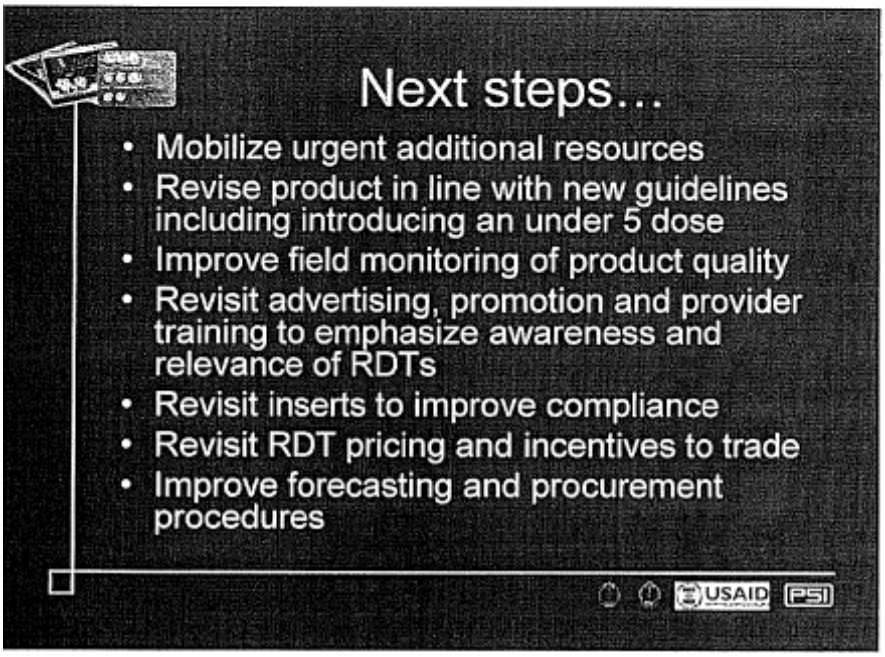
Next steps…
• Mobilize urgent additional resources
• Revise product in line with new guidelines including introducing an under 5 dose
• Improve field monitoring of product quality
• Revisit advertising, promotion and provider training to emphasize awareness and relevance of RDTs
• Revisit inserts to improve compliance
• Revisit RDT pricing and incentives to trade
• Improve forecasting and procurement procedures
USAID
PSI

Next steps…

- Mobilize urgent additional resources
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- Revisit inserts to improve compliance
- Revisit RDT pricing and incentives to trade
- Improve forecasting and procurement procedures

USAID PSI

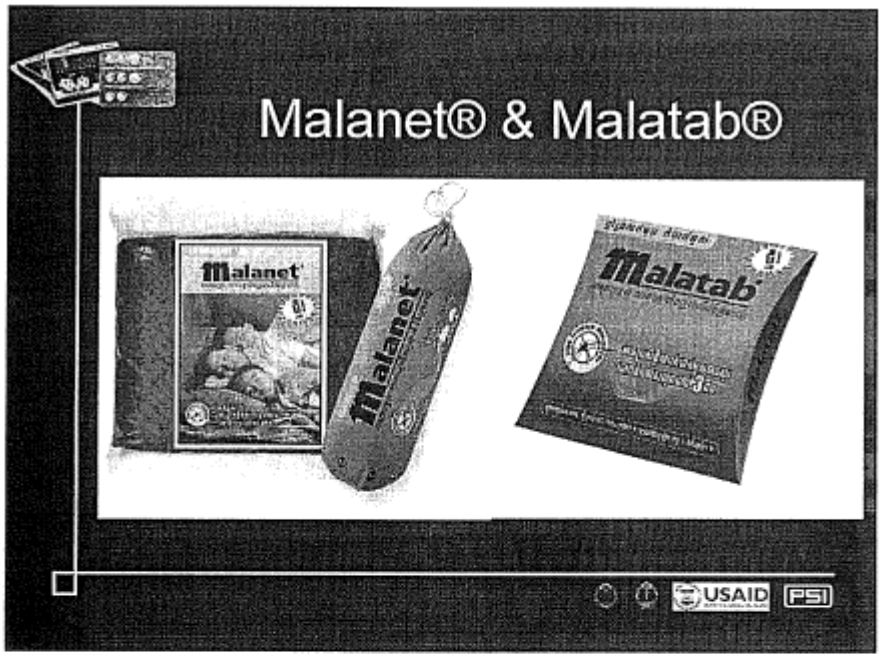
New Product - Prevention

Social marketing:

Malanet®: Long lasting insecticide treated net (LLITN).

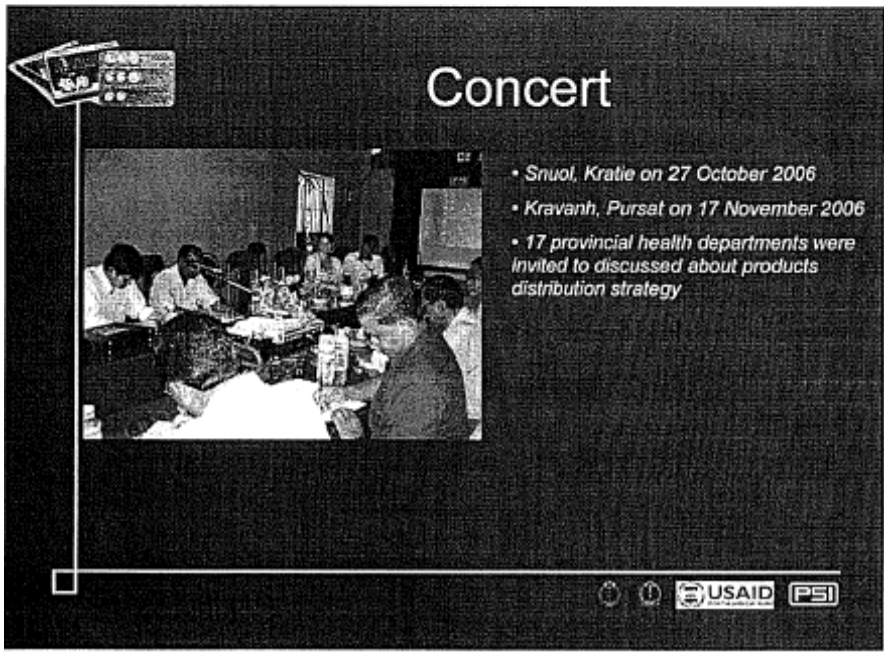
Malatab®: Insecticide treatment kit (ITK).

USAID PSI


Malanet® & Malatab®
Malanet
Malanet
Malatab
USAID
PSI

Product Development
• Work closely with CNM and SMCC on
– packaging and information insert development
– Educational Video
– Pricing and Distribution Strategy
– Training Outlets
USAID
PSI

Official Launch - guest arrival
H.E Profesor Eng Huot graced occasional attendance by taking his busy time to join Malanet and Malatab official launch at Intercontinental Hotel
USAID
PSI


Concert
• Snuol, Kratie on 27 October 2006
• Kravanh, Pursat on 17 November 2006
• 17 provincial health departments were invited to discussed about products distribution strategy
USAID
PSI

Thank you
USAID
PSI

ANNEX 5. REQUEST FOR COUNTRY CLEARANCE

TO: Kate Crawford/USAID/Cambodia/Director OPH

FROM: Management Sciences for Health (MSH)/ Presidential Malaria Initiative (PMI)/Rational Pharmaceutical Management Plus (RPM Plus) Program Cooperative Agreement No. HRN-A-00-00-00016-00

SUBJECT: Request for Country Clearance for travel to Phnom Penh, Cambodia from Dec 1-10, 2006 for Marion Lynders, Kathy Webb and Rima Shretta.

COPY: Jonathan Ross, USAID/Cambodia/ PHN Officer
Chanta Chak, USAID/Cambodia/Infectious Diseases Team Leader
Hen Sokun Charya/USAID/Cambodia/Development Specialist for MCH/RH
John MacArthur, USAID/RDM/A/OPH, Infectious Disease Advisor
Anthony Boni/ GH/HIDN/HS, CTO RPM Plus
Kama Garrison/GH/HIDN
Douglas Keene, Director, MSH/RPM Plus
Maria Miralles, Deputy Director, RPM Plus
Olya Duzey, Program Manager, ANE, MSH/RPM Plus
Malick Diara, Program Manager – Malaria, MSH/RPM Plus

The RPM Plus Program wishes to request country clearance for the proposed travel to Phnom Penh, Cambodia of the following RPM Plus staff; Marion Lynders, Senior Program Associate, Rima Shretta, Senior Program Associates, and Kathy Webb, Program Associate for the Pharmaceutical Management for Malaria training course for the period of December 4-8, 2006.

Background:

With an incidence rate of 7.5 per 1,000 and 382 deaths in 2004, malaria in Cambodia is currently the third most common cause of outpatients, the fifth main health problem among inpatients and the second most common cause of hospital mortality, despite the limited areas of the country where transmission occurs (forested hilly areas). Also, malaria treatment and control is hampered by the spread of resistance to common antimalarial drugs, especially along the Cambodian-Thailand border where multi-drug resistant malaria is prevalent. Another compounding problem has been the high prevalence of counterfeit and substandard antimalarial drugs sold across the country.

Management Sciences for Health's (MSH) Rational Pharmaceutical Management Plus (RPM Plus) Program has received funds from USAID to develop strategies to implement malaria policies and to provide technical assistance in pharmaceutical management issues for malaria. RPM Plus in partnership with the National Center for Parasitology, Entomology and Malaria Control will conduct a national training course on pharmaceutical management for malaria from December 4-8, 2006 in Phnom Penh, Cambodia. The course is being organized by the United States Agency for International Development. The Pharmaceutical Management for Malaria workshop will focus on developing capacity at all levels to manage medicines and supplies for the national malaria control program. It will provide information and hands-on practice to

facilitate staff members understanding and implementation of basic pharmaceutical management concepts and methods.

Since 2002, RPM Plus has been an ACTMalaria partner and has participated in ACTMalaria annual meetings. Previously, RPM Plus shared with the group, methodologies and findings from malaria drug use surveys conducted in Cambodia and Thailand (2002, 2003).

In 2004, RPM Plus completed a community drug management assessment for childhood illnesses in Cambodia. Data were collected from 3,000 households and 1,379 providers from public and private sectors in five provinces, to identify potential household and provider drug management problems that may affect the treatment of childhood illness. ACTMalaria requested RPM Plus to participate at the Regional Symposium on Malaria entitled: *"StrateGems Against Malaria in Asia: Harmonizing Malaria Control Along and Beyond Borders"* and present key findings from the 2004 Community Drug Management of Childhood Illnesses (C-DMCI) survey. This presentation will focus specifically on how malaria in children under five is managed at the community level in Cambodia.

Purpose of Proposed Visit:

Marion Lynders, Kathy Webb and Rima Shretta will travel to Phnom Penh to facilitate a pharmaceutical management for malaria training course. Approximately, 40 participants from the national malaria program as well as pharmacists and medical store staff at the central, provincial and operational district levels will attend the course.

Also, Marion Lynders will present select findings from the C-DMCI survey at the ACTMalaria symposium in Manila, Philippines, November 28-30, 2006.

Scope of work:

Marion Lynders will:

- Participate in and present findings from the Cambodian C-DMCI survey at the ACTMalaria symposium in Manila, Philippines, November 28-30, 2006
- Provide technical assistance to the workshop participants during the pharmaceutical management for malaria training course
- Coordinate logistics for the PMM workshop with assistance from local RPM Plus and malaria program staff
- Meet with USAID and key Ministry of Health representatives to discuss current RPM Plus work and upcoming activities

Kathy Webb and Rima Shretta will:

- Provide technical assistance to workshop participants in pharmaceutical management for malaria.

Anticipated Contacts:

- Kate Crawford, Jonathan Ross, Hen Sokun Charya, Chanta Chak, USAID;

- Key representatives from the Ministry of Health including the National Malaria Control Program

Logistics: Marion Lynders will arrive in Manila, November 27, 2006, on flight Northwest 71 and depart December 1, 2006, on flight Thai Air 621 to Phnom Penh. Ms. Lynders will depart Phnom Penh, December 8, 2006, on flight Thai Air 699 to return to the US. Kathy Webb and Rima Shretta will arrive in Phnom Penh, December 2, 2006 and depart December 10, 2006. Flight details will follow. All MSH staff will be staying at the Himawari Apartment Hotel in Phnom Penh. No mission assistance is required.

Funding: USAID/RDM/A funds to RPM Plus

Action: Please send country clearance for the proposed visit of Marion Lynders, Kathy Webb and Rima Shretta. Please reply via e-mail to the attention of Anthony Boni, USAID/GH/HIDN/HS, e-mail: aboni@usaid.gov, tel: (202) 712-4789, fax: (202) 216-3702. Please send carbon copies to Kama Garrison at kgarrison@usaid.gov, John MacArthur at jmacarthur@usaid.gov, Douglas Keene at dkeene@msh.org, Maria Miralles at mmiralles@msh.org; Olya Duzey at oduzey@msh.org; Malick Diara at mdiara@msh.org; Marion Lynders at mlynders@msh.org; and Nicolette Regis at nregis@msh.org.

Thank you for Mission cooperation.

ANNEX 6. LIST OF PARTICIPANTS

CNM
Ngouv Vanthon
Ouk Rada
Tou Sothea

CMS
Bun Saren
Than Khaily

Planning Unit
Son Thyda

NLDQC
Poeund Kimchheng, Vice Director

Malaria Supervisor of Phnom Penh Municiple Hospital
Dr Nom Chan Dasakhon

CDC
Thai Savuth

Provinces

Mondul Kiri

- Heat Sreng, Provincial Health Department
- Mr Phok Ly Vitol, Malaria Program Supervisor
- Kim Sareth, Provincial Medical Store (Pharmacist)

Preah Vihear

- Mak Sambath, Provincial Health Department
- Dr Meas Samon, Malaria Program Supervisor
- Mr. So Lain, Provincial Medical Store (Pharmacist)

Koh Kong

- Ph Chhun Hour, Director of Provincial Health Department
- Dr Keth Vuthy, Malaria Program Supervisor
- Dr Ou Kem San, Chief of Provincial Medical Store
- Mr Koy Sokha, Sre Ampel Operational District Medical Store
- Mr Chan Phom, Smach Mean Chey Operational District Medical Store

Odear Meachey

- Dr Ouk Kimsoen, Director of Provincial Health Department
- Dr Khon Pong, Malaria Program Supervisor
- Hean Kim Siet, Provincial Medical Store (Pharmacist)

Battambang

- Ngek Bun Chhup, Director of Provincial Health Department
- Ouk Vithiea, Malaria Program Supervisor
- Kor Virak, Provincial Medical Store(Pharmacist)
- Hang Chhe, Operational District Medical Store (Pharmacist)
- Mr Kong Noeun, Operational District Medical Store

Pailin

- Yok Sovann, Vice Director of Provincial Health Department
- Soun Chen, Malaria Program Supervisor
- Nut Tet, Provincial Medical Store

Participants from Other Organizations

RACHA
Kov Buntor

PSI
Diane Freeman

ACTMalaria
Cecil Hugo

BASICS III
Dr. Steve Solter

WHO
Dr. Micheal O'Leary
Dr. Junko Yasuoka
Dr. Rashid Abdur

USAID
Jonathan Ross
Dr. Chanta Chak

Guest Presenters

Pharmacist Association of Cambodia
Dr. Yim Yann

USP/DQI
Abdelkrim Smine

PSI
Mean Samol

ANNEX 7. COURSE AGENDA

Day	Time	Activity	Presenter/Facilitator
Day 1	8:30–9:00	Registration	
	9:00–9:15	Welcome	MSH/RPM Plus
	9:15–9:45	Opening of the course and group photo	Jonathan Ross, USAID/Cambodia Dr. Michael O' Leary, WHO; Dr. Doung Socheat, CNM, Dr. Lon Chanthap, CNM Marion Lynders, MSH/RPM Plus
	9:45–10:15	Introduction of presenters and participants	
	10:15–10:30	**Break**	
	10:30–11:00	Introduction and format of the course, formation of groups, daily evaluation, logistics	MSH/RPM Plus
	11:00–12:00	**Session 1:** Introduction to Management of Malaria Medicines and Supplies	MSH/RPM Plus
	12:00–13:00	**Lunch**	
	13:00–13:30	Group Activity (Worksheet 1.1)	
	13:30–14:00	Presentation of Group Activity (2 groups)	Group presentations
	14:00–15:30	**Session 2:** Monitoring and Evaluation	MSH/RPM Plus
	15:30–15:45	**Break**	
	15:45–17:00	Monitoring and evaluation exercise (Worksheet 2.1)	
Day 2	8:30–8:45	Plenary (questions and clarifications)	
	8:45–10:00	**Session 3:** Selection	MSH/RPM Plus
	10:00–10:15	**Break**	
	10:15–11:30	**Session 4:** Quantification	
	11:30–12:00	Group Activity (Worksheets 4.1 and 4.2)	
	12:00–13:00	**Lunch**	
	13:00-13:30	Group Activity Continued (Worksheets 4.1 and 4.2)	
	13:30–14:45	**Session 5:** Procurement	MSH/RPM Plus
	14:45–15:00	**Break**	
	15:00–15:30	Cambodia and counterfeit drugs	Dr. Yim Yann (PAC)
	15:30–17:00	Group Activity (Worksheet 5.1)	

Day	Time	Activity	Presenter/Facilitator
Day 3	8:30–8:45	Plenary (questions and clarifications)	
	8:45–10:30	**Session 6:** Storage, Distribution, and Inventory Management	MSH/RPM Plus
	10:30–10:45	**Break**	
	10:45–11:00	Group Activity (Worksheet 6.1)	
	11:00-12:00	Inventory management at provincial and district level drug stores-challenges and opportunities	Director of Provincial Health Department-Battambang province
	12:00–13:00	**Lunch**	
	13:00–15:00	**Session 7:** Quality Assurance	USP/DQI
	15:00–15:15	**Break**	
	15:15–16.00	Group Activity (Worksheet 7.1)	
	16.00-17.00	Dealers In Death video-Produced by WHO	
Day 4	8:30–8:45	Plenary (questions and clarifications)	
	8:45–10:00	**Session 8:** Rational Medicine Use	MSH/RPM Plus
	10:00–10:15	**Break**	
	10:15–11:00	Experience with community drug management in Cambodia-Results from the Community Drug Management of Childhood Illnesses survey	MSH/RPM Plus
	11:00–12:00	Group Activity (Worksheet 8.1)	MSH/RPM Plus
	12:00–13:00	**Lunch**	
	13:00–14:00	Role of Private sector	PSI
	14:00–15:30	Session 9: Preparation for fieldwork	MSH/RPM Plus
	15:30–15:45	**Break**	
	15:45–17:00	Group Activity (Worksheet 9.1)	

Day	Time	Activity	Presenter/Facilitator
Day 5	8:30	Depart CNM for field visits (participants must be ready at 8:15 for a prompt 8:30 departure)	
	9:00–11:30	Fieldwork	
	11:30–12:00	Group Activity (Worksheet 9.1, preparation for presentation)	
	12:00–13:00	**Lunch**	
	13:00-14:00	Group Activity (Worksheet 9.1, preparation for presentation continued)	
	14:00–15:00	Presentation of group activity	Group presentations
	15:00–15:15	**Break**	
	15:15–16:45	Presentation of group activity	Group presentations
	16:45–17:00	Closing Remarks and presentation of participation certificates	CNM and MSH/RPM Plus