Mekong Malaria Initiative
Antimalarial Drug Quality Monitoring and Evaluation

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Acronyms and Abbreviations

BG	Background indicator
BP	British Pharmacopoeia
DRA	Drug regulatory authority/agency
EP	European Pharmacopoeia
GLP	Good laboratory practices
IP	Impact indicator
Int.P	International Pharmacopoeia
JP	Japanese Pharmacopoeia
MOH	Ministry of Health
NGOs	Non-governmental organizations
NLDQC	National Laboratory for Drug Quality Control
NMC	National Malaria Control Program
OC	Outcome indicator
PC	Process indicator
QA/QC	Quality assurance and quality control
RBM	Roll Back Malaria
THL	Temperature, humidity and light
TLC	Thin-layer chromatography
USAID	United States Agency for International Development
USP	United States Pharmacopeia
USP DQI	United States Pharmacopeia Drug Quality and Information Program
WHO	World Health Organization

1. Background

The use of poor quality drugs is thought to contribute to the increase in drug-resistant malaria in South-East Asia. In October 2002, the U. S. Pharmacopeia Drug Quality and Information (USP DQI) program embarked on a project to assist the Mekong Region countries to improve the quality of antimalarial medicines. Toward achieving this goal, USP DQI has collaborated with the World Health Organization's (WHO) Roll Back Malaria initiative in the Mekong Sub-Region, WHO Country Offices, and national health authorities to conduct training courses on enhanced drug quality measures in the Mekong Sub-Region. The courses, held in Cambodia, Laos, and Thailand during March, April, and July 2003 respectively, focused on good laboratory practices, basic tests, sampling procedures, and drug quality data reporting.[1] Selected drug regulatory officials, laboratory personnel, and malaria control program staff were trained to use low-technology methods and techniques (basic tests – physical/visual inspections, simple disintegration, and thin-layer chromatography) to screen antimalarial drugs for quality in the field.

2. Objectives and Rationale for Monitoring

Drug quality monitoring aims to strengthen drug quality assurance programs and quality control systems at the national and program levels. There are two primary objectives:

1. To obtain evidence-based data from the field on the quality of selected antimalarial drugs; and

2. To present recommendations to policymakers on developing and implementing appropriate strategies to address drug quality problems.

More specifically, antimalarial drug testing data will be collected, analyzed, classified, and disseminated among Mekong Sub-region countries and shared with other regions and interested organizations as appropriate. The findings from data analysis will be documented and used to help national malaria programs, including government agencies and NGOs, develop and implement appropriate strategies that address the problems of counterfeit and substandard drugs, which will ultimately improve the quality of antimalarial medicines. In addition, the findings of this project will strengthen collaboration and cooperation among Mekong Sub-region countries that wish to introduce measures to deal with illegal cross-border pharmaceutical trade, one factor believed to contribute to the high prevalence of fake and substandard medicines in this area. In order to maximize efforts, a proper tool must be developed for monitoring and evaluation.

Why monitor and evaluate?

Monitoring and evaluation are key elements in any project operation. Performance-based outcomes must be monitored continuously to determine the extent to which established targets are being met. With a monitoring system in place, when problems do occur, appropriate corrective action can be taken immediately.

Several methods for monitoring and evaluation of drug quality assurance and control activities exist. One common method used is to collect standardized data to measure specific

indicators. To calculate indicators, data are needed about the program. These data should be available within the drug quality assurance, control, and information system.

Based on what criteria?

Ideally, indicators should be:

a) understandable;
b) specific;
c) available;
d) verifiable;
e) relevant;
f) measurable; and
g) representative.

All countries in the Mekong Sub-Region officially have national drug policies and malaria control policies in place; some publish them as laws, regulations, or procedures. The rules vary from country to country but generally support the same goal: Making good quality, effective, safe, low-cost essential medicines available to the entire population at an affordable cost and ensuring that they are used rationally. With an effective drug quality monitoring and evaluation system in place, a malaria control program can support national drug policy goals.

3. Methodology

The methodology of this monitoring is based on a framework consisting of the following elements:

- Review the national malaria situation and assess capability in drug quality assurance and drug quality control;
- Identify and select sentinel sites to participate in drug quality monitoring activities, where other malaria activities, such as drug resistance monitoring, are also being monitored. The sites are selected for their geographic location (bordering with neighboring countries), their high level of drug resistance, their high malaria prevalence, and the appearance of cross-border illegal trade in medicines;
- Organize training courses on GLP, sampling, basic testing, drug quality data management, and reporting for national drug laboratory control labs, drug regulatory agencies, and selected sentinel sites staff;
- Develop and implement in-country field operations, i.e., sample collection, testing (including verification and confirmation), and data documenting and reporting;
- Collect testing data, analyze, report, and present suggestions for appropriate strategies to address any drug quality control problems;
- Organize regional meetings to share and disseminate findings and propose recommendations; and
- In the medium- and long-term, monitor suggestions and recommendations for implementation.

Figure 1 summarizes the methodological framework for monitoring.

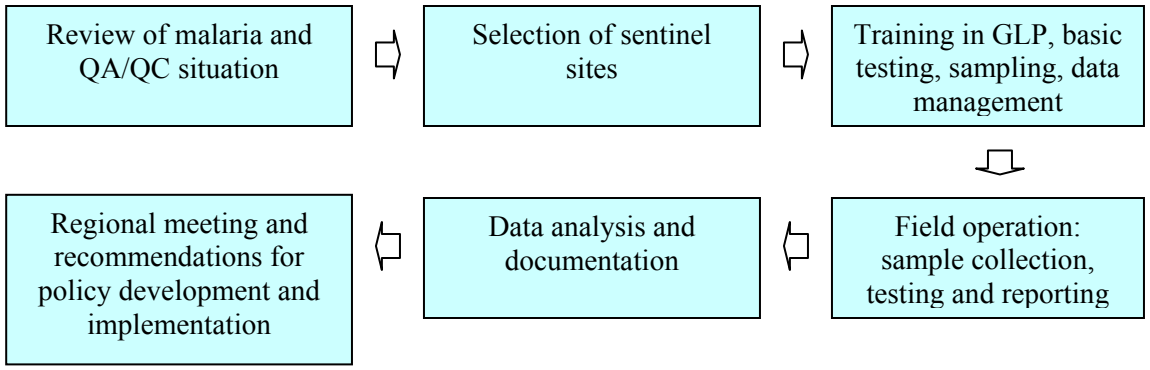


Figure 1.

3.1. Data collection methods and techniques[2]

Data will be collected using pre-defined indicators; a proposed list is provided. (See Annex.)

Combined techniques will be used to collect data, such as:

1. Conduct formal or semi-formal discussions and consultations with responsible officials, including directors or deputies of chief divisions within the drug regulatory agency (DRA), government and other procurement agencies, selected key NGOs, drug testing labs, and selected key pharmaceutical establishments.

2. Review technical documents and records from primary and secondary sources. Records could include drug laws, executive orders, inspection records, and DRA and National Lab annual or mid-term reports. Other convenient techniques, such as email, fax, and telephone are also used.

3. Obtain quantitative data on samples, tests, and testing results from field operations in each country.

3.2. Methods for data analysis and reporting

Both qualitative and quantitative data collected for each indicator will be examined, analyzed and, where appropriate, computed into percentages by USP DQI personnel in close consultation with collaborating organizations, such as WHO RBM Mekong and national/local experts in related fields. Where necessary and appropriate, these data will be presented in tables or other graphic depictions for better visual data comparisons between countries. In the analysis, both number and proportion (numerator/ denominator) expressed in percentage (%) are used for selected indicators. Most indicators are expressed in numbers to explicitly reflect the actual data, which may not provide a true picture if expressed in percentage.

The analysis attempts to address the following questions:

1. What is the magnitude of the problem of poor quality antimalarial drugs both in the public and private sectors (chloroquine tablets; quinine tablets/injections; sulfadoxine+pyrimethamine tablets; artesunate tablets; tetracycline tablets/capsules; mefloquine tablets; amodiaquine tablets; primaquine tablets; and dihydroartemisinin derivatives preparations).

2. *What* problems related to QA/QC system need to be addressed and *how* can the problems be approached?

The analysis will provide the following information:

- Background information - Covers brief background information on health and on pharmaceuticals, with indicators about key aspects of pharmaceutical services (procurement, storage and distribution) in both the public and private sectors, drug regulatory system, and functions.

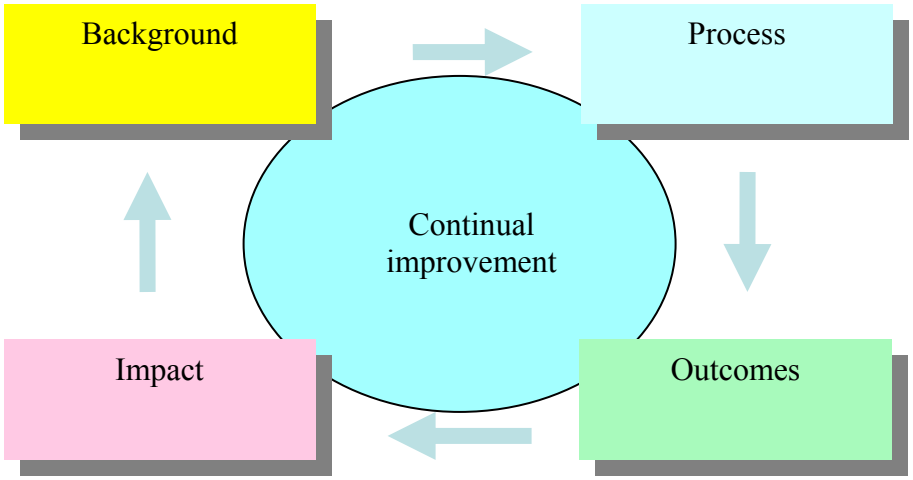
- Process – Reflects the mechanisms used and activities performed by the sentinel sites, malaria control program, national laboratory and reference labs, and DRA. Process indicators are used to assess the effectiveness of these mechanisms and activities.

- Outcomes – The achievement of common objectives of each country's DRA to address poor quality antimalarial drugs as well as that of this monitoring project. Outcome indicators will be used to demonstrate the degree to which these objectives are being met.

- Impact – The overall impact of the monitoring activity on the national malaria program, e.g., reduction of poor quality medicines over time and an increased budget allocation of government in QA/QC work.

- Continual improvement – The overall goal for the government (including ministry of health, drug regulatory authority, malaria control program, the national laboratory for drug quality control) and others to achieve.

Analysis is based upon the principles depicted in Figure 2, below.



3.3. Testing methods[3]

For screening test at the sentinel site level: The German Pharma Health Fund Minilab testing procedures and the techniques taught during training are used to screen for quality of testing at the sentinel sites. This testing includes physical/visual examinations, simple disintegration, and thin layer chromatography.

Verification and confirmation tests at national and reference laboratories will be carried out using the latest analytical methods and procedures, consistent with specifications described in the monographs of the *U. S. Pharmacopeia* (USP) and *International Pharmacopoeia* (Int.P). USP DQI and the WHO Country Office will ensure that these monographs are available at all national labs.

The following antimalarial drug preparations are included in this monitoring project: chloroquine tablets; quinine tablets/injections; sulfadoxine/pyrimethamine tablets; artesunate tablets; tetracycline tablets/capsules; mefloquine tablets; amodiaquine tablets; primaquine tablets; and dihydroartemisinin derivatives preparations. For preparations that have neither USP nor Int.P monographs, other pharmacopeias will be used, including the *British Pharmacopoeia* (BP), *European Pharmacopoeia* (EP), *Japanese Pharmacopoeia* (JP), and, if necessary, other national pharmacopoeias. In most cases, two primary tests will be used: Identification and assay for content of active ingredient(s). Other tests are used for selected samples on a case-by-case basis. Test such as dissolution of solid dosage forms, sterility for injection forms, or some other critical tests should be carried out by reference labs to address specific issues.

4. Proposed antimalarial drug quality monitoring indicators

Several of the malarial drug quality indicators listed here are solely for use by national malaria programs participating in the USP DQI Mekong Antimalarial Drug Quality Surveillance Project. These indicators have not yet been field-tested. A few of them, however, have been adapted from WHO guidelines, which have been field-tested and used in their original form by WHO national drug policy programs and by some countries.[4] The following indicators are classified as background, process, outcome, and impact indicators. Seven indicators (out of 18) are selected as *core indicators* (BG1, BG7, PC2, PC3, OC1, OC2 and IP2 –in bold-faced below) which should be collected by each country's point person or team for the USP DQI project. Others are complementary and should be adapted to each country's environment and the sentinel sites settings.

To determine the feasibility of adopting certain indicators within a malaria drug quality assurance and control system, the following information must be considered:

- Name of the indicator;
- Rationale for the indicator;
- Use of the indicator;
- Computation/calculation; and
- Location and provider of the data.

4.1. Background Indicators

Drug legislation and regulation

1. **Existence of legislation and regulations concerning drug registration, licensing of pharmaceutical establishments, inspection, control of drug production, importation, and exportation.**

Procurement, storage, and distribution

2. Number of occasions or times that antimalarial drugs were procured at central or provincial level from qualified suppliers in the past two years.

3. Number of provincial site warehouses and health facilities that store antimalarial drugs under appropriate storage conditions in terms of temperature, humidity, and protection from light.

4. Number of drug retail outlets visited that store antimalarial drugs in appropriate storage conditions in terms of temperature, humidity, and protection from light.

5. Number of antimalarial drug samples beyond their expiry date collected over one-year period.

Rational drug use

6. Number of pharmacies and drug outlets with good awareness about the existence of substandard or counterfeit antimalarial drugs and the associated health risks of using them.

Drug quality assurance and quality control

7. **Existence of operational drug registration, inspection, licensing, and laboratory services at the national level.**

8. Number of antimalarial drugs registered out of the total number available in the country.

4.2. Process Indicators

The process indicators described below have been tailored specifically to the USP DQI antimalarial drug quality surveillance project.

Malaria sentinel site

1. Number of antimalarial drug samples collected during each defined monitoring period (every three, four, or six months)

2. **Number of antimalarial drug samples tested that failed initial screening test(s) at sentinel surveillance site (by physical/visual inspection, simple disintegration, or TLC).**

National laboratory for drug quality control

3. Number of samples received from the sentinel sites that were tested for verification.

Reference lab(s)

4. Number of samples received and tested by Reference Lab(s) for confirmation.

4.3. Outcome Indicators

1. **Number of batches/lots failing quality tests that are removed from National Malaria Program (or from the market).**

2. **Administrative or regulatory actions taken against providers or manufacturers that sell poor quality antimalarial drugs.**

3. Decreased number of illegal or unlicensed drug outlets over time at the sites participating in the project.

4.4. Impact Indicators

1. Quantified reduction of poor quality antimalarial drugs used in the National Malaria Program and in the market over time.

2. **An increase in government budget allocated for DRA to carry out improved QA/QC activities over time.**

5. Determinants of indicators

Note: The following abbreviations are used below to determine the type of indicator:
BG – Background indicator;
PC – Process indicator;
OC – Outcome indicator; and
IP – Impact indicator.

BG1: Existence of legislation and regulations concerning drug registration, licensing of pharmaceutical establishments, inspection, control of drug production, importation, exportation, drug advertisement and promotion, and post-marketing surveillance.

- Rationale: The existence of adequate legislation and regulations concerning pharmaceutical activities, including drug registration, licensing of pharmaceutical establishments, inspection, control of drug production, importation, and exportation is critical since they are the legal tools used by regulatory authorities to ensure the quality assurance and control of drugs circulated in any country.

- Use: This indicator assesses whether or not a given country has legislation and regulations covering each aspect of drug quality-related activities. The existence must be in the form of a written document with required approval authorization in evidence.

- Computation: This is a YES or NO question answered by checking the appropriate box below for YES.

□ registration □ licensing of persons and pharmaceutical establishments
□ inspection service □ laboratory service

□ drug production □ importation
□ exportation □ drug advertisement and promotion
□ exportation □ post-marketing surveillance

- Location and provider of the data: Information is available from the MOH Department of Food and Drug or the Food and Drug Administration.

BG2: Number of occasions or times that antimalarial drugs were procured at central or provincial level from qualified suppliers in the past two years.

- Rationale: Purchasing medicines from qualified suppliers is one way to reduce the risk of obtaining substandard quality drugs. To be qualified, suppliers must meet predefined quality criteria, which are verified through dossier evaluation, testing, and inspection. For example, key criteria are: products registered; product certificate from WHO certification scheme provided; products produced according to GMP standards; batch certificate provided; and samples passed quality testing.

- Use: This indicator measures whether or not a country or a particular program, e.g., malaria program, is obtaining medicines from reliable suppliers.

- Computation: In the formula below, the figure for the numerator (N) is derived from the number of procurement records/reports showing that drugs have been obtained from pre-qualified suppliers during the last two years. The denominator (D) is from the total number of procurements in the same time period. Knowing these numbers, one can calculate in percentage as follows:

  % of procurement obtained from pre-qualified sources = (N÷D) x 100

  Example: 80% of procurement was from pre-qualified suppliers.

- Location and provider of the data: Information is available from the Procurement Department of the Malaria Program at the Department of Food and Drug or from Central Medical Stores, Food and Drug Administration.

BG3: Number of provincial site warehouses and health facilities that store antimalarial drugs under appropriate storage conditions in terms of temperature, humidity, and protection from light (THL).

- Rationale: Storing drugs in appropriate conditions is crucial to maintaining drug quality throughout its labeled shelf-life. Antimalarial drugs, like other medicines, should be stored in accordance with the conditions stated on the label.

- Use: This indicator assesses warehouses and health facilities for appropriate storage practices to ensure that quality will not be affected.

- Computation: In the formula below, the numerator (N) is derived from the number of warehouses or health facilities that store antimalarial drugs in appropriate storage temperature and humidity during each visit when collecting drug samples. The denominator (D) is the total number of warehouses or facilities that store antimalarial drugs. Knowing these numbers, one can calculate in percentage as follows:

% of warehouses/health facilities with appropriate storage THL= (N÷D) x 100

Example: 90% of warehouse or facilities do not keep antimalarial drugs in recommended temperature.

- Location and provider of the data: Data can be obtained during the sample collection visits at individual warehouses and health facilities.

BG4: Number of drug retail outlets visited that store antimalarial drugs in appropriate storage conditions in terms of temperature, humidity, and protection from light (THL).

- Rationale: Keeping appropriate storage temperature, humidity, and protection from direct sun light is crucial to maintaining drug quality throughout its labeled shelf-life. Antimalarial drugs, like other medicines, should be stored in accordance with the conditions stated on the label.

- Use: This indicator assesses the drug outlets for appropriate storage practices to ensure that quality will not be affected by storage conditions.

- Computation: In the formula below, the numerator (N) is derived from the number of drug outlets that store antimalarial drugs in appropriate storage temperature, humidity, and direct light protection during each visit when collecting drug samples. The denominator (D) is the total number of drug outlets that store antimalarial drugs. Knowing these numbers, one can calculate in percentage as follows:

  % of drug retail outlets with appropriate storage THL = (N÷D) x 100

  Example: 75% of warehouses or facilities do not keep antimalarial drugs in recommended temperature, humidity, and direct light protection facilities.

- Location and provider of the data: Data can be obtained during sample collection visits at individual retail drug outlets.

BG5: Number of antimalarial drug samples beyond their expiry date collected over one-year period.

- Rationale: Every drug has an expiry date which should be clearly indicated on the label. The fact that a patient can find antimalarial drugs beyond the expiry date in any health facility or drug outlet indicates a bad supply system and an ineffective quality assurance program.

- Use: To assess the effectiveness of the supply system at health facility and drug outlet level.

- Computation: In the formula below, the numerator (N) is derived from the number of drug samples beyond the expiry date collected during a one-year collection period. The

denominator (D) is the total number of drug samples collected during that one-year period. Knowing these numbers, one can calculate in percentage as follows:

% of drug samples beyond expiry dates = (N÷D) x 100

Example: 6% of drug samples collected were beyond their expiry date.

- Location and provider of the data: Data can be obtained during the sample collection visits at individual warehouses, health facilities, and retail drug outlets.

BG6: Number of pharmacies and drug outlets with good awareness about the existence of substandard or counterfeit antimalarial drugs and the associated health risks of using them.

- Rationale: Numerous reports and studies have shown that substandard and counterfeit antimalarial medicines are freely available in the market. Responsible drug outlets should be aware of the potential risk and danger of using these drugs and should make every effort to sell only good quality and genuine antimalarial products. To obtain this information, pose these questions:
  1. Have you encountered counterfeit or poor quality antimalarial drugs during the past year or recently? □ Yes □ No
  2. What would be the health risks of using fake or poor quality antimalarial medicines? □ No cure □ Prolonged illness □ Death □ Others
  3. What measures have you used to make sure that the medicines you buy are reliable for their quality?
     □ Buy medicines from reliable sources
     □ Carefully examine before buying them
     □ Other, specify _____

- Use: This indicator assesses the awareness among pharmacists and retailers about the availability of substandard and/or counterfeit antimalarial drugs and the health risk of using them.

- Computation: Good awareness – if all three questions are answered correctly
  Example: 50 (D) drug outlets visited during the survey and asked, only 20 (N) can give correct answer. This can be calculated in percentage as follows:

  % of drug outlets with good awareness = (N÷D) x 100 = 40%

- Location and provider of the data: Information can be obtained during the sample collection visit at individual pharmacies/drug outlets.

BG7: Existence of operational drug registration, inspection, licensing, and laboratory services at the national level.

- Rationale: Drug registration, inspection, licensing, and laboratory services form the basic functions of any drug regulatory agency's responsibility to ensure the quality of drugs marketed in the country.

- Use: This indicator is used to indicate the existence of core functions of a drug regulatory agency. Further questions should be posed and acceptable answers obtained to make sure that these services are working (refer to Appendix for questions and explanation).

- Computation: Based on the questions posed and answers obtained above, give a check (√) in the boxes below for acceptable answers:

  □ registration □ licensing of pharmaceutical establishments
  □ inspection service □ laboratory service

- Location and provider of the data: National drug regulatory authorities, e.g., Drug and Food Department or the Food and Drug Administration should have available the reference documents or terms of reference for the agency functions.

BG8: Number of antimalarial drugs registered out of the total number available in the country.

- Rationale: Proper registration of a drug by a drug regulatory agency provides some guarantee to the user of its quality, safety, and efficacy. Studies found a lower incidence (about three-fold) of substandard products among registered antimalarial medicines compared to unregistered products.

- Use: This indicator assesses whether an unregistered antimalarial product may be sold legally in a country. If so, it indicates a weak drug regulatory authority and a poor drug quality control system.

- Computation: In the equation below, the numerator (N) is derived from the number of antimalarial drug products registered in the country by the NDRA. The denominator (D) is the total number of antimalarial drug products available in the country. Knowing these numbers, the percentage can be calculated as follows:

  % of drugs registered = (N÷D) x 100

  Example: 95% of antimalarial drug products are registered in the country.

- Location and provider of the data: Data can be obtained from the MOH DRA Office or the agency dealing with trade/importation and wholesaling of pharmaceuticals in the country.

PC1: Number of antimalarial drug samples collected each defined monitoring period (every three, four, or six months)

- Rationale: To measure the drug sampling activity at each sentinel surveillance site.
- Use: This indicator measures the number of samples collected by staff during the defined monitoring period and provides information on the sources of the samples.
- Computation: Number of drug products (samples) collected by all trained staff from at least three sources:

  1. Periodic random sampling of retail outlets, clinics, and hospitals;
  2. Samples provided by potential suppliers (if products are procured on site) and by new stock arriving at the site warehouse(s);
  3. Samples of specific products provided by the community through complaints.

     Example: In one four-month period, two staff members collected 120 random samples, 10 samples provided by potential suppliers, and 3 samples from community members suspicious of product quality.

     120 + 10 + 3 = 133 samples for one monitoring period at one site.

     In addition, sites should record the sources of samples, e.g., 12 samples from drug retail outlet A, 10 samples from Clinic B, 5 samples from Hospital A, etc. It is important that the sample collection person make every effort to obtain as much information as possible, in accordance with the instructions described in the *Drug Sample Collection Form*.

- Location and provider of the data: Information is available from sentinel sites (or from their reports) and from the supervision team (NMC Program + NLDQC).

PC2: Number of samples collected that are screened for quality at the sentinel sites (by visual inspection, simple disintegration, or thin layer chromatography (TLC)).

- Rationale: To measure the effectiveness of the drug quality monitoring staff at each sentinel surveillance site.
- Use: This indicator measures the number of samples properly screened for quality at each sentinel site against the total number collected during the defined monitoring period. Screening must include physical/visual inspection and at least one additional method (TLC or disintegration). Test results must be properly documented.
- Computation: This indicator is expressed as the number of samples properly tested (as defined by the program) by site staff compared to all samples collected during the defined monitoring period. The higher the percentage, the more effective the staff functions.

Example:: Of 150 samples collected during a four-month period, 120 were tested properly. One can calculate these in percentage as follows:

% of samples tested = (120÷150) x 100 = 80%

- Location and provider of the data: Information can be obtained from sentinel sites (or from their reports) and from the supervision team (NMC Program + NLDQC).

PC3: Number of antimalarial drug samples tested that failed initial screening test(s) at sentinel surveillance site (by physical/visual inspection, simple disintegration, or TLC).

- Rationale: To measure an increase or decrease in poor quality products being used to treat malaria within a specific geographic area over time.

- Use: This indicator measures the number of drug products which were tested during a defined monitoring period and the total number that failed the screening test for quality.

- Computation: This indicator is expressed as the number of drug product samples that failed quality screening tests by the sentinel site compared to the total number of drug product samples tested. The lower the percentage, the more reliable the quality of the available products within the sentinel site area. For comparable evaluation purposes, however, it is important that the number of the sample size is consistent.

  Example: Of the150 drug samples tested during the past four months, 20 failed to conform to the quality standards. One can calculate this in percentage as follows:

  % of drugs sampled that failed quality testing = (20÷150) x 100 = 13.33%

  In addition, testing staff should collect any information that allows the total number of tests to be categorized by such criteria as the number initially presented for testing, reasons for testing, number of positive and negative results, and source of samples. This will help determine adequacy of the quality assurance system of the country.

- Location and provider of the data: Information can be obtained from sentinel sites (or from their reports) and from the supervision team (NMC Program + NLDQC).

PC4: Number of samples received from the sentinel sites and tested for verification by NLDQC.

- Rationale: As part of the quality assurance management practice, verification testing is integrated into the USP DQI Mekong Sub-region antimalarial drug quality monitoring project. The sampling and testing protocol recommend that the NLDQC lab test 100% of samples received. Due to the lack of equipment, analytical procedure, and/or reference substance and/or reagents, however, these samples must be sent to Reference lab(s) for confirmatory testing.

- Use: This indicator measures the capability of individual NLDQCs and their compliance with the procedures required in the antimalarial drug quality monitoring project.

- Computation: This indicator is expressed as the total number of drug samples received by the NLDQC from sentinel sites and tested for verification compared with the total number of drug samples received.

  Example: Of 100 samples received from the sites, 90 samples were tested for verification. This can be calculated in percentage as follows:

  % of drugs sent to NLDQC for verification = (90÷100) x 100 = 90%

- Location and provider of the data: Information can be obtained from the NLDQC.

PC5: Number of samples received and tested by reference lab(s) for confirmation.

- Rationale: As part of the quality assurance management practice, confirmation testing is integrated into the USP DQI Mekong Region antimalarial drug quality monitoring project. The sampling and testing protocols recommend that all samples received be tested by the reference lab(s).

- Use: This indicator measures the capability of reference lab(s) and their compliance with the procedures required in the antimalarial drug quality monitoring project.

- Computation: This indicator is expressed as the total number of drug samples received and tested by the reference lab(s) compared with the total number of drug samples received.

  Example: Of 45 samples received, 40 were tested. This can be calculated in percentage as follows:

  % of drugs tested by the reference lab(s) for confirmation = (40÷45) x 100 = 89%

- Location and provider of the data: Information can be obtained from the reference lab(s).

OC1: Number of batches or lots failing quality tests that are removed from the National Malaria Program or from the market.

- Rationale: In an effective regulatory environment, all batches or lots that fail quality standards are removed from circulation.

- Use: This indicator measures the effectiveness of drug regulatory law enforcement practices.

- Computation: This indicator is expressed as the number of batches or lots of antimalarial drugs removed from the National Malaria Program or from circulation compared to the total number of batches or lots tested and proved to be of poor quality.

Example: Of 20 batches or lots that have failed quality testing, 15 batches or lots of poor quality antimalarial drugs have been removed from circulation. Knowing these numbers, the percentage can be calculated as follows:

% of batches/lots removed from circulation = (15÷20) x 100 = 75%

The higher the percentage, the more effective the enforcement of the regulatory system.

- Location and provider of the data: Information can be obtained from the MOH NDRA Office.

OC2: Administrative or regulatory actions taken against providers or manufacturers that sell poor quality antimalarial drugs.

- Rationale: In an environment where law enforcement or effective regulatory measures are in place, DRAs take appropriate administrative or regulatory actions against repeated violations in selling poor quality medicines, including antimalarials.

- Use: This indicator measures the effectiveness of a regulatory agency or law enforcement practice to exercise a range of provisions against violators, including issuing a notice of warnings, suspending or revoking a license, or assessing a fine.

- Computation: This indicator is expressed as the number of notices, license suspensions or revocations, or fines assessed compared with the total number of violation cases during a defined period.

  Example: Of 30 violations for selling poor quality antimalarial drugs, 20 warnings and four license suspensions were issued between Oct 2003 – Sept 2004. Knowing these numbers, the percentage can be calculated as follows:

  % of administrative and regulatory measures taken = (24÷30) x 100 = 80%

  The higher the percentage, the more effective the regulatory system of a NDRA.

- Location and provider of the data: Information can be obtained from the MOH NDRA Office.

OC3: Decreased number of illegal or unlicensed drug outlets over time at the sites participating in the project.

- Rationale: Due to the ineffective enforcement of laws and regulations concerning authorization and licensing of persons and pharmaceutical establishments, there are unlicensed pharmacies or drug outlets operated in many countries. The number of these illegal drug outlets should decrease over time when QA/QC and DRA are strengthened and laws are enforced.

- Use: This indicator is used to measure whether or not there is a decreased in the number of illegal or unlicensed drug outlets over time.

- Computation: This indicator is expressed as the number of illegal/unlicensed drug outlets at the time of review compared to the total of number of drug outlets when the project started in the participating malaria sentinel site.

  Example: There were 150 illegal/unlicensed drug outlets when the project started in March 2003, and there were 130 when the project was reviewed in March 2004. The percentage can be calculated as follows:

  A decrease of 20 drug outlets (due to closure from revocation or suspension of licenses) or a decrease of 13.3%.

- Location and provider of the data: Information can be obtained from the DRA and/or the (Food and) Drug Department.

<u>IP1: Quantified reduction of poor quality antimalarial drugs used in the National Malaria Program and in the market over time.</u>

- Rationale: One objective of the antimalarial drug quality monitoring project is to reduce the use of poor quality drugs and promote the use of good quality medicines. Over time, the project will have an impact on each country's drug quality assurance and quality control system.

- Use: This indicator measures the percentage of reduction of poor quality antimalarial drugs used in the National Malaria Program and in the market over time.

- Computation: This indicator is expressed as the number of drug samples that failed testing by the NLDQC compared with the number of drug samples that failed testing in the previous review period.

  Example: 180 (out of 850 tested) drug samples failed quality testing in the April 2003 review, and 120 (out of 930 tested) in the April 2004 review period. Knowing these numbers, the percentage can be calculated as follows:

  Failure rate in 2003 = (180÷850) x 100 = 21.17%
  Failure rate in 2004 = (120÷930) x 100 = 12.90%
  There is an 8.27% reduction of poor quality drug products.

- Location and provider of the data: Information can be obtained from the MOH NDRA office or from the NLDQC.

IP2: An increased government budget allocated for DRA to carry out improved QA/QC activities over time.

- Rationale: In the best interests of the country and to improve the sustainability of the drug quality monitoring activities, USP DQI and WHO hope to see an increase in the government budget for these activities.

- Use: This indicator is used to measure whether or not there is an increase in the government budget for QA/QC over time.

- Computation: This indicator is expressed as the budget figures at the time of the project started compared to that of the review periods, e.g., at the second year of the project, and one year after USP DQI and WHO support ends.

  Example: The government budget was US$20,000 when the project started in March 2003; in March 2005 the figure is US$22,000, and in March 2007 this figure grows to US$30,000. The percentage can be calculated as follows:

  An increase of 10% over two years (2003/2005).

- Location and provider of the data: Information can be obtained from the DRA and/or the (Food and) Drug Department.

Appendix for BG7 Indicator:

A- Drug registration- give a check (√) in □ registration if at least obtaining 4 acceptable answers.

1. Does a drug registration department/unit exist? Yes_____ No_____ (Acceptable answer: Yes)

2. How many officers are responsible for routine drug registration? (Acceptable answer: at least 2)

3. Number of pharmaceutical products/preparations officially registered in the country _____ (Year_____). (Acceptable answer: if he/she can give a figure based on a documented report – drug registration record book or computer, if computer-assisted system is used)

4. Capacity to assess application dossiers for registration per year? (Acceptable answer: at least 200 per year)

5. Are guidelines/instructions on drug registration available and freely accessible? (Acceptable answer: Yes and if he/she can demonstration the location of the guidelines)

B- Inspection services- give a check (√) in □ Inspection if at least obtaining 2 acceptable answers.

1. Existence of an inspectorate: Yes _____ No _____
   If yes, provide number of inspectors. Acceptable answer: at least 3 at the central level.

2. Existence of manuals or standard operating procedures (SOPs) for inspectors: Yes_____ No_____; If yes, ask him/her to provide name and date of publication. Acceptable answer if the publication is produced.

3. Number of routine inspections (for both distribution chain and GMP) carried out per year. Acceptable answer: at least 20.

C- Laboratory control/testing - give a check (√) in □ Laboratory service on if at least obtaining 3 acceptable answers

1. Existence of a national drug quality control lab (NDQCL)
   Yes_____ No_____. Acceptable answer: Yes.

2. Number of professional analysts employed in the Lab. Acceptable answer: at least 10.

3. What kind of tests or assays the Lab can perform? Acceptable answer if all (a toe) tests can be carried out by the lab.
   a. Identification Yes_____ No_____
   b. Disintegration Yes_____ No_____

c. Dissolution Yes_____ No_____
d. Assay for content of API(s) Yes_____ No_____
e. Any of the following special tests:
    1. Sterility Yes_____ No_____
    2. Pyrogen Yes_____ No_____

4. Estimated minimum number of samples (including APIs and finished products) the Lab is able to test per year. Acceptable answer: at least 200.

D- Licensing of pharmaceutical establishments. Give a check (√) in □ Licensing service if at least obtaining 3 acceptable answers

1. Existence of unit/team in charge of issuing, variation, suspension and revocation of license for persons or pharmaceutical establishments. Acceptable answer: Yes.

2. Existence of standard operating procedures (SOPs) for licensing of persons or pharmaceutical establishments: Yes_____ No_____; If yes, ask him/her to provide name and date of publication. Acceptable answer if the publication is produced.

3. Number of licenses issued for pharmacies in the last years. Acceptable answer: if he/she gives a figure based on the record or official report.

4. Number of unlicensed drug outlets exists in the country. Acceptable answer: none.

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[3] USP DQI Anti-malarial Drug Quality Monitoring – Mekong Malaria Initiatives, 2003. Standard Operating Procedure for Sampling of Anti-malarial Drug Samples in the USP DQI Anti-malarial Drug Quality Monitoring Project in Mekong Delta Countries. Annex 1: Testing methods, procedures and testing data reporting.
[4] P Brudon, JD Rainhorn, et MR Reich, 1999. Indicators for monitoring national drug policies. A practical manual. 2nd edition. World Health Organization, WHO/EDM/PAR/99.3.