LAO PEOPLE'S DEMOCRATIC REPUBLIC
Peace Independence Democracy Unity Prosperity

Ministry of Health
Food and Drug Quality Control Center

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Comparative Study of the Quality, Availability, and Source of Antimalarial Medicines in Cambodia, Laos, Thailand, and Vietnam in PQM-MQM Covered and Non-Covered Areas in Mekong Sub-Region

Laos Case Report

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Acknowledgements

List of Acronyms and Abbreviations

AMLs	Antimalarials
APIs	Active Pharmaceutical Ingredients
BFDI	Bureau of Food and Drug Inspection
CMPE	Center of Malariology, Parasitology, and Entomology
FDD	Food and Drug Department
FDQCC	Food and Drug Quality Control Center
GFATM	Global Funds for AIDS, Tuberculosis and Malaria
GLP	Good Laboratory Practice
GMS	Greater Mekong Sub-region
GPHF	Global Pharma Health Fund
GPP	Good Pharmacy Practice
INN	
MoH	Ministry of Health
MQM	Medicines Quality Monitoring
MRA	Medicines Regulatory Agency
NMCP	National Malaria Control Program
PFDU	Provincial Food and Drug Units
PQM	Promoting the Quality of Medicines
STGs	Standard Treatment Guidelines
TLC	Thin-layer Chromatography
USP	United States Pharmacopeial Convention

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I. Background:

1. Drug resistant malaria is one of the major public health concerns in the Greater Mekong Sub-region (GMS), especially at some specific border areas between Cambodia-Thailand, Cambodia-Vietnam, Thailand-Myanmar.
2. The antimalarials (AMLs) are procured/purchased and/or distributed through different mechanisms including the Global Funds for AIDS, Tuberculosis and Malaria (GFATM), National Malaria Control Program (NMCP), and private entities; and by various players (e.g, manufacturers, distributors, and retailers) operating the country; their proper availability, source and quality are not well-documented.
3. Despite the technical assistance from the United States Pharmacopeial Convention (USP) Promoting the Quality of Medicines (PQM) and other programs' efforts to improve the quality of AMLs and other essential medicines for several years in the Greater Mekong Sub-region (GMS), sporadic availability of poor-quality AMLs and other pharmaceuticals, including antibiotics, either manufactured in-region or imported from abroad remains a concern needing persistent attention and increased interventions from medicines regulatory agencies (MRAs) and program managers/implementers at all levels.
4. Evidence data has shown a trend of reduction of poor-quality AMLs over the past years in all medicines quality monitoring (MQM) sentinel sites in the region, a valid question still remains to be answered whether or not the reduction can also be applied to non-MQM covered areas. This question led to the design and execution of this comparative survey.

II. Objective

The objective of this survey was to obtain evidence data on quality, availability and source of priority antimalarial medicines (AMLs) being produced and/or imported and circulated in PQM-supported MQM covered areas compared with non-MQM areas in Cambodia, Laos, Thailand and Vietnam.
The following specific objectives were defined:

1. Identify the pharmaceutical quality of AMLs (conformant as well as non-conformant with the quality specifications, and/or other deficiencies e.g., packaging and labeling).
2. Identify their availability (dosage forms, strengths, and brands, storage conditions observed during the sampling), source (country of origin, manufacturer/supplier, health facility and/or retailer, and whether or not they are in national standard treatment guidelines (STGs).
3. Understand their acquisition process and procedures at national malaria control program (NMCP) and health facility levels.
4. Understand challenges and constraints the stakeholders at different levels (medicines regulatory agencies, NMCP managers and healthcare providers) have been facing to ensure the quality of AMLs in the geographical areas in the study.
5. Formulate recommendations for improving sampling strategies of AMLs and other essential medicines under the PQM-supported MQM activities in the region.

The sections discussed below described the implementation of the study in Laos.

III. Activity implementation:

Methodology

This study is a descriptive, cross-sectional survey using a simple random sampling methodology for the sampling locations and AMLs.

The study team consisting of representatives of Food and Drug Department (FDD), Bureau of Food and Drug Inspection (BFDI), Food and Drug Quality Control Center (FDQCC), Center of Malariology, Parasitology, and Entomology (CMPE), Provincial Food and Drug Units (PFDUs), the provincial Malaria Station, and the PQM Focal Officer who randomly selected outlets from both the public and private sectors within MQM and Non-MQM areas representing the north, central and southern parts of the country.

The study design was developed by the PQM staff with inputs and close consultation with the national and local agencies described above. A pre-study workshop was conducted to train the country study team on the study methodology with main focus on sampling protocol and techniques as well as on testing of samples prior to study implementation.

Sample size calculations based on Yamane simplified formula generated a minimum sample size of 114 samples assuming sampling error of ±4 percent, 95% confidence interval, and a failure rate prevalence of between 5-15% and equal variability in quality of antimalarials across the study sites.
Minimum sample size = $[Z^2 \times (p) \times (1-p)] / d^2$, where:
Z = critical value (e.g., 1.96 for 95% confidence level)
p = prevalence, expressed as decimal (failure rate
d = confidence interval, expressed as decimal (e.g., 0.04)

Samples were collected, labelled and packed strictly based on the study protocol for transportation to the sentinel testing sites to ensure protection from deterioration, contamination, or physical damage.

Samples were transported to a sentinel site for basic testing using the Global Pharma Health Fund (GPHF) Minilab® techniques: The sample screening tests included physical and visual inspection, simple disintegration, and Thin-layer chromatography (TLC). A simple disintegration test checks whether uncoated, normal-release, solid-dosage forms will disintegrate within 30 minutes, which provides information about their solubility. The TLC is a simple, flexible, and effective method for checking the identity of a pharmaceutical product and for semi-quantitative determination of the product. TLC is generally used for one of three purposes: to identify the presence of Active Pharmaceutical Ingredients (APIs) in a product formulation, to determine the presence of impurities, or to quantitatively determine the estimated amount of a particular substance in a sample. Accurate estimates of quantity can be measured by comparison between the spot intensity of the test sample with that of the reference product.

A subset of these samples (those that failed, passed, or were considered doubtful- meaning the results were unclear) were then selected based on the protocol for confirmatory analysisat the Food and Drug Quality Control Center laboratory using appropriate pharmacopeial methods

(USP, International Pharmacopoeia, Chinese Pharmacopoeia, and British Pharmacopoeia, unless otherwise specified).

- Testing included correct labeling and packaging including the following information:
  - Product name (brand or trade name, and INN or generic name)
  - Dosage form and strength
  - Number of tablet or capsules (quantity) per dispensing unit
  - Manufacture date and expiry date
  - Lot or batch number
  - Name and address of manufacturer and/or distributor
  - Registration number
  - Storage condition instructions
  - Administration instruction and package insert, if applicable.

- Organoleptic (physical/visual) examination for contaminant, uniformity of shape, and other physical characteristics (color, mark, score line, etc.)
- Identification of API(s); *if passed, continue with Assay test.*
- Assay for content of API(s); *if passed, continue with Dissolution test*
- Dissolution for tablet and capsule forms.

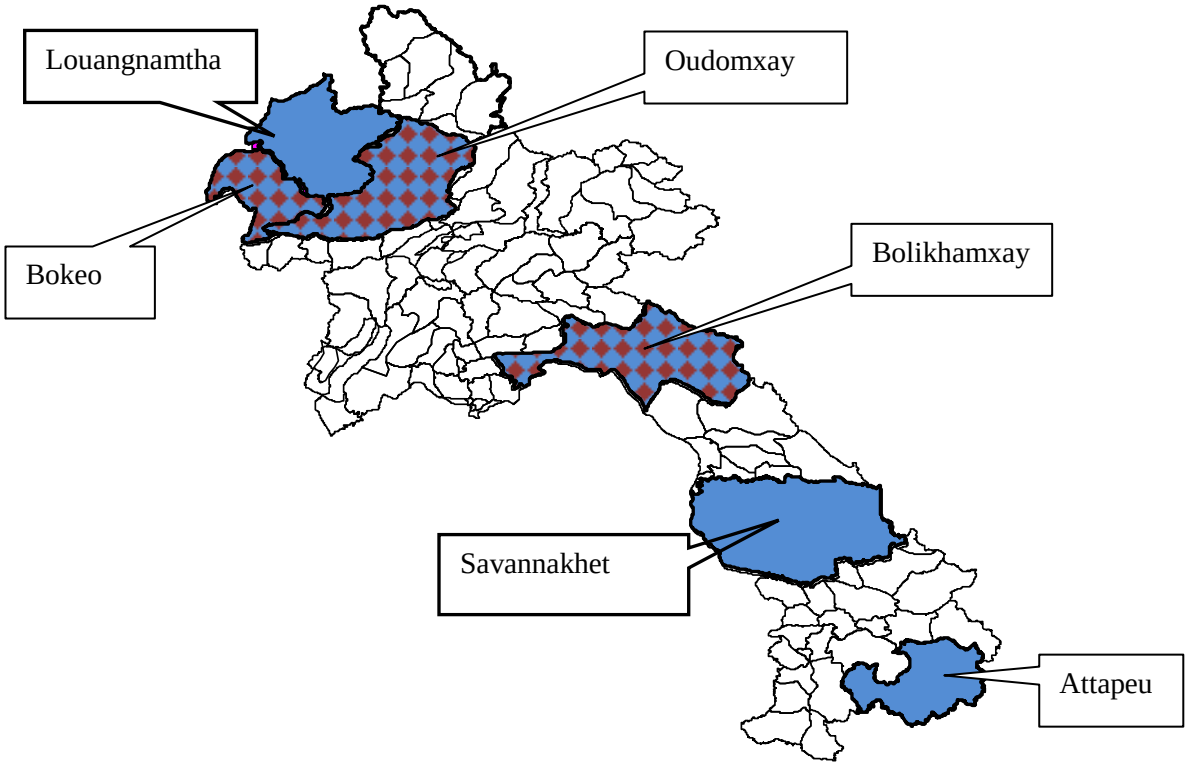
- For injectables, the following tests were performed:
  - Proper packaging and labeling
  - Organoleptic (physical/visual inspection) test
  - Identification test
  - Assay for content of API

Sample collection and testing teams

No.	FDQCC Teams (Central)	Provinical MQM Teams	NON-MQM Teams
1	- Dr. Souklatsamy Vongsack - Dr. Lamphet Khounsaknalath - Dr.Bounpone Phommachack	<u>Savannakhet</u> - Ms. Phetvong-nga F&D Prov. - Ms. Souphaphone F&D Prov. - Ms. Chansouk F&D Sepone Distr. - Ms. Oulayvanh F&D Nong Distr.	<u>Bolikhamxay</u> - Ms. Soudsada F&D Prov. - Ms. Kongmanee F&D Prov. - Ms. Maniphone F&D Bolikhan Distr. - Mr. Bouasy F&D Khamkert Distr.
2	- Dr. Phatsaly Oudomsack - Dr. Chansapha Pamanivong - Ms. Phetsamone Vongphachan	<u>Attapeu</u> - Dr. Sommack F&D Prov. - Ms. Sangvane F&D Prov. - Mr. Inpanh F&D Saysettha Distr. - Mr. Phonephet F&D Sansay Distr.	
3	- Dr. Thippaphone Koenakhone - Dr. Vannakone Sirisomphone - Mr. Somchai Chanthapany	<u>Luangnamtha</u> - Dr. Chanthee F&D Prov. - Dr. Bounmee F&D Prov. - Ms. Davone F&D Sing Distr. - Ms. Deng F&D Long Distr.	

4	- Dr. Panyphone Meksavanh - Dr. Chansapha Pamanivong - Ms. Viengkham Sayyavong		<u>Bokeo</u> - Dr. Phonepasith F&D Prov. - Dr. Siphouttha F&D Prov. - Ms. Somphet F&D Houayxai Distr. - Ms. Khammieng F&D Tonpheung Distr.
5	- Dr. Thongvang Ratsavong - Dr. Lamphet Khounsaknalath - Mr. Somchai Chanthapany		<u>Bokeo</u> - Dr. Phetchanh F&D Prov. - Ms. Pinkoe F&D Prov. - Mr. Khamko F&D Houn Distr. - Ms. Dokkhoun F&D Pakbeng Distr.

Geographical areas of sampling



Symbol:
☐ MQM Provinces
❖ NON-MQM Provinces

Level 1 outlets include the Provincial Hospitals, National Malaria Control Warehouses, and Private Distributors and Manufacturer Warehouses. Level 2 outlets include District Hospitals and private pharmacies.

Serial No.	Provinces	Province Level (Level 1)	District Level (Level 2)	
			1	2
1	Louangnamtha	- Provincial Hospital - National Malarials Control Warehouse - Distributors	Sing	Long
2	Savannakhet		Sepone	Nong
3	Attapeu		Saysettha	Sanesay
4	Bokeo		Houayxai	Tonpheung
5	Oudomsay		Houn	Pakbeng
6	Bolikhamsay		Bolikhan	Khamkert

Results

The table below shows the type and number of samples by location.

List of drug items and number of samples collected from MQM and NON-MQM

Serial No.	Item	MQM			NON-MQM			Total
		Louangnamtha	Savannakhet	Attapeu	Bokeo	Oudomsay	Bolikhamsay	
1	Artesunate Tab/Inj.	0	0	1	0	1	0	**2**
2	Artemether Tab/Inj.	1	0	0	0	0	0	**1**
3	Dihydroartemisinin Tab*	0	0	0	0	0	0	**0**
4	Mefloquine Tab./Cap.*	0	0	0	0	0	0	**0**
5	Primaquine Tab. *	0	0	0	0	0	0	**0**
6	Chloroquine Tab.	4	2	4	3	4	0	**17**
7	Quinine Tab/Inj.	1	0	0	0	1	0	**2**
8	Artemether/Lumefantrine Tab.	3	5	3	2	1	7	**21**
9	Artesunate/Mefloquine Tab.*	0	0	0	0	0	0	**0**
10	Sulfadoxine/pyrimethamine Tab.*	0	0	0	0	0	0	**0**
11	Amoxicillin Cap.	9	5	9	14	9	9	**55**
12	Cloxacillin Cap.	3	2	0	2	5	4	**16**
Grand total		**21**	**14**	**17**	**21**	**21**	**20**	**114**

* Not available in Lao PDR

Samples were collected from both the public and private sectors in each province. 24/52 (46%) of samples in MQM areas were collected from public outlets, and 28/52 (54%) of samples were collected from public outlets in Non-MQM provinces. Level 1(19 samples) and Level 2 (95 samples) were collected.

Distribution of Samples by Sector

Province	MQM		Non-MQM		Total
	Private	Public	Private	Public	
Attapeu Province	11	6			17
Louang namtha Province	11	10			21
Savannakhet Province	6	8			14
Bokeo Province			12	9	21
Borikhamxay Province			8	12	20
Oudomxay Province			14	7	21
Total	**28**	**24**	**34**	**28**	**114**

Samples were tested in the sentinel sites using Minilab methods. The basic test results suggested that all 114 samples tested at 6 provincial sentinel site laboratories (MQM and NON-MQM) met the basic quality specifications.

Basic test results using Minilab methods at the 6 sentinel sites

No.	Provincial Minilab Site	Number of samples	Kinds of products	Test results				
				Pass	Doubtful	Fail	Counterfeit	Not analysed
MQM								
1	Louangnamtha	21	06	21	0	0	0	0
2	Savannakhet	14	04	14	0	0	0	0
3	Attapeu	17	04	17	0	0	0	0
NON-MQM								
1	Bokeo	21	04	21	0	0	0	0
2	Oudomsay	21	06	21	0	0	0	0
3	Bolikhamsay	20	03	20	0	0	0	0
Total		**114**	**07**	**114**	**0**	**0**	**0**	**0**

From the 114 samples which were collected, a subset of 38 were subjected to confirmatory testing at FDQCC:

No.	Item	Number
1	Artesunate Tab/Inj.	02
2	Artemether Tab/Inj.	01
3	Chloroquine Tab.	10
4	Quinine Tab/Inj.	01

5	Artemether/Lumefantrine Tab.	09
6	Amoxicillin Cap.	10
7	Cloxacillin Cap.	05
Total		38

The results of the confirmatory tests are shown below. All 38 samples passed confirmatory testing at FDQCC according to USP 36 NF 31 2013 (Identification, Weight variation, Dissolution and Assay).

List of drug samples underwent the confirmatory analysis at FDQCC and their results:

Province	Medicine & Dosage form	Manufacturer	Country	Lot. No.	Mfg. Date	Exp. Date	Test result
Louangnamtha	1. Amoxicillin 500mg/Cap	KPN	Laos	1346084	04/07/2013	07/2016	Pass
	2. Artemether 80mg/ml	LiKPC	China	12IM02	09/2012	08/2015	Pass
	3. Chloroquine 250mg/Tab	CBF	Laos	020413	25/04/2013	04/2016	Pass
	4. Chloroquine 250mg/Tab	SSP Lab.	Thailand	I530428	28/04/2010	28/04/2015	Pass
	5. Amoxicilline 500mg/Cap	GSK	France	1620	03/2013	03/2015	Pass
	6. Cloxacilline 250mg/Cap	United Drug	Thailand	754002	22/05/2011	22/05/2014	Pass
Savannakhet	7. Chloroquine 250mg/Tab	CBF	Laos	030713	23/07/2013	07/2016	Pass
	8. Chloroquine 250mg/Tab	CBF	Laos	020413	25/04/2013	04/2016	Pass
	9. Coartem 20/120mg/Tab	Novartis	USA	F0667	02/2012	01/2014	Pass
	10. Coartem 20/120mg/Tab	Novartis	USA	F2752	05/2012	05/2014	Pass
	11. Cloxacilline 500mg/Cap	New life	Thailand	603635	22/03/2013	22/03/2015	Pass
	12. Amoxicilline 500mg/Cap	Coduphar	Laos	300218	18/07/2013	18/06/2016	Pass
Attapeu	13. Amoxicilline 500mg/Cap	KPN	Laos	1346040	28/03/2013	03/2016	Pass
	14. Chloroquine 250mg/Tab	Coduphar	Laos	110810	20/07/2011	06/2014	Pass
	15. Amoxicilline 500mg/Cap	Coduphar	Laos	300234	05/09/2013	04/08/2016	Pass
	16. Chloroquine 250mg/Tab	CBF	Laos	020413	25/04/2013	04/2016	Pass
	17. Artefan 20/120mg/Tab	Ajanta	India	P0372J	10/2013	09/2014	Pass
	18. Coartem 20/120mg/Tab	Novartis	USA	F2894	09/2012	08/2014	Pass
	19. Artesun 60mg/ml	Guilin P.	China	LA120825	18/07/2012	17/07/2015	Pass
Bokeo	20. Amoxicillin 500mg/Cap	Zhangfeng	China	120801	12/08/2012	07/2015	Pass
	21. Maraquine 250mg/Tab	CBF	Laos	020413	25/04/2013	04/2016	Pass
	22. Amoxicillin 250mg/Cap	CBF	Laos	010811	18/08/2011	08/2014	Pass
	23.Chloroquine 250mg/Tab	Laemthong	Thailand	TC030Q1	04/07/2012	03/07/2016	Pass
	24. Clozacilline 500mg/Cap	T.O. Lab.	Thailand	6426011	17/05/2013	17/05/2016	Pass
	25. Coartem 20/120mg/Tab	Novartis	USA	F2636	02/2012	01/2014	Pass
Oudomsay	26. Maraquine 250mg/Tab	CBF	Laos	030713	23/07/2013	07/2016	Pass
	27. Coartem 20/120mg/Tab	Novartis	USA	F2636	02/2012	01/2014	Pass
	28. Quinine 600mg/ml	ANB	Thailand	550032	01/2012	12/2016	Pass

	29. Cloxacilline 500mg/Cap	Seven Star	Thailand	1012	07/05/2013	07/05/2016	Pass
	30. Amoxicilline 1000mg/ml	P.F.No.2	Laos	130408	08/04/2013	08/04/2016	Pass
	31. Sinmoquin 250mg/Tab	SSP Lab.	Thailand	1560218	18/02/2013	18/02/2016	Pass
	32. Artesun 60mg/ml	Fosun P.	China	LA121/08	19/09/2012	18/09/2015	Pass
Bolikham say	33. Coartem 20/120mg/Tab	Novartis	USA	F2917	09/2012	08/2014	Pass
	34. Coartem 20/120mg/Tab	Novartis	USA	F0919	11/2012	10/2014	Pass
	35. Coartem 20/120mg/Tab	Novartis	USA	F2917	09/2012	08/2014	Pass
	36. Cloxacillin 250 mg/Cap	T.O. Lab.	Thailand	6425001	14/02/2013	14/02/2016	Pass
	37. Amoxicillin 500mg/Cap	KPN	Laos	1346111	31/07/2013	07/2016	Pass
	38. Amoxicillin 250mg/Cap	Utopian	Thailand	021011	09/10/2011	09/10/2014	Pass

Registration status of medicines

Registration Status in Lao PDR

Sector	Yes	Donated	No	% Not Registered	Total
Private	47		15	24%	62
Public	19	23	10	20%	51
Total	66	23	25	22%	114

Of the 62 samples collected in the private sector, 47/62 (76%) were registered. In the public sector, medicines that had been donated were also identified. 24% of the samples collected in the private sector were not registered. This is similar to the finding in the public sector where 20% of medicines were not legally registered in Lao PDR.

The table below identifies the source and manufacturer and registration status of medicines found by location. Thailand was the source for 21/24 (87.5%) of the unregistered medicines. Two medicines from Lao PDR and one from Vietnam were also identified. Unregistered amoxicillin was most frequently found.

Sixteen of the 25 unregistered samples (64.0%) were collected from non-MQM locations, with the remaining 36.0% from MQM provinces.

One unregistered Artemisinin injectable monotherapy was found in a private pharmacy in LouangNamtha.

Medicines by Manufacturer, Country of Origin and Registration Status

Active Pharmaceutical Ingredient(s) (API)	Name of Manufacturer		Non-MQM	MQM	Registered	Total
Amoxicillin	CBF	LPDR	1	1	Yes	2
	Codupha-Lao	LPDR	10	6	Yes	16
	Factory No 2	LPDR	2		No	2
	GSK GlaxoSmithKline	France		1	Yes	1
	H.K Pharma.	Thai	1		No	1
	KPN	Thai	11	10	Yes	21
	M & H Manufacturing	Thai		1	Yes	1
	S.K. Pharm.	Thai	1		Yes	1
	Seven Stars Pharmaceutical	Thai	1		No	1
	SO 04 Quang Trung. TP thanh Hoa	Vietnam	1		No	1
	T.P Drug Labratories	Thai		1	No	1
	Thailand	Thai	1		No	1
	The United Drug	Thai		2	No	2
	UTOPIAN	Thai	1		No	1
	Zhangfeng	China	2	1	Yes	3
Artemether	Li KPC	China		1	No	1
Artemether/ Lumefantrine	Ajanta Pharma	India		1	Yes	1
	Novartis	USA	10	10	Yes	20
Artesunate	Fosun Pharma	China	1		Yes	1
	Guilin Pharma	China		1	Yes	1
Chloroquin Phosphate	CBF	LPDR	4	7	Yes	11
	Codupha-Lao	LPDR		1	No	1
	Laemthong Medical	Thai	2	1	No	3
	S.S.P Laboratories	Thai	1	1	No	2
Cloxacillin	H.K Pharma.	Thai		1	No	1
	M & H Manufacturing	Thai		1	Yes	1
	New life pharma co. ltd	Thai		1	No	1
	Seven Stars Pharmaceutical	Thai	6	1	Yes	7
	Silam Medicare	Thai	1		No	1
	T. O. LAB. Co. LTD	Thai	3		No	3
	Thailand	Thai	1		No	1
	The United Drug	Thai		1	No	1
Quinine Dihydrochloride	A.N.B Laboratories	Thai	1	1	Yes	2
Total			62	52		114

IV. Conclusion and Evaluation

1. The implementation of Comparative Study of the Quality, Availability, and Source of Antimalarial Medicines in Cambodia, Laos, Thailand, and Vietnam in PQM-MQM Covered and Non-Covered Areas in Mekong Sub-Region was delayed due to delayed receipt of reference standards for Mini-Lab. For this reason, the sample collection was delayed until October from the planned start following training of target MQM and NON-MQM sites (11-12 July 2013).
2. This study method deviated from routine MQM practice as follows:
   - The study took place in 6 provinces; 3 in the MQM area: Louangnamtha, Savannakhet and Attapeu and 3 NON-MQM sites: Bokeo, Oudomsay and Bolikhamsay. Each province was divided into 2 levels: In Level I the province collected samples from the Hospital, the National Malaria Control program warehouse, and drug company or supplier warehouses. In Level II, samples were collected in 2 districts and in the district hospital and target pharmacy stores or clinics.
   - Targets: A random sample of 8 products out of 12 products in each location was taken from Level 1 outlets.

     A random sample of 5 of the 12 products was collected in Level II outlets.

     A minimum of 21 samples were collected in each province. The target number of samples was 128 samples, with a minimum set at 114 samples.
   - The actual implementation shows that: 2 provinces were not able to reach the target samples: Savannakhet and Attapeu (14 and 17 samples, respectively), however the total sample achieved the minimum requirement (114 samples).
3. Of the 12 products included in the study, only 7 products could be sampled in Lao P.D.R. because the others are not produced or marketed locally.
4. The National Malaria Control Center provides antimalarials Coartem, Artesunate, Artemether to the hospitals and are free of charge to all malaria patients admitted. Since the antimalarial medicines are available and accessible free of charge in the public sector, only very limited availability in numbers and types of AMLs were found in the private sector, for example, injectable Quinine, oral Chloroquine and injectable Arthemether were available in private pharmacies, but were not found in hospital. Also the pharmacies operators are becoming more and more aware of the poor-quality medicines and ethical in their practice and distribute only quality medicines with official purchase orders from companies or suppliers who they know do not produce sub-standard medicines.
5. The total number of samples collected was 114, with 7 kinds of products sampled. There were 18 samples with the same lot number. All samples passed.
6. 24 samples of non-registered medicines were identified, more came from non-MQM settings that MQM.
7. A subset of 38 samples were taken for confirmatory analysis at the Food and Drug Quality Control Center (FDQCC). All 38 samples passed according to the United States Pharmacopoeia (USP 36 2013).

Factors contributing to the quality of medicines collected from the MQM and NON-MQM are as follows:

The monitoring of antimalarial, antibiotics, anti-tuberculosis and anti-HIV drugs in 6 provinces of Lao P.D.R. has been supported by the United States Pharmacopoeia Promoting the Quality of Medicine program (USP PQM) for many years. This program provided Minilabs and supplies, trainings and technical support starting in 2003 – 2005 with 3 provinces, Xayaboury , Savannakhet and Champasak. In 2005 - 2008 the project was expanded to 3 additional provinces (Luangnamtha, XiengKhouang and Attapeu); 6 provinces in total. In complementarity to the PQM, these 6 provinces

were also supported by the Quality Control of Antimalarials in 17 Provinces program which was supported by Global Fund (GF) rounds VI Year 2008 - 2013.

- Results from the PQM program in 2009 - 2011 showed that 99.41 % of samples achieved quality standards. Non-compliant samples failing disintegration testing (0.44 %) and counterfeit drugs (0.14 %) were identified in Sekong Province, and Khammouane Province respectively.[Metronidazole 250mg/tab manufactured by CBF factory in Champasak Lot No.010409, Exp. 04/2012; Artesunate 50mg/tab manufactured in China by unknown manufacturer Lot No. 060207, Exp. 06/2010].

- In 2009, the GF project covered 4 provinces of this comparative study: Louangnamtha, Oudomsay, Savannakhet and Attapeu. Twenty product types were sampled. The total 232 samples were collected. There were 25 antibiotic samples: Amoxicillin (21 samples), Cloxacillin (4 samples) and all achieved the specification standard. There were 30 Antimalarial samples: Artesunate (2 samples), Chloroquine (21 samples), Quinine (6 samples) and Fansidar (1 sample); 29 samples achieved quality specifications, but one sample (Artesunate) was found to be a counterfeit drug. In summary, for the year 2009; 99.13 % of samples passed, one sample (0.43 %) did not comply with disintegration testing specification (not an antimalarial or antibiotic) and one counterfeit drug was found (0.43 %).
- In 2010, the program also covered the same 4 provinces of this comparative study. A total of 224 samples of 18 products were collected. A total of 25 antibiotic samples were collected: Amoxicillin (24 samples), Cloxacillin (1 sample). All achieved the specification standards. A total of 25 Antimalarials of 5 types were collected: Artesunate (1 sample), Chloroquine (21 samples), Quinine (1 sample), Fansidar (1 sample) and Coartem (1 sample). All 25 samples met the specification standards. In summary, in 2010; 99.10 % of samples passed, with 0.89 % (not antimalarials or antibiotics) not complying with the disintegration testing specification.
- In 2011, the project covered the same 4 provinces of this comparative study again. A total of 261 samples of 15 products were collected. This was an increase of 16.52% in the sample size. Antibiotics (39 samples) consisted of Amoxicillin (30 samples) and Cloxacillin (9 samples); all samples met the specification standards. Antimalarial samples (25 samples) consisted of Chloroquine (24 samples), Quinine (1 sample) and all samples met the specification standards. Despite the increase in sample size, all samples passed (100 %).
- Another factor contributing to the improved quality of medicines in Laos is that the quality assurance and quality control of medicines activities carried out by the FDD in close collaboration with the PFDUs to monitor, and manage the quality of medicines. The newly instituted Bureau of Food and Drug Inspection have also taken active measures against pharmacies selling substandard and counterfeit drugs. In addition, the FDD has recently been engaging with the consumer through advertising and awareness to ensure consumers are aware of the effects of using counterfeit drugs and sub-standards medicine and to enable consumers to select quality medicines consistently.

The factors above influenced the results of this comparative study, and contributed to the success of this program. The knowledge, skills and techniques of the analysts in the province and central labs, and their experience also contributed to the quality of the results of this study in both the MQM and NON-MQM sites.

Limitations:

Difficulties were encountered in obtaining sufficient samples and multiple trips to the field were required to achieve the minimum level of sampling. Despite these efforts, some provinces still could not meet the minimum target requirements. In addition, not all antimalarial drugs are available in Laos so this increased the required sampling from the other products. Through this process, however, the analysts of FDQCC as well as provincial labs learned lessons, gained experience in drug sampling and testing and this will lead to improved knowledge and skills in both techniques and lab management. Once the other participating countries in the study have completed their analysis, we will be able to compare the quality of antimalarial medicines and antibiotics with Vietnam, Cambodia and Thailand.

V. Recommendations.

1. The results of this study should be disseminated, and used for future planning based on the lessons learned, and recommendations included.

2. The monitoring and testing of drug quality is an essential component of drug safety in Laos and sufficient budget should be provided on an ongoing basis to make this a routine activity. Government financial contribution is essential to complement the external development and technical partners to maintain and sustain the MQM program as an integral part of its post-marketing surveillance.

3. More efforts and support should be made on the part of the Ministry of Health and FDD to help improve both the technical skill upgrades and lab management skills of FDQCC and its regional quality control laboratories. Accreditation of the central laboratory to WHO standard level will enable them to perform Good Laboratory Practices (GLP) and consistently perform high quality testing services in support of the inspection process and activities.

4. Continued vigilance by the FDD, FDQCC, BFDI and Provincial FDU in Laos to institute Good Wholesaling Practice, Good Pharmacy Practice and Good Manufacturing Practice will help ensure that poor quality medicines entering and circulating in the country are readily identified and withdrawn from the market in a timely manner, and that the manufacturers and importers/distributors of these products are prosecuted according to the law and regulations. More enforcement on ensuring medicines available to the public are registered is required.

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