



**REPORT ON THE MEETING ON
THE SURVEY OF THE QUALITY OF ANTIMALARIALS
IN SUB-SAHARAN AFRICA (QAMSA)**

SILVER SPRINGS HOTEL, NAIROBI, KENYA

6 - 8 JULY 2010

This document contains the Report of the QAMSA participating countries and does not represent the decisions or policies of the World Health Organization

Contents

Executive summary	2
Introduction	3
Meeting agenda.....	4
Opening remarks.....	4
Presentations.....	4
Observations from presentations	6
Group work	8
Limits and future	8
Surveillance of antimalarials – proposal for country plans to follow up and collaborative efforts at regional level/future of antimalarial surveillance	8
Recommendations	8
Prequalification and registration	8
Minilab testing	9
Post-marketing surveillance	9
Pharmaceutical manufacturing companies	9
Regional collaboration	9
Conclusions	10
Annexure	11
Meeting agenda	
List of participants	

EXECUTIVE SUMMARY

The Survey of the Quality of Antimalarials in sub-Saharan Africa (QAMSA) was initiated by the World Health Organization (WHO), in collaboration with the United States Pharmacopeia (USP) and the national medicines regulatory authorities (NMRAs) of ten sub-Saharan African countries: Cameroon, Ethiopia, Ghana, Kenya, Madagascar, Malawi, Nigeria, Senegal, Uganda and the United Republic of Tanzania.

Following completion of the survey, a meeting was held in Nairobi, Kenya, 6–8 July 2010, to review the survey results. Six of the ten countries who participated in the survey — Cameroon, Ethiopia, Ghana, Kenya, Nigeria and the United Republic of Tanzania — were represented at this meeting.

Overall, survey results demonstrated high antimalarial failure rates¹ in the West African countries of Ghana, Nigeria, Senegal, and in Cameroon in the Central Africa sub-region. Failure rates were relatively low in Kenya and the United Republic of Tanzania. No failures were observed for Ethiopia.

Ghana, Kenya, Ghana and the United Republic of Tanzania had participated in an earlier WHO survey of the quality of antimalarials. Lessons learnt were implemented by their NMRAs, which may have contributed to the better results that they achieved during this second survey. Ethiopia's successful results may be attributable to strict implementation of regulations concerning which products can be imported for use in its public hospitals and private pharmacies.

During the meeting, the results of Minilab testing and laboratory quality control (QC) tests were presented by country teams and WHO Headquarters and thereafter evaluated. The post-marketing surveillance activities of the United Republic of Tanzania were also presented as a possible means of supervising the medicines market of a country. Reports from three other countries — Madagascar, Senegal and Uganda — were presented by the representative of laboratory of the United States Pharmacopeia (USP).

The meeting encouraged inter-country collaboration to solve several common problems that contribute to the incidence of low-quality pharmaceuticals on national and international markets. Specific recommendations in the areas of regulatory control, Minilab and QC laboratory testing, post-marketing surveillance, and product stewardship by pharmaceutical manufacturers, were agreed upon.

¹ The percentage of samples, for which results of quality control testing did not comply with pre-set specifications, in relation to the total number of samples tested in the laboratory.

INTRODUCTION

The Survey of the Quality of Antimalarials in sub-Saharan Africa (QAMSA) was initiated by the World Health Organization (WHO), in collaboration with the United States Pharmacopeia (USP) and the national medicines regulatory authorities (NMRAs) of ten sub-Saharan African countries. Six of these countries — Cameroon, Ethiopia, Ghana, Kenya, Nigeria and the United Republic of Tanzania — were supported by WHO with funding from the European Commission (AIDCO). Madagascar, Senegal, Malawi and Uganda were supported by the United States Pharmacopeia (USP)/United States Agency for International Development (USAID).

Before this meeting, two other meetings were held with the national survey teams. The first (in the United Republic of Tanzania in 2007) was held to design the survey protocol and the second (in Ethiopia in February 2008) focused on training on the GPHF-Minilab.

The survey evaluated the quality of artemisinin-based combination therapies (ACTs), sulfadoxine/pyrimethamine (SP) and sulfamethoxypyrazine/pyrimethamine products (SPP).

The major processes in the survey included:

- designation of national focal persons for the survey by the NMRAs
- training on the survey protocol and methodology (in the United Republic of Tanzania, 4-5 July 2007)
- preparation of a national sampling plan
- training on Minilab testing for six countries (in Ethiopia, 11-15 February 2008)
- training of data collectors in participating WHO Member States
- sample collection (in country)
- WHO Headquarters validation of sampling undertaken in the respective countries
- Minilab testing of collected samples
- sending of sample collection forms to WHO Headquarters
- sending of selected samples to the WHO prequalified laboratory in South Africa for QC testing
- sending copies of package inserts to WHO Headquarters
- review of the results of Minilab and QC testing, in Nairobi, Kenya, 6–8 July 2010.

Survey aim

The survey's aim was defined as:

- to evaluate the quality of selected antimalarial medicines in a defined number of African countries.

Specific objectives of the survey

The survey's specific objectives were defined as:

- to estimate the proportion of ACTs and SP products, meeting specific quality standards in the selected countries at different points of the regulated and informal distribution system at different points of the regulated and informal distribution system

- to estimate the proportion of counterfeit ACT and SP products in selected countries at different points of the regulated and informal distribution system
- to identify possible causes of the above findings and to propose possible strategies and implementation plans to address the problems identified by the study.

Nairobi meeting, July 2010

The meeting in Nairobi was held to enable countries to share their survey results and strategies, and to deliberate on areas of common concern, including how best to reduce the incidence of substandard antimalarials within sub-Saharan Africa. The six WHO-supported countries participated in the meeting. In addition, reports for three of the four USP/USAID-supported countries were presented by a USP representative.

MEETING AGENDA

The participating countries adopted an agenda (see Annexure) for the meeting.

OPENING REMARKS

The representative of the Kenyan Ministry of Health, Dr Steven M. Kimatu, welcomed all participants to the meeting and thanked WHO for initiating and providing support for the countries throughout the survey.

Dr Clive Ondari, WHO Headquarters, also welcomed participants and congratulated country teams for their hard work, which had ensured successful completion of the survey. He added that their efforts had led to the development of a protocol for post-marketing surveillance (PMS) and to the results of the survey being addressed at national levels. He emphasized that these achievements were to be consolidated at the meeting through development of strategies aimed at maintaining the quality of antimalarials after marketing authorization or product registration had been granted.

PRESENTATIONS

Presentations were made on agenda items. Copies of these can be requested from WHO Headquarters. The highlights of each presentation are summarized below.

1. Quality of antimalarial drugs in sub-Saharan Africa (QAMSA) - Dr Clive Ondari, WHO Headquarters

The general performance of the survey was reviewed: 935 samples were collected from the six countries, 893 samples (95.5%) of which underwent Minilab evaluation in their respective

countries. Of the 935 samples, 306 samples (32.7%) were sent to the WHO collaborating centre in South Africa and USP laboratories for QC testing.

NMRAs were advised to seriously consider thorough evaluation of the critical parameters of products to compendia conformity prior to product marketing authorization and PMS programmes.

2. Quality of Antimalarial drugs in sub-Saharan Africa (QAMSA) – Dr Amor Toumi, WHO Headquarters

This presentation described in broad terms the survey outline, protocol, logistics and Minilab results for the six WHO-supported countries. It also examined the registration status of collected samples according to product type and distribution levels for each of the six countries.

The antimalarial medicines evaluated were ACTs (co-packed and fixed-dose combinations), and SP products. Sampling was carried out at three levels:

- Level 1: Manufacturers, importers, public and nongovernmental organization (NGO) medical stores
- Level 2: Wholesalers, public, private and NGO retail pharmacies, hospitals, clinics and dispensaries
- Level 3: Informal markets.

3. Results of Laboratory Testing – Dr Jitka Sabartova, WHO Headquarters

Of the 935 samples, 306 samples (32.7%) were selected, based on complex criteria.

Products tested in the laboratory included:

- artemether/lumefantrine
- artesunate/amodiaquine (co-packed and fixed dose combinations)
- sulfadoxine/pyrimethamine
- sulfamethoxypyrazine/pyrimethamine

As required by specifications of the International Pharmacopoeia and the United States Pharmacopoeia, samples were tested for identity, content of each active pharmaceutical ingredient (API), related substances or impurities, and dissolution and uniformity of mass of dosage units,

In total, 76 samples failed one or more tests; 191 samples complied with specifications set for this survey; and 22 samples were inconclusive (dissolution failed in stage 1 or 2, and the number of dosage units available was not sufficient to finalize a dissolution test). Testing for 17 samples was completed after the expiry of their shelf life. Detailed analysis of test failure by product type, parameters tested, country of manufacture, country of use, geographical regions within countries, different distribution levels of sampling and WHO-Prequalification status were examined.

4. Implementing Post Marketing Surveillance Strategies - Dr Hiiti Sillo, Acting Director-General, Tanzanian Food and Drugs Authority (TFDA)

The experience of TFDA in conducting PSM within the context of its strategic plans was presented. In Tanzania, PMS is recognized as an important regulatory measure that both helps to assure members of the public regarding the quality of pharmaceutical products, and to combat substandard and counterfeit pharmaceutical products. It can help NMRA to conduct "registered products stewardship". Effective PMS depends upon sound planning and commitment. Those responsible for conducting PMS must recognize that the commitment of all stakeholders, and the participation of trained and specialized inspectors and analysts, are critical to a successful PMS programme.

Some of the challenges in implementing PMS were identified. They include: inadequate human resources and funds; poor attitude of local manufacturers to Good Manufacturing Practices (GMP); and poorly-designed PMS activities.

5. Overview of QAMSA USP/USAID – Dr Daniel Bempong, USP

Madagascar, Malawi, Senegal and Uganda received support from USP/USAID to enable them to participate in the QAMSA survey. Survey results for three of the countries (i.e. excluding Malawi) were presented and discussed. (The survey results and associated report for Malawi are yet to be made available.)

6. Country presentations (by the different country teams)

Six individual country reports were presented and discussed. From the reports it became clear that the countries fall into two distinct groups: countries with high product failure rates (Cameroon, Ghana and Nigeria) and countries with relatively low failure rates (Kenya and the United Republic of Tanzania) or a zero no failure rate (Ethiopia). The situation in Ethiopia can be attributed to strict observance of regulatory provisions, such as prohibition of orders containing products not included on approved medicines lists for public and private sector uses. Other relevant factors include the relatively few product brands available in Ethiopia and the presence of only one local manufacturer of antimalarials.

OBSERVATIONS FROM PRESENTATIONS

Key issues that were underscored by the presentations include the following:

1. In relation to products tested under the survey, Cameroon, Ghana and Nigeria had the highest failure rates, Kenya and the United Republic of Tanzania had relatively low failure rates, and Ethiopia had a zero failure rate.

2. Kenya, Ghana and the United Republic of Tanzania participated in an earlier survey conducted in 2003 and had adopted PMS measures to address product counterfeiting and substandard medicines.
3. There are no informal medicines markets in the United Republic of Tanzania. There are a few informal medicines markets in Ethiopia, but no counterfeit or substandard products were found during the survey.
4. Private clinics are not allowed to procure or store medicines in Ethiopia. Patients have their prescriptions filled by regulated pharmacies and dispensaries only.
5. In Ethiopia, public sector medicines procurement is based on the Essential Drug List while importation is based on the National Drug List. This limits the number of products that can be imported.
6. In contrast to the Ethiopian situation, several brands of the same chemical entities, sourced from several pharmaceutical manufacturers, were collected in those countries with high product failure rates (Cameroon, Ghana and Nigeria).
7. During sample collection it was observed that storage conditions in informal markets are far from being ideal, and that product regulation and control of these markets are usually very difficult. It may be necessary to conduct a survey that specifically addresses these aspects of products sold on informal markets.
8. Currently, in the United Republic of Tanzania, 95% of imported antimalarials are WHO-prequalified.
9. The failure rate for samples of WHO-prequalified products was much lower than for non-prequalified products: 4% (3 of 83 WHO-prequalified samples) vs. 40% (73 of 184 non-WHO-prequalified samples).
10. High failure rates were recorded for a well-known global brand of SP produced in Nigeria, but this was not the case with respect to the same brand produced elsewhere.
11. The QC test results indicate that the dissolution of SP is of some concern and warrants further attention.
12. Impurities (related substances) were of concern for artesunate products.
13. The API was found to be absent from two survey samples: artemether in an artemether/lumefantrine product and pyrimethamine in an SP product.
14. No antimalarial product of any pharmaceutical manufacturing company in sub-Saharan Africa (except South Africa) had been prequalified by WHO at the time of the meeting.
15. It was observed that the fewer the number of pharmaceutical companies (both foreign and domestic) in a country, the better the regulatory control.

16. Minilab testing has its limitations and so cannot be used as a substitute for pharmacopoeia assay and dissolution.

GROUP WORK

Two group discussion sessions were held to examine specific issues raised by the survey and possible improvements to the survey protocol, and to discuss the potential for PMS at sub-regional levels.

1. Limits and future:

Participants were divided into groups to deliberate and make recommendations for improving various aspects of the survey (including protocol, sampling, Minilab analysis, management of results and budget allocated), for the benefit of any future surveys. The impact of the survey on the structure of PMS at country level was also discussed.

2. Surveillance of antimalarials – proposal for country follow up and for collaborative efforts at regional level; future of antimalarial surveillance:

Given the significant differences in survey results between the East and West African regions (including Cameroon), the two regions were mandated to discuss areas of common concern, indicate areas of potential collaboration and highlight follow-up country activities.

RECOMMENDATIONS

Prequalification and registration:

- ✓ WHO should begin prequalification of APIs, as well as continue prequalification of finished pharmaceutical products.
- ✓ Sub-Saharan African countries should consider harmonization of some regulatory requirements, such as product licensing or registration, to enable uniform assessment of quality parameters.
- ✓ NMRAs should adopt a formal protocol for PMS of registered products.
- ✓ As much as practicable, Member States should attempt to limit the number of brands of a particular chemical entity to be registered or licensed, so as to facilitate regulatory control.
- ✓ The registration number should be inscribed on registered products so that products can be readily identified in the field. However, this requirement may decrease availability of medicines.

Minilab testing:

- ✓ Minilab testing results should be regarded as preliminary. Decisions regarding compliance of products should be taken only after the confirmatory QC results have been obtained.
- ✓ Proficiency testing of all new users of Minilabs should be undertaken to ensure that Minilab testing is carried out competently and that misleading results are avoided.
- ✓ The thin layer chromatographic test of the Minilab should be used to test for the presence of related substances/impurities in APIs and in ACTs and SP products.

Post-marketing surveillance:

- ✓ All NMRAs should have a PMS plan. (PMS plans can be incorporated into the NMRAs' strategic plans).
- ✓ Criteria for the choice of products to be monitored after marketing authorization should be clearly defined.
- ✓ Research into the reasons for treatment failure (such as the on-going research to investigate observed reactions to artemether/lumefantrine in Nigeria and in the United Republic of Tanzania) may be considered in support of future licensing activities.

Pharmaceutical manufacturing companies:

- ✓ In addition to obtaining the certificates of analysis, the quality of all APIs should be tested, including for purity, at the time of importation.
- ✓ Regulatory supervision of local manufacturers should be strengthened.

Regional collaboration:

- ✓ Exchange of information between NMRAs should be promoted regarding:
 - substandard/counterfeit products circulating on markets within countries
 - registered products
 - pharmaceutical industry
 - regulatory decisions
 - PMS plans and outcomes of PMS activities.
- ✓ Registration requirements and regulations on GMP and PMS should be harmonized between countries. (Common Technical Documents should conform with the requirements of the International Conference on Harmonisation.)
- ✓ Joint inspection of facilities and joint evaluation of medicines by NMRAs, and collaboration of NMRAs with the WHO Prequalification Medicines Programme, should be encouraged.
- ✓ Joint operations between countries COUNTRIES to combat counterfeit products should be organized.
- ✓ Existing sub-regional NMRA collaboration such as that promoted by the West African Drug Regulatory Authorities Network should be sustained.
- ✓ Sharing by NMRAs of facilities and exchange of expertise (e.g. QC laboratory expertise) should be promoted.
- ✓ NMRAs should work with local manufacturers who are seeking WHO prequalification of medicines.
- ✓ Exchange programmes and working visits to enable NMRA personnel to share experiences and learn best practices should be organized.

CONCLUSIONS

The chairman thanked and commended participants for their hard work, commitment and contributions, both in the course of carrying out the survey and during the three-day meeting.

In the closing remarks of the meeting it was noted that the:

- draft meeting report will be circulated by the end of August 2010 for review and comments by participants
- report would be published on the WHO web site thereafter
- final report on the QAMSA survey would be published by the end of September 2010.

ANNEXURE:

Nairobi meeting agenda

List of participants

NAIROBI QAMSA Meeting

6-8 July 2010

Agenda

Tuesday 06 July 2010

08h30 - 08h50: Declaration of interest - Final verification

09h00 - 09h30: Opening Ceremony

- WHO representative, Kenya
- Ministry of Health representative
- WHO/HQ representative

09h30 - 10h30: Progress of QAMSA survey (1)

- Overview objectives and essential steps : Dr Clive ONDARI
- Protocol, registration status and Minilab results : Dr Amor TOUMI

10h30 - 11h00: Coffee break

11h00 - 11h30: Progress of QAMSA survey (2)

- Full analysis results: Dr Jitka SABARTOVA

11h30 - 12h30: Implementing post-marketing surveillance strategies: Dr Hiiti SILLO

12h30 - 14h00: Lunch break

14h00 - 15h30: Country presentations of QAMSA results: Cameroon, Ethiopia and Ghana

15h30 - 16h00: Coffee break

16h00 - 17h30: Country presentations of QAMSA results: Kenya, Nigeria and Tanzania

Wednesday 07 July 2010

09h00 - 10h30: QAMSA survey - Limits and future (Group discussion)

10h30 - 11h00: Coffee break

11h00 - 11h45: QAMSA survey - Limits and future (Group discussion - Continuing)

11h45 - 12h30: Plenary - results and recommendations from group discussion

12h30 - 14h00: Lunch break

14h00 - 15h30: What future for market surveillance of antimalarials and strategic approaches in countries? (group discussion)

15h30 - 16h00: Coffee break

16h00 - 16h45: What future for market surveillance of antimalarials and strategic approaches in countries? (group discussion)

16h45 - 17h30: Plenary - results and recommendations from group discussion

Thursday 08 July 2010

09h00 - 10h30: Surveillance of antimalarials - Proposal for country plans to follow up and collaborating efforts at regional level (Separate discussion with countries)

10h30 - 11h00: Coffee break

11h00 - 12h30: Future of antimalarial surveillance and closing ceremony



Meeting on Quality of Antimalarials in Sub-Saharan Africa (QAMSA)

6-8 July 2010

Silver Springs Hotel

Nairobi, Kenya

List of Participants

Cameroon

Dr David Singhe
Chef de Division Technique, Lanacome
Ministere de la Sante Publique
Yaounde
Tel: +237 99 67 46 94
Email: singhe@yahoo.fr

Dr Hans Hanny Eyongorock
Chef de Service des Visas
Direction de la Pharmacie et du Médicament
Ministere de la Sante Publique
Yaounde
Tel: +237 77 75 12 33
Email: heyongorock@yahoo.com

Ethiopia

Mr Afework Nida Berga
Inspector
Drug Administration & Control Authority of Ethiopia
P.O. Box 5681, Addis Ababa
Email: afe.2000@yahoo.com

Mr Kemal Hussien Seid
Senior Analyst
Drug Quality Control Laboratory
Drug Administration & Control Authority of Ethiopia
P.O. Box 5681, Addis Ababa
Email: kemhuss80@yahoo.com

Ghana

Mr Geoffrey Arthur
Zonal Head, Volta Region
Food and Drugs Board
P.O. Box CT 2783
Cantonments - Accra
Email: geoffreyarthur@rocketmail.com

Mr Samuel Kwakye
Deputy Head of Laboratory
Food and Drugs Board
P.O. Box CT 2783
Cantonments - Accra
Email: koowa2001@yahoo.com

Kenya

Dr Steven M Kimatu
Ministry of Health

Nigeria

Dr Nelson Agaba Ocheke
Department of Pharmaceutical Chemistry
University of Jos
Plateau State, Nigeria
Email: ochekpen@yahoo.com

Mrs Hassatu Hadi Sirika
Principal Regulatory Officer
Technical Services Unit
National Agency for Food and Drug Administration and Control
NAFDAC Headquarters
Plot 2032, Olusegun Obasanjo Way
Wuze Zone 7
Abuja
Email: sirika.h@nafdac.gov.ng

United Republic of Tanzania

Mr Emanuel Alphonse
Food and Drugs Authority
P.O: Box 77150
Dar Es Salaam
The United Republic of Tanzania
Email: emma_25551@yahoo.com

Dr Yonah Hebron Mwalwisi
Food and Drugs Authority
P.O. Box 77150
Dar Es Salaam
The United Republic of Tanzania
Email: hebony502004@yahoo.com

Special Advisor:

Dr Hiiti B. Sillo - Ag. Director General
Tanzania Food and Drugs Authority
Mabibo External
P.O. Box 77150

Dar Es Salaam
United Republic of Tanzania
Tel:+255 22 2450751/2450512
Mob: +255 754 307179, Fax: +255 22 2450793
Email: hiiti@yahoo.com/hiiti.sillo@tfda.or.tz

WHO Regional Staff

Dr Rose Ngono Mballa - **Cameroon**
National Programme Officer
Boîte postale 155, OMS Yaoundé
Tel: +237 752 92903
Fax: +237 222 11077
Email: ngonor@cm.afro.who.int

Mr Bekele Tefera - **Ethiopia**
P.O. Box 3069
Addis-Ababa, Ethiopia
Tel: + 251-115-53 15 50 (Office)
Mobile : +251-911- 169663
Fax: + 251-111-514037
Email: bekelet@et.afro.who.int

WHO Headquarters Staff

Dr Clive Ondari
Coordinator
Medicines Access and Rational Use
Tel: +41 22 791 3676
Fax: +41 22 791 4167
Email: ondaric@who.int

Dr Jitka Sabartova
Technical Officer
Quality Assurance and Safety: Medicines/ Prequalification
Medicines Programme
Tel: + 41 22 791 3376
Fax: + 41 22 791 4730
Email: sabartovaj@who.int

Dr Amor Toumi
Technical Officer
Medicines Regulatory Support
Tel: + 41 22 791 3471
Fax: + 41 22 791 4889
Email: toumia@who.int