SURVEY OF THE QUALITY OF SELECTED ANTIMALARIAL MEDICINES CIRCULATING IN SIX COUNTRIES OF SUB-SAHARAN AFRICA

World Health Organization

WHO/EMP/QSM/2011.1

Survey of the quality of selected antimalarial medicines circulating in six countries of sub-Saharan Africa

January 2011

Quality Assurance and Safety: Medicines
Essential Medicines and Pharmaceutical Policies

Printed in Malta

Acknowledgements

The principal survey developers and organizers, and the report authors were Jitka Sabartova, Amor Toumi and Clive Ondari, Department of Essential Medicines and Pharmaceutical Policies, World Health Organization (WHO), Geneva.

The following National Professional Officers for Essential Medicines in WHO country offices provided invaluable assistance in organizing the country studies:

Edith Andrews, Ghana, Bekele Tefera Jembere, Ethiopia, Rose Ngono Mballa, Cameroon, Regina M. Mbindyo, Kenya, Rose Shija, United Republic of Tanzania and Ogori Taylor, Nigeria.

This report is the result of a survey carried out by WHO in cooperation with the National Drug Regulatory Authorities of Cameroon, Ethiopia, Ghana, Kenya, Nigeria and the United Republic of Tanzania. WHO thanks these National Drug Regulatory Authorities for their cooperation and assistance.

National Professional Officers for Essential Medicines and for HIV/AIDS from WHO country offices worked with senior inspectors from National Drug Regulatory Authorities to collect samples. Special acknowledgement is due to the country teams and to participants at the meetings that developed the survey protocol and discussed the results, in particular to:

David Singhe, Head of Technical Division, National Quality Control Laboratory, Cameroon

Fasika Mekete Alemu, Inspector, Drug Administration and Control Authority, Ethiopia

Samuel K. Kwakye, Deputy Head of Laboratory, Food and Drugs Board, Ghana

Geoffrey Arthur, Zonal Head, Volta Region, Food and Drugs Board, Ghana

Stephen M. Kimatu, Head of Medicines Information Department, Pharmacy and Poisons Board, Kenya

Otulukpe Ibrahim Ali, National Agency for Food and Drug Administration and Control, Nigeria

Nelson Agaba Ochekpe, Department of Pharmaceutical Chemistry, University of Jos, Nigeria

Yonah Hebron Mwalwisi, Manager, Medicines and Cosmetics Analysis Department, Tanzania Food and Drug Authority, United Republic of Tanzania.

Protocol development and results discussion was undertaken by:

Fasika Mekete Alemu, Emanuel Alphonce, Edith Andrews, Geoffrey Arthur, Afework Nida Berga, Ibrahima Diallo, Hans Hanny Eyongorock, Ravony Harintsoa, Yonah Hebron, Bekele Tefera Jembere, Stephen Kimatu, Samuel Kwakye, Myers Lugemwa, Regina M. Mbindyo, Rose Ngono Mballa, Anthonia Nakamya, Nelson Agaba Ochekpe, Clive Ondari, Valerio Reggi, Jitka Sabartova, Kemal H. Seid, Rose Shija, Margareth Ndomondo Sigonda, Hiiti B. Sillo, David Singhe, Hassatu Hadi Sirika, Fred Moin Siyoi, Ogori Taylor, Amor Toumi, Wondie Alemu Woldemedhin, Eshetu Wondemagegnehu. At the United States Pharmacopeia by: Natalia Davydova, Latifa Elhadri, Patrick Lukulay.

Thanks are also due to: Isaac O. Kibwage from the University of Nairobi, Kenya, who assisted in the preparation of the survey report, particularly the Literature Review, and Theo Dekker, an expert consultant, who helped with the interpretation of test results. Lembit Rägo and Milan Smid, WHO, provided valuable technical input and support. Philip Jenkins edited the text and Monika Zweygarth was responsible for revision, design and layout.

This document has been produced with the financial assistance of the European Union, the Bill and Melinda Gates Foundation and UNITAID. The views expressed herein are those of the authors and can in no way be taken to reflect the official opinion of the European Union, the Bill & Melinda Gates Foundation or UNITAID.

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Abbreviations

A&A co-packed	Artesunate + amodiaquine co-packed tablets
A&SP	Artesunate + sulfadoxine/pyrimethamine
A&SPP	Artesunate + sulfamethoxypyrazine/pyrimethamine
AA	Artesunate/amodiaquine
AA FDC	Artesunate/amodiaquine fixed-dose combination
ACT	Artemisinin-based combination therapy
AL	Artemether/lumefantrine
AM	Artesunate/mefloquine
API	Active pharmaceutical ingredient
BP	British Pharmacopoeia
DQI	Drug Quality and Information Program (US Pharmacopeia)
FDC	Fixed-dose combination
FPS	Focal Point for Sampling
GMP	Good Manufacturing Practices
GPHF	German Pharma Health Fund
HPLC	High-performance liquid chromatography
INN	International Nonproprietary Name
JP	Japanese Pharmacopoeia
LC-MS	Liquid chromatography – mass spectrometry
NGO	Nongovernmental organization
NMRA	National Medicines Regulatory Authority
Ph. Eur.	European Pharmacopoeia
Ph.Int.	International Pharmacopoeia
PMS	Post-marketing surveillance
QAMSA	Quality of antimalarial medicine in sub-Saharan Africa
Q	(in dissolution testing): The amount of dissolved active ingredient specified in the individual monograph, expressed as a percentage of the content stated on the label.
QC	Quality control
SP	Sulfadoxine/pyrimethamine
SPP	Sulfamethoxypyrazine/pyrimethamine
TLC	Thin-layer chromatography
USP	United States Pharmacopeia
UV	Ultraviolet-visible
WHO	World Health Organization

Executive summary

Aim and objectives

The survey aimed at evaluating the quality of selected antimalarials in six countries of sub-Saharan Africa (Cameroon, Ethiopia, Ghana, Kenya, Nigeria and the United Republic of Tanzania). These countries have been supported by WHO to strengthen their regulatory controls over antimalarial products[1]. The survey was organized independently of manufacturers of antimalarial medicines.

The specific objectives of the survey were to:

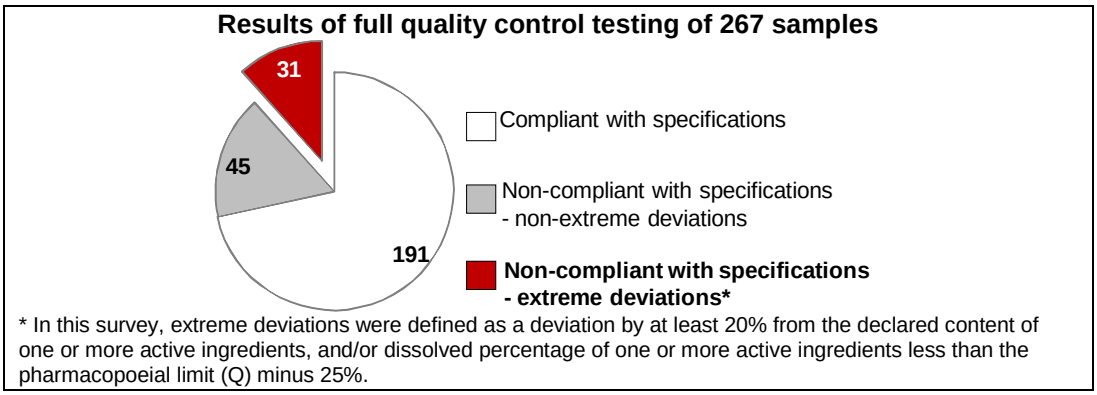
- estimate the proportion of artemisinin-based combination therapy (ACT) products and sulfadoxine/pyrimethamine (SP) products meeting specific quality standards at different points of the regulated and informal distribution systems;
- estimate the proportion of counterfeit ACT and SP products at different points of the regulated and informal distribution systems;
- identify possible causes for any findings;
- propose possible strategies and implementation plans to address the problems identified.

Method

The survey was conducted through WHO cooperation with the national drug regulatory authorities from participating countries. Trained survey teams in each country were responsible for collecting samples according to national sampling plans from different distribution levels including the informal market in at least three geographical regions of high malaria prevalence. In total 935 samples were collected in the period April - June 2008 and were screened using GPHF-Minilab® kits. Based on predefined criteria, 306 samples (from 64 manufacturers and 218 sampling sites) were selected for full quality control testing in the WHO-prequalified laboratory in South Africa and in the United States Pharmacopeia (USP) laboratory in the USA. Testing was coordinated by WHO, and specifications of the International Pharmacopoeia or USP were used. During the survey, data were collected that made it possible to relate the results of quality testing to distribution levels, geographical regions, domestic production or import, registration status and prequalification status.

Findings

Of 306 samples selected for laboratory testing, 267 were fully tested and 28.5% of them failed to comply with specifications. Although non-compliance with pre-established criteria cannot be directly related to a risk for patients' health, such a high failure rate indicates a substantial problem in the quality of antimalarials present in distribution channels. Focusing only on extreme deviations from specifications (as defined in this report), which are likely to be associated with health implications, the failure rate reached 11.6%.



[1] A study according to the same protocol was performed in parallel and supported by USP-DQI, Drug Quality and Information Program of the US Pharmacopeia in Madagascar, Senegal and Uganda. Results of the parallel study have been reported elsewhere.

Discussion

Limitations of study

Samples were collected and selected for QC laboratory testing according to the pre-defined criteria in a way that strived to achieve a representative picture of the quality of selected antimalarials in the supply chain. It should be noted that because of relatively small numbers of samples tested from individual countries and individual manufacturers, interpretation of results is subject to certain limitations. Although the results cannot be considered as fully representative, relevant conclusions may be drawn.

Findings in countries

In individual countries substantial differences in failure rates were observed. It is a positive observation that in Kenya and Tanzania the quality of antimalarials seems to be reasonably under control. Although no failing sample was detected in Ethiopia, it is of concern that a high proportion of samples of collected antimalarials was not registered (41%), and this suggests vulnerability of the market towards penetration of products with unknown properties. In other countries results are less positive because of a substantial proportion of samples that did not comply with pre-set specifications.

In Nigeria, the country with the highest incidence of failing samples according to the survey results (63.9%), the possibility to be treated with an antimalarial medicine complying with international quality standards is less than that of receiving substandard medicine. In Ghana and Cameroon (failure rates 39.5% and 36.6%, respectively), the patient has an approximately 60% chance of obtaining medicine of good quality. In these countries the strengthening of regulatory systems and market supervision seem to be of primary importance. A strong indication for the need to improve regulatory capacity may be the observation in Ghana, namely that the failure rate for unregistered medicines was lower than that for registered ones. In countries with high failure rates, products were collected from a larger number of manufacturers compared to countries with low failure rates. The complexity of markets in terms of the number of products from different manufacturers therefore seems to be one of the contributing factors in making medicines regulation more difficult and in increasing the possibility of substandard medicines on the market.

Types of failures and possible causes

For ACTs a common problem seems to be the lower content of active pharmaceutical ingredients (APIs) and higher content of related substances, SPs failed mainly in dissolution. Failures in mass uniformity tests were observed in the survey, which, in association with the heterogeneity of testing results frequently seen inside individual batches, suggests quality problems originating from non-compliance with Good Manufacturing Practices (GMP).

Within the survey, two samples were identified in which one of the APIs was missing (ACT in one case and SP in the other). Data collected within the survey were insufficient for further investigation of counterfeiting.

As regards the influence of distribution conditions, the collected data do not provide consistent findings. With a limited number of samples and no specific pattern of results, the data do not indicate systematic quality deterioration during distribution, but such a possibility cannot be excluded in individual settings.

Manufacturing source and regulatory status of products

It appears that there is a trend of higher failure rates among domestically manufactured products compared to imported ones. This indicates the need to strengthen monitoring of domestic production in countries that have pharmaceutical manufacturers in their territory, and to apply the same regulatory standards for domestically produced and imported medicines. So far medicines manufactured in the countries participating in the survey appeared in general very rarely on the market in any other than the producing country. This situation may easily change and export to neighbouring countries may become more common. The solution to prevent the movement of substandard antimalarials among countries is again competent regulatory supervision of domestic manufacturers and domestically produced medicines, together with regulatory oversight over imported medicines and cooperation between regulatory bodies. Low failure rate was specifically observed for imported products manufactured by established globally acting manufacturers and for products prequalified by WHO. The total failure rate of samples of WHO-prequalified medicines collected from all six countries participating in the survey was astonishingly low - below 4%. This justifies WHO prequalification as an effective mechanism for quality assurance of procured medicines.

Value of minilab testing

Comparison of results obtained during laboratory testing with the GPHF-Minilab® screening method indicated a substantially lower sensitivity of GPHF-Minilab® to detect non-compliance in dissolution and in assay/related substances test (15% and 42% detected, respectively). Considering the final outcomes of testing, GPHF-Minilab® underestimated negative laboratory results approximately three times, irrespective of the seriousness of deviation. In situations requiring regulatory or forensic decisions, laboratory QC testing should always be applied.

Follow-up

Survey results were discussed on several occasions with regulators from participating countries. All countries approached survey results in a positive spirit, and outcomes of the survey led in several countries to the adoption of regulatory actions and system measures. Recommendations were agreed about the strategies necessary to strengthen medicines regulation, strengthen supervision of manufacturers and improve their adherence to GMP principles, extend post-marketing surveillance, harmonize regulatory requirements, facilitate exchange of information and cooperation among countries in a region as well as between regions, and support the participation of local manufacturers in WHO prequalification and utilization of WHO-prequalified products. These changes should be reflected in updated pharmaceutical policies prepared by regulators in cooperation with all the stakeholders, such as manufacturers, importers/distributors, central medical stores and national malaria programmes.

Three countries with high failure rates in the survey subsequently organized national stakeholders' consultations to review the survey findings and to address the gaps identified. The conclusions of these consultations address a broad range of recommendations and actions.

Conclusion

Although overall survey results indicate a relatively high proportion of antimalarials that are outside specifications set up in recognized pharmacopoeias, survey outcomes should not be generalized as 'catastrophic'. In several countries results of quality testing were quite encouraging and many detected non-compliances were not extreme. Moreover, observed quality failure rates cannot be always directly related to therapeutic failures of these medicines. The relationship between quality and health implications is more complex and was not a subject investigated in this survey. Nevertheless, out-of-specification results documented in the survey are always of concern and, if present in such rates as observed, call for rapid action.

The information obtained through the survey has led to a better understanding of the quality profile of antimalarials in sub-Saharan Africa. It has contributed to evidence-based regulatory actions, the development of regulatory systems and their enforcement capacity, the advancement of post-marketing surveillance, and increased cooperation between national drug regulatory authorities.

1. Introduction

Malaria continues to be a major health threat to tropical countries and especially to countries in sub-Saharan Africa. Combating malaria is identified by the United Nations in the Millennium Development Goals as an objective and is one of the priorities for the World Health Organization (WHO).

Antimalarial medicines are central to any strategy for effective reduction of mortality related to malaria. Efficacy and safety of antimalarial medicines, as measured by their quality, are therefore essential in mitigating morbidity and reducing deaths. Assured quality is also a principle for slowing down the development of resistance to antimalarial medicines and is important for the perception of quality of health care and good treatment by health-care professionals and patients.

Specifications to measure the quality of medicines are defined by their manufacturers. Quality is thus built into medicines during product development and production. Before placing a medicine on the market, quality is reviewed by National Medicines Regulatory Authorities (NMRA) through a complex process. This process normally includes the assessment of documentation on product quality, safety and efficacy, and inspection of compliance with Good Manufacturing Practices (GMP). NMRA assessors review if product specifications, which may be either developed by the manufacturer or established in pharmacopoeias, assure the appropriate quality of a particular product. Adherence to GMP requirements during product manufacture ensures that each batch consistently complies with approved specifications. NMRAs normally follow registered products on their markets through approving changes in product documentation and regular inspection of manufacturers. Additional assurance concerning acceptable quality is achieved by different schemes of sampling and testing of medicines, either sampled from the market or controlled at different entry points to the country. Some indications of substandard quality may also be obtained from pharmacovigilance, i.e. systematic evaluation of reported adverse events.

Quality may easily deteriorate through improper handling of medicines during distribution or storage before they reach patients. Quality control of medicines in the distribution system according to proper specifications is therefore an important prerequisite in ensuring optimal treatment outcomes. Quality surveys of marketed products are thus another tool used by NMRAs in ensuring quality of medicines. They provide information on handling and storage conditions that affect quality of product so that corrective actions can be implemented. Surveys would also act as a deterrent against dumping of substandard medicines by manufacturers and importers.

2. Literature review

2.1 Pharmacopoeial methods

Pharmacopoeial analyses of medicines follow well-tested methods according to published monographs. Pharmacopoeial methods change over time with advancement in available technologies. There are a number of pharmacopoeias, including the International Pharmacopoeia (Ph. Int.), European Pharmacopoeia (Ph. Eur.), United States Pharmacopeia (USP), British Pharmacopoeia (BP) and Japanese Pharmacopoeia (JP). Pharmacopoeial specifications for quality that should be met by products include requirements for identity, content of active pharmaceutical ingredient (API), related substances and tests of dosage forms such as uniformity of mass/content, friability, hardness, disintegration, dissolution, etc. They further include the general requirements on packaging and labelling of the marketed formulations. Various methods are specified for evaluating the quality of antimalarial medicines, as discussed hereafter.

2.2 Rapid testing methods

Endeavours to ensure quality of medicines moving in international commerce have led to the development of a number of simple and accessible analytical methods. These methods have been developed for high throughput screening of medicines for indications of identity, content and changes in physical attributes. They generally give indicative or estimated results. It is important to note that if a product fails in a rapid testing method, its quality is questionable.

- A simple, inexpensive colorimetric test to determine artesunate in tablets, based on a reaction between an alkali decomposition product of artesunate and a diazonium salt, Fast Red TR, was reported by Green et al. (2000). The test is specific for artesunate at pH 4. Only 1% of the total weight of a standard tablet containing 50 mg of artesunate is needed, and the test can be completed within 10 minutes. A modification of the method to involve acid decomposition made it possible to specifically detect artemether, dihydroartemisinin and artesunate in tablets. In both cases, the appearance of a yellow colour indicates the presence of active ingredient (Green et al., 2000, 2001).
- In 2004, the German Pharma Health Fund (GPHF), a charity organization established by research-based pharmaceutical companies in Germany, released a mini-laboratory developed to help low-income countries detect counterfeit and substandard quality medicines. The GPHF-Minilab® provides a reliable, simple and inexpensive method for rapid drug quality verification of antituberculosis, antimalarial and antiretroviral drugs, as well as major antibiotics and some other essential medicines (Jahnke, 2004).
- Green et al. (2007) studied the suitability of refractometric and colorimetric methods alone or in combination for the rapid field assessment of the quality of artesunate, chloroquine, quinine and sulfadoxine. Results obtained were compared with those from high-performance liquid chromatography (HPLC) assays. The combination of refractometry and colorimetry had high accuracy ranging from 0.96 to 1.00 for artesunate, injectable chloroquine, quinine and sulfadoxine but low accuracy (0.78) for enteric coated chloroquine.
- Ioset and Kaur (2009) reported the development of a simple thin-layer chromatography (TLC) method for the detection of artemisinin and its derivatives in antimalarials. The method involves the use of 2,4-dinitrophenylhydrazine or 4-benzoylamino-2,5-dimethoxybenzenediazonium chloride hemi (zinc chloride) salt as spray reagents. The reagents give a pink or blue product, respectively, in the presence of artemisinin and its derivatives. However, the sensitivity of the method is limited; at least 10% of artemisinin and its derivatives in antimalarials have to be present to be detectable in an antimalarial.

2.3 Published data on quality of antimalarials

There have been various reports on the level of quality of medicines in a number of countries, as summarized below.

2.3.1 Africa

Angola, Burundi and Democratic Republic of Congo

Gaudiano et al. (2007) reported findings of a study that assessed the quality of antimalarial tablet samples (chloroquine, quinine, mefloquine, sulfadoxine and pyrimethamine) purchased in the informal market in Angola, Burundi and the Democratic Republic of Congo. The assay of active substance by means of validated liquid chromatographic methods, uniformity of weight determination, disintegration and dissolution tests was carried out. Official or modified USP methods were used whenever possible. Visual inspection was also carried out. Out of 30 antimalarial tablet samples one failed to meet specifications for content of active ingredients, one had a non-declared active substance different from that stated on the label while out-of-specification dissolution profiles were observed in 46% of samples.

Burkina Faso

Medicines were tested for quality using the GPHF-Minilab®. Detected low-standard drugs were re-tested with European Pharmacopoeia standards for disintegration and UV spectroscopy. The samples analysed were 50% (39/77) chloroquine, 13%sulfadoxine-pyrimethamine (SP), 12% quinine, 8% amodiaquine, 12% artesunate and 5% artemether/lumefantrine (AL). About 42% of the drug samples were found to be substandard, with 28 samples failing the visual inspection and 9 containing substandard amounts of the active ingredient. Four samples failed the disintegration test while one sample contained no active ingredient. The failure rates among the various antimalarials analysed were 61.5%, 11.1%, 40% and 33.0%, for chloroquine, artesunate, SP and quinine, respectively. All amodiaquine and AL samples complied with the various tests. The illicit market contributed 90.0% of substandard drugs (Tipke et al., 2008).

Cameroon

A study carried out in Cameroon to investigate the quality of antimalarials in the illicit pharmaceutical sector found that 38% of chloroquine, 74% of quinine and 12% of antifolate (SP) products had either no active ingredient, insufficient active ingredient, the wrong ingredient or unknown ingredient(s). Simple colour tests and semi-quantitative TLC analysis was employed in the study. The failure rate ranged from 10% to just less than 30% in the six states sampled. Samples obtained from public institutions had a failure rate almost three times that obtained from private sources. Finally, 84% of the failure rate was due to change in the physical characteristics of drugs, while assay and dissolution were each responsible for 8% of the failures (Basco, 2004).

Ghana

The artesunate content of tablets sampled in Kumasi varied between 47.9% and 99.9%. Six (35.3%) samples passed the International Pharmacopoeia content uniformity test while 11 failed the test. Only three (17.6%) of the samples met the European Pharmacopoeia requirements for content of active ingredients (Ofori-Kwakye et al., 2008).

Kenya

In 2000, a report on the quality of SP products on the Kenyan market revealed that one batch out of 26 analysed failed in the assay for API while 23 out of 33 batches failed in the dissolution test. The liquid chromatographic method used for simultaneous analysis of pyrimethamine and sulfadoxine was modified from that described in the USP with the incorporation of phosphate buffer, while dissolution studies were conducted using the USP paddle method (Kibwage and Ngugi, 2000).

A report by Thoithi et al. (2002) on the quality of drugs reported an overall failure rate of 21.1%. Antimalarial drugs had a failure rate of 27.7% out of 83 samples comprising amodiaquine, quinine, SP and chloroquine products. Of the 23 samples that failed 15 were SP products. SP and chloroquine products had failure rates of 40.5% and 13.3%, respectively.

A study on the most commonly available amodiaquine and SP products in four districts in Kenya using USP methods for assay and dissolution found 47 out of 116 products studied to be substandard. This comprised 45.3% of SP and 33.0% of amodiaquine samples (Amin et al., 2005).

The Drug Analysis and Research Unit reported a failure rate of 26.8% among antimalarial drugs analysed between 2001 and 2005. Official Pharmacopoeial methods were used in the assays. Most of the drugs reported as failing were SP products, with the major contributing factor being dissolution. In all, 41 antimalarials including amodiaquine, quinine, SP and artemisinin derivatives were included. Ten out of 20 SP tablets and one of the three artemisinin-derived antimalarials failed (Thoithi et al., 2008).

The National Quality Control Laboratory for Drugs and Medical Devices in Kenya reported a failure rate of 42% out of 229 antimalarial samples analysed between 2002 and 2005. SP products accounted for 39% of the failure rate. Official Pharmacopoeial methods were employed (Chepkwony et al., 2007).

In another study, artemether, arteether, artesunate and dihydroartemisinin formulations in Kenya and Democratic Republic of Congo were assessed for quality. The content of active ingredients and preservatives was determined quantitatively using validated HPLC-UV methods according to European Pharmacopoeia requirements. Nine of the 24 drug samples analysed did not comply with the pharmacopoeial specifications for content, with seven samples (more than half of them containing dihydroartemisinin) having too little and two samples an excess of the active ingredient. The range in drug content varied between 77.0% for arteether injection to 110.0% for dihydroartemisinin dry powder. Two-thirds of the dry powder suspensions were either substandard or fake. About 77% and 67%, respectively, of the tablets and injections analysed, complied with pharmacopoeial specifications. Three tablets containing artemether, artesunate and dihydroartemisinin were identified as fake, since the Belgian company named on the pack did not exist, as confirmed by the Belgian Ministry of Health. Unidentified peaks were observed on the chromatograms of arteether injections and a dihydroartemisinin dry powder (Atemnkeng et al., 2007).

Multicountry Africa

In 2003, WHO reported a study on the quality of chloroquine and SP products in seven African countries, namely Gabon, Ghana, Kenya, Mali, Mozambique, Sudan and Zimbabwe (WHO, 2003). Substandard samples were found in all countries for at least one of the formulations studied (chloroquine tablets, chloroquine syrup and SP tablets).

Nigeria

A study on the quality of drugs supplied by Nigerian pharmacies was conducted using validated HPLC methods against BP specifications. Overall 48% (279/581) of drugs analysed failed to comply with BP specifications. Chloroquine phosphate formulations had a failure rate of 70% (20/29) for the capsule samples, 100% (20/20) for the syrups, 94% (17/18) for the tablets and 93% (14/15) for the injections. Chloroquine sulfate syrup and tablets had failure rates of 73% (8/11) and 79% (15/19), respectively, while the capsule sample analysed complied with BP specifications. All the 19 proguanil tablet samples, 10 quinine injection samples and the only quinine syrup sample analysed complied with BP specifications. Among the SP antimalarials, 13/100 tablet and 8/26 syrup samples failed to comply with BP specifications (Taylor et al., 2001).

Using USP methods, Onwujekwe et al. (2009) studied the dissolution profile of artesunate, dihydroartemisinin, SP, quinine, and chloroquine formulations available in south-east Nigeria. The authors further used a non-official HPLC method to carry out the assay for active ingredient in four artesunate and 24 dihydroartemisinin tablet samples. Of the antimalarials studied, 37% failed to meet pharmacopoeial specifications, with some products containing no active ingredient at all. None of the artesunate samples studied failed, while 46% and 39%, respectively, of the quinine and SP products were substandard.

In a six-country study in the most malaria-prone regions in Africa, Bate et al. (2008) reported that 35% of the 210 antimalarials studied were substandard. The authors used a semi-quantitative TLC method in addition to dissolution studies. The failure rates among specific drug classes were 38% of SP, 48% of amodiaquine, 24% of mefloquine, 31% of artesunate, 27% of artemether, 55% (12/22) of dihydroartemisinin and 19% of AL fixed-dose combinations. The overall failure rate for the six countries ranged from 32% to 38% (35% Ghana, 38% Kenya, 32% Nigeria, 33% Rwanda, 32% Tanzania and 35% Uganda).

A study by Shakoor et al. (1997) on chloroquine formulations sampled from Nigeria and Thailand found two formulations from Nigeria and three from Thailand that did not contain any active ingredient and were classified as counterfeits. A total of 10 out of 32 chloroquine formulations did not meet BP specifications.

The researchers used HPLC methods and BP specifications. The overall failure rate for the drugs (antimalarial and antibacterial) studied was 36% for samples from Nigeria and 40% for those from Thailand.

Odeniyi et al. (2003) investigated eight SP tablet brands by evaluating uniformity of weight, friability, crushing strength, disintegration and dissolution tests, and assay. All brands complied with BP standards for uniformity of weight, disintegration and crushing strength. Three brands failed the friability test. One brand did not comply with specifications for content of active ingredients while another brand did not comply with the USP specifications for the dissolution test. No significant differences were observed in the amounts of pyrimethamine and sulfadoxine released from the different brands. Thus only three out of eight brands investigated met all pharmacopoeial specifications

In a study on the quality of chloroquine in Lagos State general hospital using BP specifications, all the tablet samples passed the dissolution and disintegration tests. Over 85% of the tablet samples complied with specification for the content of active ingredient while about 21% failed the friability test. All the tablet samples passed the uniformity of weight. Over 90% of the syrup samples had a greater content of active ingredient than that specified in the BP. About 23% of the syrup samples failed in the specifications for microbial growth. All the injection samples failed the assay for active ingredient (Aina et al., 2007).

Senegal

The USP Drug Quality and Information Program (USP DQI) analysed samples of amodiaquine, chloroquine and SP tablets collected from the public sector health system, private sector licensed pharmacies, and the informal market in different regions of Senegal using USP and BP methods. Chloroquine tablets contained more than the claimed amount in 35% of the tested samples while SP tablets contained less than the claimed amount in 55% of the samples. All of the amodiaquine samples passed the monograph tests. The majority of failed SP and chloroquine samples (57% and 64%, respectively) came from the formal private sector (Smine, Diouf & Blum, 2002).

Sudan

Alfadl et al. (2006) carried out a surveillance of the quality of chloroquine, quinine, artemether and mefloquine formulations in Northern, Eastern, Western and Central Sudan. Physical inspection, pharmacopoeial methods and manufacturers' methods (in the absence of compendia methods) were employed. For the six states included in the study, the failure rates were 10%, 13%, 20%, 22%, 25% and 29% respectively. Most of the failures were attributed to changes in physical properties, such as colour (84%), while assay and dissolution each contributed 8%. Samples obtained from public institutions had a failure rate almost three times that of those obtained from private sources.

Tanzania

Four studies looking at the quality of antimalarial drugs in Tanzania have all given similar findings.

A study in 2000 on the quality of SP tablets marketed in Dar es Salaam, Tanzania reported that all the products analysed passed in the assay for APIs, but only four out of nine passed the dissolution test. The authors used the USP method (Jande et al., 2000).

In a study by Minzi et al. (2003) on the quality of amodiaquine and SP products marketed in Dar es Salaam, all samples passed the identity test. However, 13% of the amodiaquine samples failed the dissolution test, whereas 11% and 44% of SP samples failed the assay and dissolution test, respectively.

Hebron et al. (2005) investigated the chemical and pharmaceutical equivalence of 11 SP brands marketed in Tanzania. All products complied with pharmacopoeial specifications for content. However, one brand failed both the hardness and disintegration tests, one failed the hardness test while another failed the friability test.

Kaur et al. (2008) analysed 304 antimalarial products to determine the amount of the active ingredient and dissolution profile as per USP monographs. Where no official monograph was available only the amount of active ingredient present was determined. Overall 12.2% of the samples were found to be substandard. This figure comprised 13.4% of antifolate antimalarials (SP), 23.8% of quinine tablets and 7.5% of amodiaquine formulations. All artemisinin formulations samples contained the stated amount of active ingredient when analysed using HPLC.

Uganda

A 1998 study analysed chloroquine tablets and parenteral samples in Kampala, Uganda, for content using the BP (1988) method. Up to 30% of the tablet samples and 33% of injection samples contained less than the stated amount of the active ingredient. Based on these findings, the authors recommended the establishment of a drug quality control laboratory in Uganda (Ogwal-Okeng et al., 1998).

A subsequent study was conducted on chloroquine tablet and injection dosage forms. These were assayed for content of active ingredient using the HPLC method described in the USP. The failure rates reported were 39% for tablets samples and 51% for injections (Ogwal-Okeng et al., 2003).

2.3.2 Asia

A total of 451 drug samples was analysed by TLC and disintegration tests using the GPHF-Minilab® kits in Cambodia. The average failure rate of quinine was 71.8% (61 samples), artesunate 19.8%, tetracycline 26.6%, chloroquine 8.5% and mefloquine 7.7%. In this study, only 22 samples of dihydroartemisinin and two samples of artemether passed the tests. Overall, 122 (27.1%) of the samples failed TLC and/or disintegration tests. Of the samples which failed testing, 100 were obtained from unlicensed or illegal drug outlets (Lon et al., 2006).

Newton et al. (2001) conducted a study between 1999 and 2000 on the quality of artesunate tablets in South-East Asia (Cambodia, Laos, Myanmar, Thailand and Viet Nam). The study aimed to check for the presence of the active ingredient in the tablets. It was based on the reaction between an alkali-decomposition product of artesunate and the diazonium dye, Fast Red TR. The researchers reported that 25%, 38%, 40%, 11% and 64%, respectively, of the samples analysed from Cambodia, Laos, Myanmar, Thailand and Viet Nam did not contain artesunate.

A follow-up study in the same region reported the problem of counterfeit medicines to be on the increase with 53% of the 188 artesunate tablets containing no artesunate. The qualitative dye test described in the earlier study was used. The inspection of packaging was found to be a less reliable means of detecting fakes in this study than in the earlier one, indicating that the counterfeiters were responding to sensitization campaigns by improving the appearance of their packaging. In addition to artesunate, 44 mefloquine samples were quantitatively analysed using an HPLC method. About 9% of these were found to contain less than 10% of the stated amount of mefloquine (Dondorp et al., 2004).

A liquid chromatography – mass spectrometry (LC-MS) analysis of 34 artesunate tablet samples revealed 23 to contain no artesunate. This finding was fully in agreement with the rapid Fast Red TR test. Of the 23 counterfeit samples, 8 contained the wrong active ingredients which were identified as erythromycins and paracetamol (Hall et al., 2006).

In Yemen, chloroquine and SP formulations were analysed using pharmacopoeial methods or other validated methods (UV and HPLC) for content and dissolution where applicable. Failure rates of 6.7% and 20.0%, respectively, were reported for chloroquine syrup and tablets as far as content of active ingredient was concerned. Dissolution testing gave a failure rate of 8% for chloroquine tablets and 70% for SP tablets. All the SP tablet samples tested complied with pharmacopoeial specifications for content but poor dissolution, especially of pyrimethamine, was a serious problem (Abdo-Rabbo et al., 2005).

Bate et al. (2009) reported a failure rate of 7% for chloroquine formulation samples obtained from Delhi and Chennai in India. The samples were analysed using semi-quantitative TLC and disintegration testing.

In 2004, a sentinel study in the Yunnan Province of China on 39 antimalarial samples using visual inspection, dissolution and TLC confirmed 35 samples to be authentic. Confirmatory testing of the substandard samples using TLC and HPLC found two artesunate samples to contain no active ingredient (USP DQI, 2004).

In a survey conducted in 1998, a total of 218 antimalarial samples were collected and tested by the Vietnamese Institute of Drug Quality Control; over 96% passed testing. However, re-testing of 10% of the samples by the WHO-assigned laboratory in Malaysia gave a lower pass rate: 70% of the samples did not meet the BP specifications for API content; 3.2% and 0.4% of the samples failed in the quantitative and qualitative analyses, respectively. Assessed by type of antimalarial, 4.3%, 3.3%, 50%, 2.1% and 10% of the

samples failed the analysis for artemisinin, chloroquine, primaquine, quinine sulfate and pyrimethamine, respectively (Cong et al., 1998).

The study also concluded that there was an urgent need to improve the capability and monitoring procedures of the testing authority in Viet Nam. In 2008 the Institute proved compliance with WHO-recommended standards for quality control laboratories and became WHO-prequalified.

2.4 Rationale for this survey

Malaria is prevalent in many countries. The major management strategy is curative with antimalarial medicines, the quality of which varies from country to country as reviewed above. With the introduction of artemisinin combination therapy into most countries and the availability of various generics, it was decided to study the level of quality of antimalarial medicines.

It would be of interest to observe the levels of contribution by substandard medicines circulating in the markets of selected countries and consider whether they contribute to emerging resistance to antimalarials and observed recrudescence of the malaria parasite.

3. Scope of the survey

The survey covered six malaria-endemic countries, namely Cameroon, Ethiopia, Ghana, Kenya, Nigeria and the United Republic of Tanzania. These countries have been supported by WHO to strengthen their regulatory controls over antimalarial products through a grant from the European Commission.

A study according to the same protocol was performed in parallel and supported by USP-DQI, Drug Quality and Information Program of the US Pharmacopeia in Madagascar, Senegal and Uganda (USP/USAID, 2009).

3.1 Objectives of the survey

The survey aimed at evaluating the quality of selected antimalarials in these six countries. Its specific objectives were to:

- estimate the proportion of artemisinin-based combination therapy products (ACT) and sulfadoxine/ pyrimethamine (SP) products meeting specific quality standards at different points of the regulated and informal distribution systems;
- estimate the proportion of counterfeit ACT and SP products at different points of the regulated and informal distribution systems;
- identify possible causes for any findings;
- propose possible strategies and implementation plans to address the problems identified.

3.2 Antimalarial products surveyed

This survey investigated oral solid preparations of ACTs in co-packed and fixed-dose combination products available in each participating country and products containing the SP combination. In the regulated sector, sampling was based on the products most sold and/or recommended by national guidelines. In the informal sector, the sample collectors asked for the "best ACT and the best SP".

ACTs were selected for this survey as they are relatively new products in the markets of the participating countries and have a pivotal role in malaria treatment. SP products were included as they continue to play a significant role in malaria treatment protocols and were evaluated in a previous study. It was foreseen that a re-evaluation of SP products in the markets would offer an insight as to the improvement, if any, of the quality of these products in the selected markets.

3.3 Main activities

These were as follows:

- Collect and test samples of selected antimalarials from selected sites of the regulated private and public sector, as well as from the informal market.
- Analyse findings and write a report describing overall results and country-specific results.
- Identify the elements of a strategy aimed at addressing the problems identified by this survey.

4. Methodology

The methodology followed in this survey is detailed in the survey protocol attached as Appendix 1. Survey teams were jointly trained to ensure that the protocol was uniformly applied across participating countries.

The survey protocol was developed based on lessons learned in the WHO study published in 2003 (WHO, 2003). Joint meetings and trainings were organized between the participating countries and teams from WHO and the USP Drug Quality and Information Program (USP-DQI) to ensure the survey protocol was uniformly applied in all participating countries. Particularly:

- In July 2007, the team members met in Tanzania and discussed how the survey protocol was to be implemented.
- In February 2008, during the meeting in Ethiopia, sampling strategies were discussed to ensure national sampling plans were based on guidelines provided in the survey protocol. In this meeting, analysts were given hands-on training on GPHF-Minilab® basic tests.
- In July 2010 team members met in Kenya and discussed the study results and their impact for strategies and plans for market surveillance in individual countries.

4.1 Sampling

In each country a survey team, consisting of staff of the national drug regulatory authority, national quality control laboratory and malaria control programme, prepared a national sampling plan. The sampling plans targeted ACT and SP tablet products, with a focus on those most utilized and/or recommended by national guidelines in each respective country. Based on the prevalence of malaria and the national malaria control strategy, a country was divided into geographical zones (regions). Sampling sites in each country were selected in such a way as to cover at least three regions and all levels of the distribution system. Samples were collected from three distribution levels as follows:

- **Level 1** - the highest level of the distribution system, i.e. importers, central medical store, manufacturers, and central stores of nongovernmental organizations (NGOs), both public and private sector (referred to as "**Central**" level in this report).
- **Level 2** - wholesalers, regulated retailers, including various dispensing facilities, both public and private sectors (referred to as "**Outlets**" level in this report).
- **Level 3** - informal sector, i.e. outside the approved distribution system (referred to as "**Informal**" level in this report).

The target number of samples was established by each country depending on the available budget.

Samples were collected by the staff of the national drug regulatory authority over the period of April–June 2008. Each sample was given a code to ensure traceability, and for each sample the Sample Collection Form was completed. All collected samples were stored at room temperature prior to GPHF-Minilab® testing and dispatch to the designated QC laboratories. Fuller details can be found in the survey protocol in Appendix 1.

4.2 The two-stage testing approach

The quality of the samples was evaluated using a two-stage testing approach. This used the GPHF-Minilab® procedures and full-scale QC laboratory testing.

In the first stage, all the collected samples (except those for which GPHF-Minilab® procedures were not available) were screened by GPHF-Minilab®. This screening procedure was performed by the staff of the national drug regulatory authorities in individual countries with the aim of identifying active ingredients, estimating content and predicting drug release rates. It consisted of the following parts:

- visual inspection - description of the dosage form, label and packaging;
- TLC identification and semi-quantitative active ingredients content by comparison with the reference;
- simple disintegration - with the requirement to be disintegrated in not more than 30 minutes.

The first stage was used also to evaluate the compliance with the national requirements on the information accompanying products (on external and primary packaging, as well as in the package leaflet). The evaluation was performed by the staff of national drug regulatory authorities in individual countries using the standardized forms. As national requirements for labelling and package leaflets vary in individual countries, the results were used for regulatory purposes by authorities and are not part of this report.

At the second stage, a subset of samples was selected for testing in designated QC laboratories. The selection was organized to ensure that: (a) the subset of selected samples was representative of the total collected samples in each country and included samples from various distribution levels and different regions; (b) there was a balance between ACTs and SPs; and (c) it provided the possibility to validate the outcomes of GPHF-Minilab® screening. The following criteria were considered for the selection:

- product samples collected in more than one country;
- samples represent several regions and cover all distribution levels in each country;
- samples represent as many manufacturers as possible;
- samples from one manufacturer represent as many batches as possible;
- samples have not expired;
- number of dosage units collected for the sample was higher than 40;
- samples that had failed as well as those that had passed GPHF-Minilab® testing for disintegration or TLC;
- approximately one-third of collected samples subjected to QC laboratory testing.

4.3 Quality control testing laboratories

All samples (except samples of sulfamethoxypyrazine/pyrimethamine (SPP) products) were tested at the Research Institute for Industrial Pharmacy, incorporating CENQAM, North-West University, Potchefstroom, South Africa, which is a laboratory prequalified by WHO and a WHO Collaborating Centre. Samples of SPP products were tested at the USP Laboratory, Rockville, USA.

4.4 Tests conducted and test methods used

4.4.1 Tests conducted

QC laboratory testing included the following tests as required by the respective specifications:

- appearance
- identity
- content of each active ingredient
- related substances
- dissolution
- uniformity of mass of dosage units.

4.4.2 Test methods used

Test methods used for testing at QC laboratories were methods in the respective monographs from the International Pharmacopoeia or USP. If no pharmacopoeial monograph was available, the laboratory-validated method or the method from a manufacturer with the appropriate transfer was used, as detailed below.

Artemether/lumefantrine tablets	- International Pharmacopoeia monograph - Dissolution by laboratory-validated method, similar to method used for lumefantrine and artemether tablets in USP Non–US Monograph (authorized 1.3.2009)
Artesunate + amodiaquine tablets co-packed	Artesunate tablets: - International Pharmacopoeia monograph - Dissolution by laboratory validated method, which has been included in the revised International Pharmacopoeia monograph for artesunate tablets (published in December 2009) Amodiaquine tablets: - USP monograph
Artesunate/amodiaquine tablets FDC	Laboratory-validated methods
Sulfadoxine/pyrimethamine tablets	USP monograph
Sulfamethoxypyrazine/pyrimethamine tablets	Manufacturers' methods

4.4.3 Specifications

The following specifications were used for the different tests:

- **Appearance**
  Tablets should be undamaged, smooth and usually of uniform colour. Presence of excessive powder and/or pieces of tablets in the container, cracks or capping, chipping in the tablet surfaces or coating, swelling, mottling, discoloration, fusion between tablets, and appearance of crystals on the container walls or on the tablets demonstrate physical instability.

  Capsules should be smooth and undamaged.

  For powders, physical and/or chemical instability is demonstrated by noticeable changes in physical appearance, including texture (e.g. clumping) or colour.

- **Identity**
  Identity was confirmed by matching the retention time of active peak in the standard and sample HPLC chromatograms obtained in the assay.

- **Content of active ingredient**
  The limits for content of the active ingredient(s) applied to the individual products are shown in each table of results in Appendices 2-6. The limits vary, depending on the respective specifications.

- **Related substances**
  Specifications for testing of related substances applied to the individual products are shown in each table of results in Appendices 2-6.

- **Dissolution**
  The methods specified in section 4.4.2 were used for dissolution tests. As far as the sample size allowed, dissolution was tested in three stages, with the following acceptance criteria:

Stage	Number of units tested	Acceptance criteria*
S1	6 units	Each unit is not less than Q + 5%
S2	Another 6 units	Average of 12 units (S1 + S2) is equal to or greater than Q, **and** no unit is less than Q – 15%
S3	Another 12 units	Average of 24 units (S1 + S2 + S3) is equal to or greater than Q, **and** not more than 2 units are less than Q –15%, **and** no unit is less than Q –25%

* Q is the amount of dissolved active ingredient specified in the individual monograph, expressed as a percentage of the content stated on the label. The testing is continued through the three stages unless the results conform at either stage 1 or stage 2.

Specifications applied, in terms of Q values and testing time limits, are shown in each table of results in Appendices 2-6, where applicable.

- **Uniformity of mass of dosage units**
  The following acceptance criteria were used:

Pharmaceutical form	Average mass	Acceptable deviation in %	Number of units (of 20 units tested)
Tablets (uncoated and film-coated)	less than 80 mg	± 10.0 ± 20.0	minimum 18 maximum 2
	80 mg to 250 mg	± 7.5 ± 15.0	minimum 18 maximum 2
	more than 250 mg	± 5.0 ± 10.0	minimum 18 maximum 2
Capsules	less than 300 mg	± 10.0 ± 20.0	minimum 18 maximum 2
	300 mg or over	± 7.5 ± 15.0	minimum 18 maximum 2

4.4.4 Compliance of samples with specifications

All out-of-specification results were investigated and tests were repeated, as appropriate, according to the laboratory standard operation procedure on handling out-of-specification results.

All samples containing the same combination of active ingredients were tested according to the same specification in order to enable comparison of samples from different manufacturers. This specification was used to decide on compliance or non-compliance of tested samples for the purposes of this survey.

It should be noted that individual manufacturers may use different specifications and different methods for testing their products and that these specifications and methods may be approved by regulatory authorities in individual countries. Non-compliance with the specifications selected for this survey does not necessarily imply non-compliance with the specifications approved in the country.

5. Results

5.1 Overview of samples collected

In total, 935 samples were collected in six African countries over the period of April–June 2008 according to the protocol requirements described in Chapter 4.

The number of collected samples varied from 102 in Ethiopia to 200 in Nigeria. In total, 14.1% of collected samples were from level 1 (central level), 75.5% from level 2 (outlets) and 10.4% from level 3 (the informal market).

Of the 935 samples, 543 were ACTs, the remaining 392 were pyrimethamine combinations containing either sulfadoxine/ pyrimethamine (SP – 362 samples) or sulfamethoxypyrazine/pyrimethamine (SPP – 30 samples).

The registration status of the sampled products at the time of collection was recorded on the Sample Collection Forms and later clarified with country focal points. In total, 86% of collected samples were identified as registered (i.e. authorized for use in the country of collection by the National Medicines Regulatory Authority) and 14% samples as not registered.

In total, 330 samples of eight WHO-prequalified ACT products were identified, which represented 35% of all collected samples and 61% of all ACT samples.

Details are shown below.

5.1.1 Regions

As required by the protocol, in all countries samples were collected in several geographical regions identified as regions of high malaria prevalence, and from different levels of the distribution system. In Nigeria five cities in different regions were selected for sampling. Numbers of samples collected in each region are shown in Table 1.

Table 1: Samples collected in different regions

Country	Total number of samples	Region*				
		A	B	C	D	E
Cameroon	160	58	34	34	34	n/a
Ethiopia	102	13	16	24	49	n/a
Ghana	175	87	52	36	n/a	n/a
Kenya	154	22	57	36	39	n/a
Nigeria	200	91	33	29	30	17
Tanzania	144	27	24	34	24	35
Total	**935**	**935**				

***Regions:**	A	B	C	D	E
Cameroon:	Centre	West	South-West	Coast	
Ethiopia:	Central	Southern	Eastern	Northern	
Ghana:	Southern	Middle	Northern		
Kenya:	Central	Nyanza	Western	Coast	
Nigeria:	Lagos (South-West)	Kano (North-West)	Jos (North-Central)	Onitsha (South-East)	Calabar (South-South)
Tanzania:	Dar es Salaam	Mtwara	Kigoma	Tabora	Mwanza

5.1.2 Distribution levels

The proportion of samples collected at different levels in the distribution chain corresponded to the protocol requirements. Despite the fact that it was difficult to collect the requested number of tablets from one batch in the non-regulated "informal" market, this was done in all countries except Tanzania; the number of samples from the informal sector varied from three in Kenya to 40 in Cameroon (see Table 2).

Table 2: Number of samples collected at different distribution levels

Country	Total number of samples	Distribution level*		
		Level 1 (Central)	Level 2 (Outlets)	Level 3 (Informal)
Cameroon	160	24	96	40
Ethiopia	102	12	79	11
Ghana	175	23	140	12
Kenya	154	22	129	3
Nigeria	200	42	127	31
Tanzania	144	9	135	-
Subtotals		**132**	**706**	**97**
Total	**935**	**935**		

***Distribution levels:**

Level 1 (Central): Manufacturers, importers, central medical stores

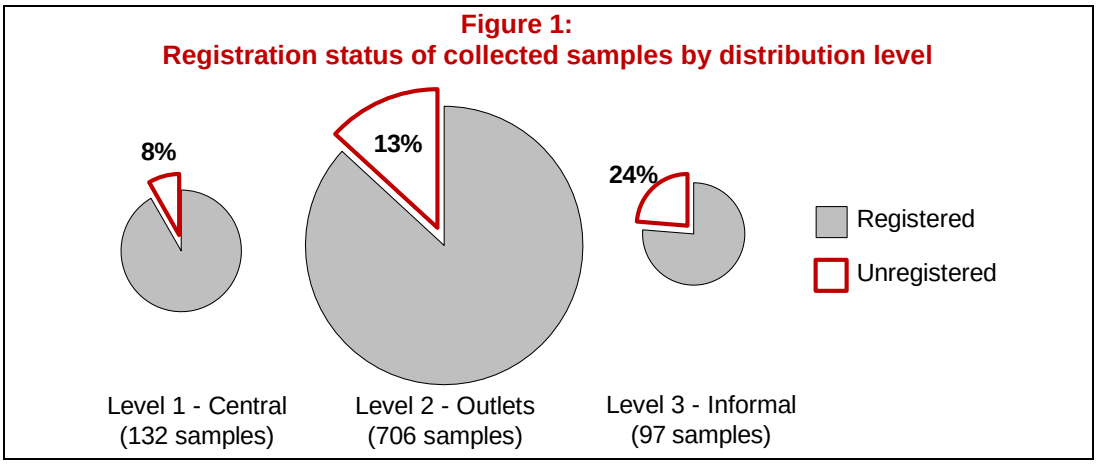
Level 2 (Outlets): Wholesalers, regulated retailers, such as pharmacies, dispensaries, retail outlets, drug stores/vendors; hospitals, clinics, health/medical centre

Level 3 (Informal): Informal (unregulated) market

Registration status at each distribution level

Overall, 14% of collected samples were not registered by the NMRA. The proportions at each distribution level are shown in Figure 1.

Figure 1:
Registration status of collected samples by distribution level



As Figure 1 shows, the percentage of samples not registered by the NMRA of the country of collection was highest in the informal market at level 3, and lowest at the central distribution level 1, where only 11 samples (three from Ethiopia and eight from Ghana) were unregistered.

Further details were recorded for 47 of the unregistered samples: 23 were collected at the Ministry of Health, for 16 the respective product registration was pending, for 5 it was expired and had not been renewed, and for 3 the product was exempt from registration as a donation.

5.1.3 Products

The survey protocol required sampling of ACTs, which were mostly sold and/or recommended by national guidelines without further specification of products. AL products were sampled in all six countries, while significant numbers of samples of AA combination products (both co-packed tablets and fixed-dose combination) were collected in Cameroon, Ghana and Nigeria only (see Table 3).

Table 3: Numbers of samples collected per product

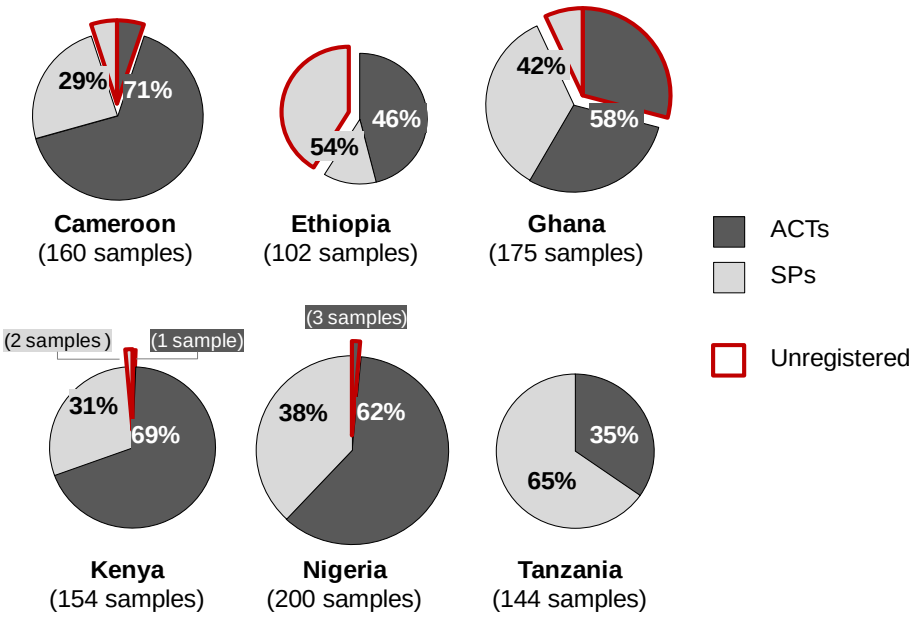
Country	Total number of samples	Artemisinin-based Combination Therapies (ACTs)				Pyrimethamine combinations (SPs)	
		Arte-mether/ lumefan-trine **(AL)**	Artesunate and amodia-quine, co-packed **(A&A cop.)**	Artesu-nate/amodia-quine fixed-dose comb. **(AA FDC)**	Other ACTs*	Sulfa-doxine/ pyri-methamine **(SP)**	Sulfa-methoxy-pyrazine/ pyrimethamine **(SPP)**
Cameroon	160	52	53	8	-	47	-
Ethiopia	102	47	-	-	-	55	-
Ghana	175	46	44	5	7	72	1
Kenya	154	96	1	-	10	46	1
Nigeria	200	43	58	13	10	75	1
Tanzania	144	43	3	-	4	67	27
Subtotal		**327** (60.2%)	**159** (29.3%)	**26** (4.8%)	**31** (5.7%)	**362** (92.3%)	**30** (7.7%)
Total	**935**	**543** (100%)				**392** (100%)	

* **Other ACTs:** Dihydroartemisinin/piperaquine (16 samples: 9 from Kenya, 6 from Ghana and 1 from Nigeria), Artesunate/mefloquine co-packed (2 samples from Nigeria), Artemisinin/piperaquine (1 sample from Ghana), Artemisinin/naphthoquine fixed-dose combination (1 sample from Nigeria), Artesunate + SPP (6 samples: 4 from Tanzania, 1 each from Kenya and Nigeria) and Artesunate + SP (5 samples from Nigeria).

Registration status of ACTs and SPs

Overall the percentage of SPs identified as unregistered was higher than that of ACTs (16.3% and 11.6%, respectively). Details for the different countries are shown in Figure 2.

Figure 2: Registration status of ACTs and SPs



In Tanzania no unregistered samples were found. In Nigeria three samples were identified as unregistered, however they were donations exempt from registration and so were legally on the market. On the other hand, high proportions of unregistered samples were found in Ethiopia (SPs only) and in Ghana (both ACTs and SPs).

5.1.4 Manufacturing source

The number of different manufacturers of the samples collected in individual countries varied substantially, ranging from 11 in Ethiopia to 52 in Nigeria. In countries where antimalarial products from many different manufacturers were on the market, such as in Nigeria, more samples were collected even if this was not clearly required by the survey protocol. Table 4 shows the number of manufacturers of collected samples separately for each product type. Some manufacturers produced more than one product type, so that the total number of manufacturers overall was lower than the sum of the numbers shown in the table.

Table 4: Number of manufacturers for each product group

Country of collection (total samples collected)		Number of manufacturers of collected samples for each product type					
		AL	A&A co-packed	AA FDC	Other ACTs	SP	SPP
Cameroon	(160)	2	8	2		13	
Ethiopia	(102)	3				9	
Ghana	(175)	8	10	2	3	16	1
Kenya	(154)	7	1		3	11	1
Nigeria	(200)	10	21	7	8	23	1
Tanzania	(144)	1	1		1	7	4

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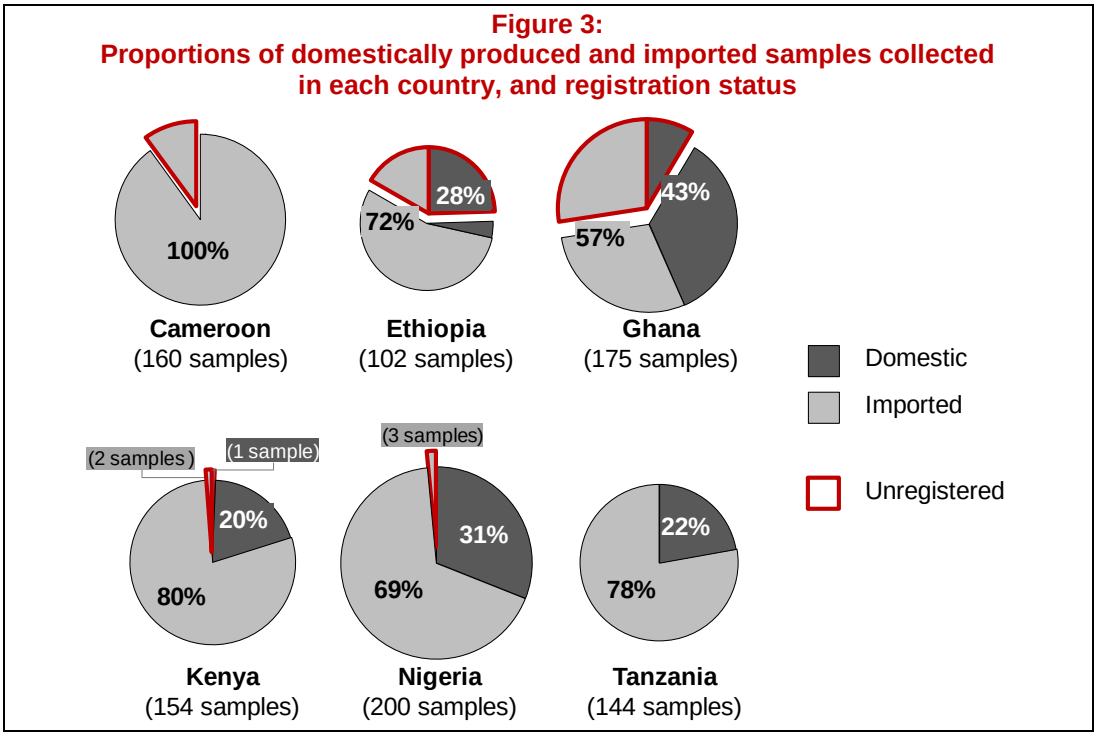
Registration status of domestically produced and imported products

In countries with domestic production of antimalarial medicines, samples collected represented both production of domestic manufacturers and imported medicines. Figure 3 gives an overview of the proportions of domestically produced and imported samples, and of their registration status.

Figure 3:
Proportions of domestically produced and imported samples collected in each country, and registration status



5.1.5 WHO prequalification

The WHO prequalification status of samples collected within the survey was reviewed. Sampled products were classified as prequalified if they were listed by WHO at the time of processing the survey results (June 2010). Only products of the same dosage form and strength, in the same immediate packaging and from the same manufacturing site as listed by WHO were characterized as prequalified.

Table 5 gives an overview of collected samples of WHO-prequalified products,.

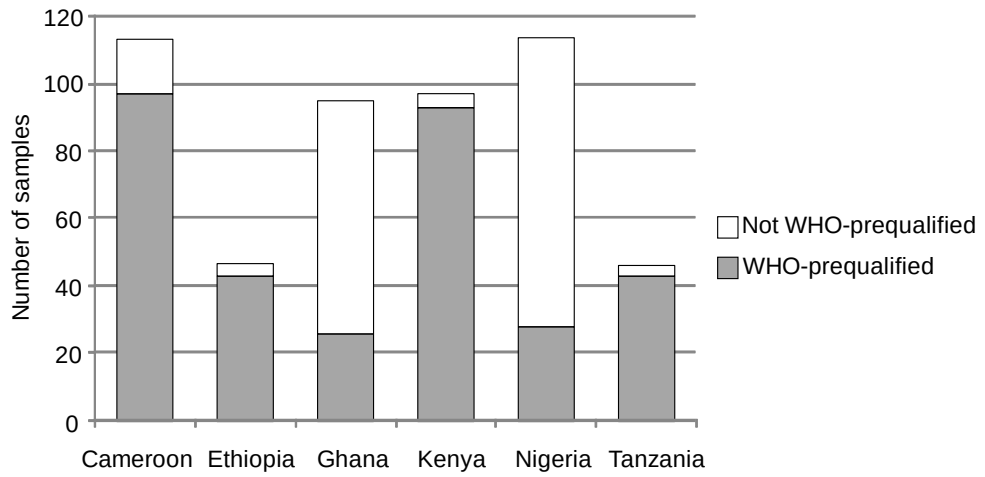
Table 5: Overview of samples of WHO-prequalified products collected in the survey

Product * Manufacturing site, country	**Date of prequali-fication**	**Number of samples of WHO-prequalified products**							**Total collected in survey**
		Came-roon	Ethio-pia	Ghana	Kenya	Nigeria	Tan-zania	**Total**	
AL 20/120mg tablets								**251**	**327**
Novartis, USA/China	Apr 2004	43	39	10	89	11	43	235	
Ajanta Pharma Ltd, India	Dec 2008	7	4	-	2	-	-	13	
Cipla Ltd, India	May 2009	-	-	-	1	1	-	2	
Ipca Laboratories Ltd, India	Dec 2009	-	-	-	1	-	-	1	
A&A co-packed tablets 153/50mg or 150/50mg								**70**	**159**
Cipla Ltd, India	Nov 2008	39	-	-	-	4	-	43	
Guilin Pharmaceutical Co Ltd, China	Aug 2007	2	-	2	-	-	-	4	
Ipca Laboratories Ltd, India	Apr 2008	1	-	12	-	10	-	23	
AA FDC 270/100mg tablets								**9**	**26**
Sanofi Aventis/Maphar, Morocco	Oct 2008	5	-	2	-	2	-	9	
Total (AL, A&A co-packed and AA FDC)		**97**	**43**	**26**	**93**	**28**	**43**	**330**	**512**

* **AL**: artemether/lumefantrine; **A&A co-packed**: artesunate + amodiaquine co-packed products; **AA FDC**: artesunate/amodiaquine fixed-dose combination

Figure 4 shows numbers of samples of WHO-prequalified products and non-prequalified products of the relevant product types collected in individual countries.

Figure 4:
Numbers of WHO-prequalified and non-WHO-prequalified AL, A&A co-packed and AA FDC samples



5.2 GPHF-Minilab® testing results

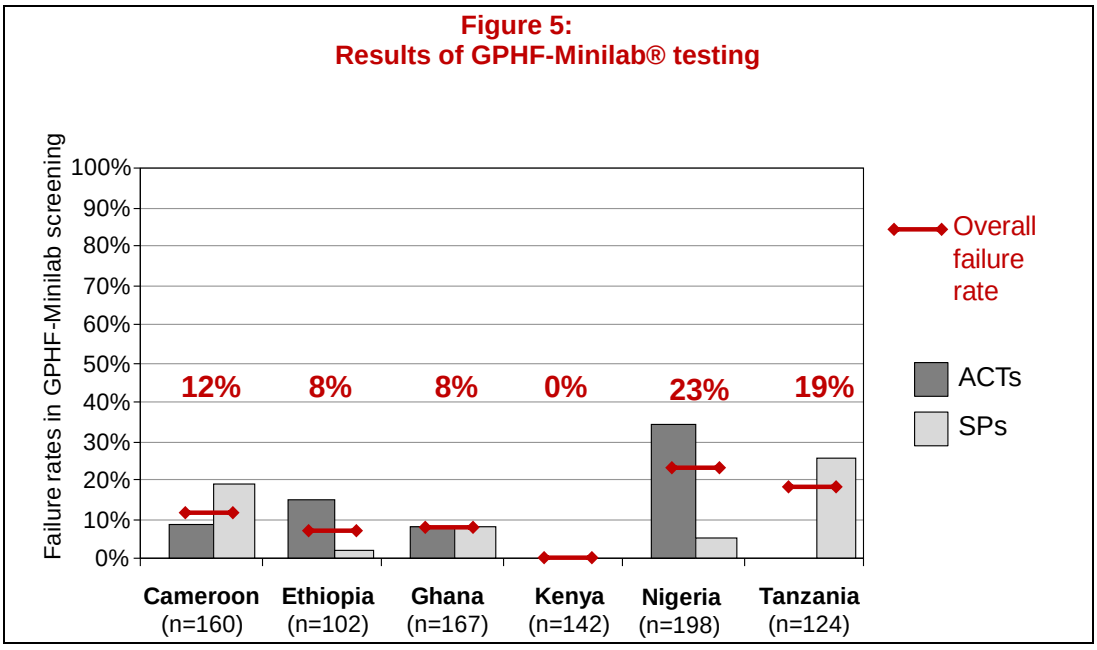
Most (893) of the collected samples were first subjected to a screening using GPHF-Minilab® kits. The screening consisted of visual inspection, TLC identification and semi-quantitative active ingredient content and simple disintegration testing. A detailed report was generated for each sample tested with the GPHF-Minilab® kit by the staff of national drug regulatory authorities in individual countries.

Forty-two samples were not tested because either collected samples were expired at the time of collection or because no GPHF-Minilab® kit was available for the particular product (combinations of dihydroartemisinin/piperaquine, artemisinin/piperaquine, artemisinin/naphthoquine, and SPP). In Tanzania and Nigeria SPP products were screened using the kit for SP.

Visual inspection within the screening procedure includes description of dosage form, label and packaging. However, as national requirements on labelling and packaging vary in individual countries and as the reports showed very different level of detail of observations in individual countries, the outcomes of assessment of labels and packaging were not considered comparable. Therefore, the results of visual inspection in this report reflect only visual inspection of the dosage form.

Figure 5 gives an overview of failure rates in individual countries for ACTs, SPs and overall.

Figure 5:
Results of GPHF-Minilab® testing



As Figure 5 shows, there were large differences among countries, and between failure rates for ACTs and SPs.

Non-compliance in visual inspection of the dosage form was the cause of all failures in Tanzania (19%), and of most failures in Cameroon (10%). On the other hand, in Nigeria and Ethiopia most failures were detected in TLC testing (19% and 7%, respectively). Disintegration was the aspect that contributed least to failure in all six countries. Details are shown in Table 6.

Table 6: Details of GPHF-Minilab® testing results

Country	No. of samples		Number of samples failed and reason for failure		
	Tested	Failed	Disintegration (should be <=30 min)	TLC	Visual inspection of dosage form appearance
Cameroon	**160**	**19**			
AL	**52**	**4**	-	-	**4** stain/powder on tablet, non-uniform colour
AA	**61**	**6**	-	**3** lower content and additional spot for artesunate	**3** black spots or dirty marks on tablet, powder on tablet
SP	**47**	**9**	-	-	**9** powder, breaks on tablet, counterfeit-different batch number on blister and box, only part of package leaflet in each box
Ethiopia	**102**	**8**			
AL	**47**	**7**	-	**7** 2x -artemether spot darker than standard 5x -lumefantrine spot intensity higher than standard	-
SP	**55**	**1**	-	-	**1** abrasions and broken tablets - hospital pack (bulk packing)
Ghana	**167**	**14**			
AL	**46**	**2**	-	-	**2** doubtful colour and spots on tablet
AA	**49**	**6***	-	**5** additional spot for artesunate	**2** chipped, eroded tablet
SP	**72**	**6**	**2** 45min/>1h	**1** additional spot	**3** chipped tablet, with pin holes, stain
Kenya	**142**	**0**			
AL	**96**	-	-	-	-
SP	**46**	-	-	-	-
Nigeria	**198**	**46**			
AL	**43**	**4**	**2** 40/60 min	**1** additional spot for artemether	**1** stain on tablet
AA	**71**	**38**	**3** AMQ 32/40/80 min	**1** no artesunate spot **34** additional spot for artesunate	-
A&SP	**5**	-	-	-	-
A&SPP	**1**	-	-	-	-
AM	**2**	-	-	-	-
SP	**75**	**4**	**4** 33/40/ 47min/> 1h	**1** no pyrimethamine spot in sample with disintegration of 47min	-
SPP	**1**	-	-	-	-
Tanzania	**124**	**23**			
AL	**31**	-	-	-	-
A&SPP	**4**	-	-	-	-
SP	**63**	**19**	-	-	**19** abrasion, erosion, breaks, foreign particles, damage, dirty marks on some tablets, non-uniform shape, sticky tablets
SPP	**26**	**4**	-	-	**4** erosion, breaks, dirty marks on some tablets
All countries	**893**	**110**			

AL: artemether/lumefantrine; **AA**: artesunate/amodiaquine; **SP**: sulfadoxine/pyrimethamine; **SPP**: sulfamethoxypyrazine/pyrimethamine; **A&SP**: artesunate + sulfadoxine/pyrimethamine; **A&SPP**: artesunate + sulfamethoxypyrazine/pyrimethamine; **AM**: artesunate/mefloquine

* One sample had 2 defects

5.3 Selection of samples for laboratory testing

From each country, approximately one-third of the total number of collected samples was selected using the pre-established criteria as listed at the end of section 4.2. A subset of 306 samples, including 93 samples of WHO-prequalified products, was thus selected for laboratory testing. Numbers of samples and batches selected in each country are shown in Table 7.

Table 7: Total collected samples and subset of samples selected for laboratory testing

Country	Total samples collected	Samples selected for laboratory testing	Number of batches	Ratio of samples per batch selected for laboratory testing
Cameroon	160	46 (29%)	26	1.8
Ethiopia	102	40 (39%)	21	1.9
Ghana	175	56 (32%)	34	1.6
Kenya	154	44 (29%)	29	1.5
Nigeria	200	75 (38%)	59	1.3
Tanzania	144	45 (31%)	26	1.7
Total	**935**	**306 (33%)**	**195**	**1.6**

5.3.1 Sampling sites and geographical regions

Samples selected for QC laboratory testing were collected a total of 218 sampling sites in different regions of each country (see Table 8). In general, in the subset selected for QC testing not more than two samples were collected at the same site.

Table 8: Number of sampling sites and number of samples selected per region

Country	Total no. of samples	No. of sampling sites	Regions and number of samples selected									
Cameroon	46	26	Centre	20	West	9	South-West	9	Coast	8		
Ethiopia	40	35	Central	9	Southern	12	Eastern	7	Northern	12		
Ghana	56	46	Southern	34	Middle	12	Northern	10				
Kenya	44	31	Central	14	Nyanza	12	Western	7	Coast	11		
Nigeria	75	43	Lagos	49	Kano	8	Jos	8	Onitsha	7	Calabar	3
Tanzania	45	37	Dar es Salaam	9	Mtwara	10	Kigoma	8	Tabora	7	Mwanza	11
Total	**306**	**218**										

5.3.2 Distribution levels

Table 9 shows the numbers of samples from each distribution level that were selected for QC laboratory testing. As large numbers of samples were collected at level 2, a higher proportion of samples from level 1 was selected for laboratory testing, to ensure substantial numbers from all levels.

Table 9: Number of samples selected from different distribution levels

Country	Level 1 (Central)	Level 2 (Outlets)	Level 3 (Informal)
Cameroon	12 of 24 (50%)	22 of 96 (23%)	12 of 40 (30%)
Ethiopia	8 of 12 (67%)	28 of 79 (35%)	4 of 11 (36%)
Ghana	16 of 23 (70%)	37 of 140 (26%)	3 of 12 (25%)
Kenya	14 of 22 (64%)	28 of 129 (22%)	2 of 3 (67%)
Nigeria	29 of 42 (69%)	35 of 127 (28%)	11 of 31 (35%)
Tanzania	7 of 9 (78%)	38 of 135 (28%)	0 of 0 n/a
Total	**86** of 132 **(65%)**	**188** of 706 **(27%)**	**32** of 97 **(33%)**

5.3.3 Products and strengths

Table 10 gives an overview of the proportions of samples of each product type selected for laboratory testing.

Table 10: Samples of different product types selected for laboratory testing

Country	AL	A&A co-packed	AA FDC	SP	SPP
Cameroon	15 of 52 (29%)	10 of 53 (19%)	5 of 8	16 of 47 (34%)	-
Ethiopia	15 of 47 (32%)	-	0 of 0	25 of 55 (45%)	-
Ghana	19 of 46 (41%)	17 of 44 (39%)	1 of 5	19 of 72 (26%)	0 of 1
Kenya	23 of 96 (24%)	1 of 1	0 of 0	19 of 46 (41%)	1 of 1
Nigeria	21 of 43 (49%)	22 of 58 (38%)	6 of 13	25 of 75 (33%)	1 of 1
Tanzania	15 of 43 (35%)	0 of 3	0 of 0	23 of 67 (34%)	7 of 27
Total	**108** of 327 **(33%)**	**50** of 159 **(31%)**	**12** of 26	**127** of 362 **(35%)**	**9** of 30

AL: artemether/lumefantrine
A&A co-packed: artesunate + amodiaquine co-packed products;
AA FDC: artesunate/amodiaquine fixed-dose combination;
SP: sulfadoxine/pyrimethamine;
SPP: sulfamethoxypyrazine/pyrimethamine

As regards dosage forms, all the samples selected for QC laboratory testing were tablets except for two samples, which were in powder form. The overview of product strength represented in the subset of samples is shown in Table 11. Strength is given in mg in the same order as the order of active ingredients in the column heading (in the case of amodiaquine the strength is expressed as the amount of amodiaquine base).

Table 11: Product strengths of samples tested

AL (108 samples)		A&A co-packed (50 samples)		AA FDC (12 samples)		SP (127 samples)		SPP (9 samples)	
Strength	No. of samples	Strength (mg)	No. of samples	Strength (mg)	No. of samples	Strength (mg)	No. of samples	Strength (mg)	No. of samples
20/120	98	50/150	5	50/150	2	500/25	127	500/25	9
40/240	8	50/153	10	50/200	3				
80/480	2	50/153.1	20	100/270	2				
		50/153.8	1	100/300	1				
		50/200	2	100/306.2	3				
		100/300	8	200/600	1				
		200/600	4						

AL: artemether/lumefantrine
A&A co-packed: artesunate + amodiaquine co-packed products;
AA FDC: artesunate/amodiaquine fixed-dose combination;
SP: sulfadoxine/pyrimethamine;
SPP: sulfamethoxypyrazine/pyrimethamine

5.3.4 Manufacturers and batches

There were large differences in numbers of products produced by different manufacturers. Applying the selection criteria, the number of manufacturers of products selected for testing was adapted proportionately to the situation in the countries surveyed.

The 306 samples selected for full testing were produced by 64 manufacturers and represented a total of 195 batches. In the subset of samples selected for testing from individual countries, the number of samples and number of batches correlated approximately with the number of manufacturers (see Table 12).

Table 12: Number of manufacturers of samples selected for laboratory testing

Country	Number of manufacturers of samples selected for laboratory testing	AL	A&A co-packed	AA FDC	SP	SPP
Cameroon	15	2	4	2	7	0
Ethiopia	6	2	0	0	5	0
Ghana	18	8	6	1	10	0
Kenya	8	4	1	0	5	1
Nigeria	27	8	9	3	13	1
Tanzania	6	1	0	0	3	4
Total number of manufacturers	**64***	**18***	**18***	**6***	**38***	**6***
Total number of batches	**195**	**72**	**31**	**9**	**76**	**9**
Total number of samples	**306**	**108**	**50**	**12**	**127**	**9**

AL: artemether/lumefantrine
A&A co-packed: artesunate + amodiaquine co-packed products;
AA FDC: artesunate/amodiaquine fixed-dose combination;
SP: sulfadoxine/pyrimethamine;
SPP: sulfamethoxypyrazine/pyrimethamine

* The total number of manufacturers is lower than the sum of the numbers in countries or across product areas because some manufacturers produced more than one product type and/or supplied more than one country.

5.3.5 GPHF-Minilab® status

The GPHF-Minilab® procedure is, by design, a screening tool that may indicate doubtful quality of a product but requires confirmation by full QC laboratory testing. As there were big differences in screening results in individual countries, samples that passed as well as those that failed in screening were selected for QC laboratory testing with the aim of validating the results of GPHF-Minilab® testing (see Table 13).

Table 13: GPHF Minilab conclusion for samples selected for QC laboratory testing

Product type	Number of samples selected for laboratory testing			Total samples selected
	Passed GPHF-Minilab® testing	Failed GPHF-Minilab® testing	Not tested	
AL	95	13		108
A&A co-packed	31	19		50
AA FDC	4	8		12
SP	105	22		127
SPP	6	2	1	9
Total	**241**	**64**	**1**	**306**

AL: artemether/lumefantrine
A&A co-packed: artesunate + amodiaquine co-packed products;
AA FDC: artesunate/amodiaquine fixed-dose combination;
SP: sulfadoxine/pyrimethamine;
SPP: sulfamethoxypyrazine/pyrimethamine

5.4 Outcomes of QC laboratory testing

This section presents the results of QC laboratory testing of 306 samples from the six countries. Details and tests results are listed in Appendices 2-6, grouped by active ingredients. Samples in each Appendix are sorted according to the countries in which they were collected.

Compliance statements reflect the results of tests for identity, assay for each active ingredient, related substances, dissolution and uniformity of dosage units as required by the respective specifications. Failures in appearance of dosage forms were taken as a supportive indicator of quality problems.

5.4.1 Limitations of QC laboratory testing in this survey

Visual inspection

Assessment of appearance of dosage form through visual inspection did not provide consistent results.

- In the QC laboratory the appearance of 28% of samples (87 samples out of 306) was assessed as compliant. For the remaining 72% of samples, various observations were reported by testing laboratories, such as tablets mottled, chipped, broken, with spots, flaws, foreign particles embedded, uneven surface, rough edges, faulty engraving, with powder or crystals on surface and powder in blisters.
- The appearance assessment of the same samples performed during GPHF-Minilab® screening by the staff of national drug regulatory authorities in countries resulted in significantly fewer observations, i.e. only for 8% of samples (25 of 306) were observations reported. Only Cameroon (9 samples), Ghana (5 samples) and Tanzania (11 samples) reported observations. It seems that assessment of appearance performed by testing laboratories was more thorough than assessment done by the staff of national drug regulatory authorities in individual countries. The single exception was Tanzania, where the regulatory authority reported 11 observations compared to one observation in testing laboratories for the same set of samples.

Failures in appearance of dosage form are generally taken as an indicator of quality problems. In this survey assessment of appearance obviously depended on the experience of the assessor and was subjective, as is demonstrated by major discrepancies between the observations of national authorities and testing laboratories. Having objective laboratory data available for assessment of quality, the outcomes of appearance assessment were not reflected in compliance assessment and were not considered a critical indicator. Nevertheless, all appearance observations are included in Appendices 2-6.

Number of dosage units collected

Owing to the low number of dosage units collected for some samples, dissolution tests could not be completed and compliance statements could not be made for 22 of the 306 samples. Dissolution results for all these samples were borderline; they did not fulfil criteria in Stage 1 or Stage 2 and there were not enough tablets for confirmation in a further stage. Detailed results for these samples are included in Appendices 2-6 with the outcome of testing as "Inconclusive". They were not counted as "Non-compliant" samples and were not considered in further evaluation.

Expired samples

The QC testing of 22 other samples was completed after expiry of their shelf-life. For five of these samples, all the results fully complied with specifications and they were further considered as compliant, not being handled differently from other compliant samples; a note was added in Appendices 2-6 indicating that testing was completed 1-4 months after expiry. For 17 samples the test results were concluded as being either inconclusive or non-compliant with specifications. These samples were not included in the Appendices or further considered.

5.4.2 Number of samples with conclusive results

Table 14 shows the total number of samples selected for testing, tested with inconclusive results due to reasons explained under 5.4.1, and fully tested with conclusive results. Failure rates presented further in this report were calculated as percentages of non-compliant samples out of the total number of samples with conclusive results.

Table 14: Numbers of samples selected and fully tested

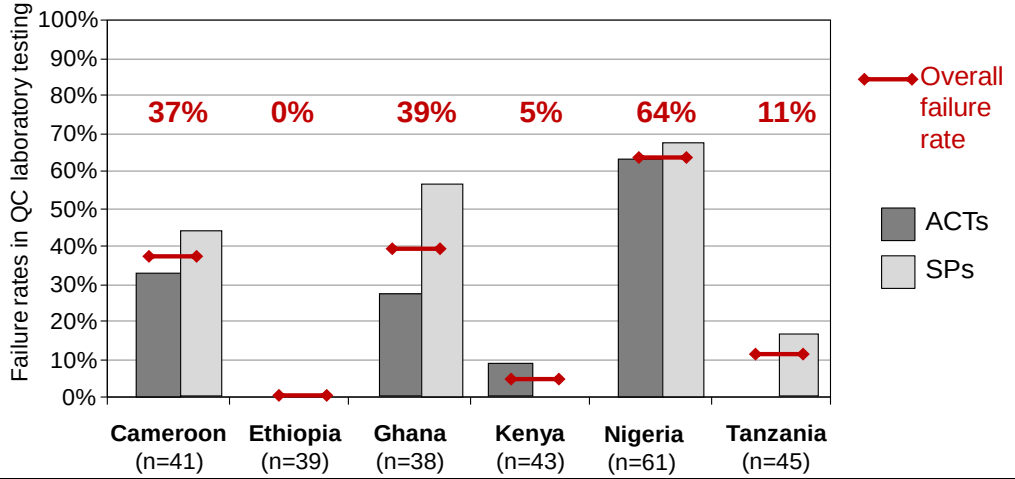
Country	Product type	Selected	Inconclusive		Conclusive	Total conclusive
			Too few units	Expired		
Cameroon	AL	15	3	-	12	**41**
	A&A co-packed	10	-	-	10	
	AA FDC	5	-	2	3	
	SP	16	-	-	16	
Ethiopia	AL	15	1	-	14	**39**
	SP	25	-	-	25	
Ghana	AL	19	9	-	10	**38**
	A&A co-packed	17	1	4	12	
	AA FDC	1	-	1	0	
	SP	19	3	-	16	
Kenya	AL	23	-	-	23	**43**
	A&A co-packed	1	-	-	1	
	SP	19	-	-	19	
	SPP	1	1	-	0	
Nigeria	AL	21	-	1	20	**61**
	A&A co-packed	22	-	8	14	
	AA FDC	6	-	-	6	
	SP	25	4	1	20	
	SPP	1	-	-	1	
Tanzania	AL	15	-	-	15	**45**
	SP	23	-	-	23	
	SPP	7	-	-	7	
All	**AL**	**108**	**13**	**1**	**94**	**267**
	A&A co-packed	**50**	**1**	**12**	**37**	
	AA FDC	**12**	**0**	**3**	**9**	
	SP	**127**	**7**	**1**	**119**	
	SPP	**9**	**1**	**0**	**8**	

AL: artemether/lumefantrine; **A&A co-packed**: artesunate + amodiaquine co-packed products; **AA FDC**: artesunate/amodiaquine fixed-dose combination; **SP**: sulfadoxine/pyrimethamine; **SPP**: sulfamethoxypyrazine/pyrimethamine

5.4.3 Testing outcomes by product types

Failure rates in each country overall and for ACTs and SPs are shown graphically in Figure 6.

Figure 6:
Results of QC laboratory testing in six African countries



The highest failure rate was found in Nigeria, followed by Ghana and Cameroon. Considerably lower failure rates were found for samples from Tanzania and Kenya. No sample from Ethiopia failed in QC laboratory testing. In all countries except for Ethiopia (no failure) and Kenya (only 2 ACTs and no SP failed), the failure rate was higher for SPs than for ACTs.

Failures were found for all tested product types in the survey. Non-compliance rates below 30% were found for AL, SP and SPP. Considering the number of manufacturers from which samples of AL and SP were collected (18 and 38, respectively), failure rates may be considered representative for the market situation. Too few SPP samples were collected to allow valid conclusions.

A failure rate of almost 50% was found for A&A co-packed samples produced by 18 manufacturers, meaning that every second sample randomly collected was non-compliant with specifications.

All AA FDC products failed testing. Although the number of samples in this case was relatively low (12 samples produced by six manufacturers; although testing of only nine samples from four manufacturers was completed before expiry and further evaluated). Such a high failure rate indicates a quality problem for this product.

Detailed data concerning failures in individual tests are presented in section 5.5.

5.4.4 Testing outcomes by geographical regions

Table 15 shows the numbers of samples tested and number non-compliant in the different regions.

Table 15: Failures observed in different regions

Country	Region, and numbers of non-compliant samples, of samples fully tested (shaded: more than one in five samples failed; **bold and shaded**: half or more samples failed)									
Cameroon	Centre	6/18	West	2/7	South-West	4/9	Coast	3/7		
Ethiopia	Central	0/9	Southern	0/11	Eastern	0/7	Northern	0/12		
Ghana	Southern	**13/22**	Middle	1/9	Northern	1/7				
Kenya	Central	1/13	Nyanza	0/12	Western	0/7	Coast	1/11		
Nigeria	Lagos	**28/40**	Kano	3/7	Jos	**5/6**	Onitsha	**3/6**	Calabar	0/2
Tanzania	Dar es Salaam	1/9	Mtwara	3/10	Kigoma	1/8	Tabora	0/7	Mwanza	0/11

The numbers of failures in different regions shown in Table 15 gave a heterogeneous picture; from some regions the numbers of samples tested with conclusive results were relatively low.

- In Cameroon, comparable proportions of substandard samples were found in all four regions, ranging from 29% to 44%.
- No substandard samples were found in Ethiopia.
- In Ghana, the highest percentage of failed samples (59%) was found in the Southern zone, where the capital Accra is located.
- The only two failing samples in Kenya were found in the Central and Coast regions.
- In Nigeria, the highest failure rate was found in Jos (83%), followed by Nigeria's largest city Lagos (70%), Onitsha (50%) and Kano (43%). No failure was found in Calabar. Low numbers of samples were collected in all cities except Lagos.
- In Tanzania, the highest failure rates were found in Mtwara (30%), followed by Kigoma (13%) and the capital Dar es Salaam (11%). No failure was found in either Tabora or Mwanza.

5.4.5 Testing outcomes by distribution levels

One of the objectives of the survey was to compare the proportion of substandard ACTs and SPs at different distribution levels and different geographical regions in the selected countries. The results are summarized in Table 16.

Table 16: Results of QC laboratory testing of samples according to distribution levels

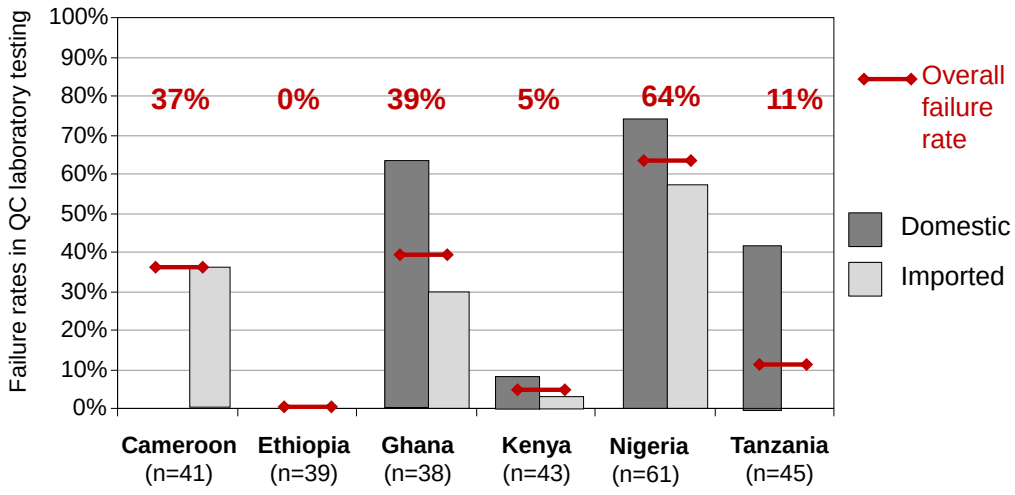
Country	Level 1 (Central)	Level 2 (Outlets)	Level 3 (Informal)
	Numbers of non-compliant samples, of those fully tested (shaded: more than one in five samples failed; **bold and shaded**: half or more samples failed)		
Cameroon	3/10	5/21	**7/10**
Ethiopia	0/8	0/27	0/4
Ghana	5/11	8/25	**2/2**
Kenya	1/13	1/28	0/2
Nigeria	**20/24**	**16/28**	3/9
Tanzania	2/7	3/38	n/a

In all countries (except Ethiopia where no failing samples were found) failure rates at level 1 were higher than failure rates at level 2.

5.4.6 Testing outcomes by country of manufacture of tested products

Information on differences in quality between medicines produced locally and those imported into the country may be useful for regulators in countries participating in the survey. Figure 7 shows the corresponding failure rates.

Figure 7:
Failure rates of domestically produced and imported product samples



Except for Cameroon (where no domestic products were collected in this survey) and Ethiopia (where no failure was found either in locally produced or imported samples), a higher failure rate was found for domestic samples than for imported samples.

A more detailed breakdown is shown in Table 17.

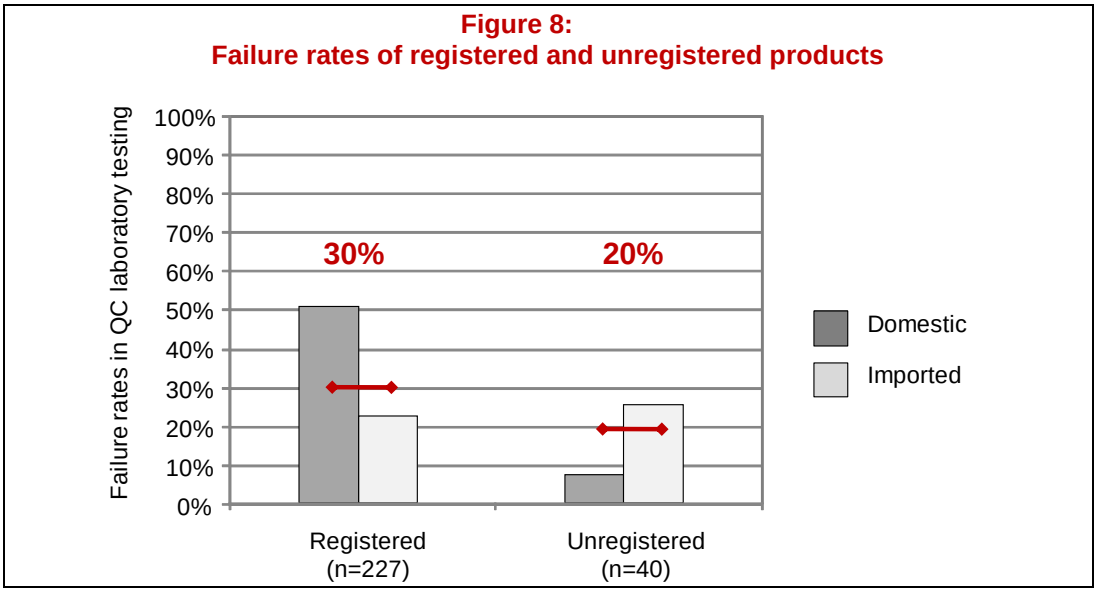
Table 17: Testing outcomes for domestically produced and imported samples

Country of manufacture		Number of compliant samples		Number of non-compliant samples	
Domestically produced:	**Cameroon**	**0**		**0**	
Imported from:	India	**26**	15	**15**	7
	China		4		3
	USA		5		0
	South Africa		2		0
	Mauritius		0		1
	Nigeria		0		2
	UK		0		2
Domestically produced:	**Ethiopia**	**13**		**0**	
Imported from:	India	**26**	10	**0**	0
	USA		10		0
	China		2		0
	Kenya		2		0
	South Africa		2		0
Domestically produced:	**Ghana**	**4**		**7**	
Imported from:	India	**19**	12	**8**	7
	China		6		0
	USA		1		0
	Bangladesh		0		1
Domestically produced:	**Kenya**	**11**		**1**	
Imported from:	USA	**30**	11	**1**	1
	India		8		0
	China		6		0
	South Africa		5		0
Domestically produced:	**Nigeria**	**6**		**18**	
Imported from:	India	**16**	10	**21**	14
	China		4		6
	Viet Nam		1		1
	USA		1		0
Domestically produced:	**Tanzania**	**7**		**5**	
Imported from:	Kenya	**33**	15	**0**	0
	USA		8		0
	China		7		0
	Italy		2		0
	India		1		0

5.4.7 Testing outcomes by registration status

Overall, 68 of 227 registered samples failed (30%), compared with 8 of 40 unregistered ones (20%). Among 227 registered samples, 59 were from local production and 30 of them failed (51%), while of 168 registered imported samples 38 failed (23%). Among unregistered samples, 13 were locally produced and one failed (8%), while 27 were imported samples and seven of them failed (26%) - see Figure 8.

Figure 8:
Failure rates of registered and unregistered products



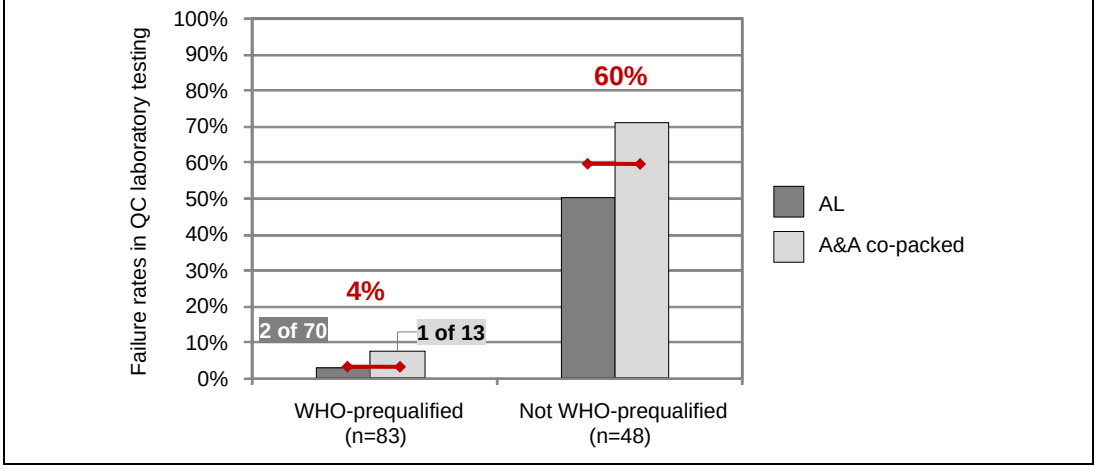
The aggregated results illustrated in Figure 8 combine different findings in the individual countries. Only one unregistered sample was selected for QC testing from Nigeria and none from Tanzania or Kenya. For the other countries, the results were as follows:

- All samples from Ethiopia passed QC testing, including 20 registered and 19 unregistered samples.
- Cameroon: 11 of 37 registered samples (30%) and all five unregistered samples failed QC testing.
- Ghana: 12 of 23 registered samples (52%) and three out of 15 for unregistered samples (20%) failed QC testing.

5.4.8 Testing outcomes by WHO-prequalification status

Of the 306 samples selected for QC laboratory testing, 93 samples were of WHO-prequalified products. Of these 93 samples, 10 gave inconclusive results because they were tested after their expiry date (7) or because there were insufficient tablets to complete the dissolution test (3). Conclusive results were obtained for 83 samples, including 70 AL and 13 A&A co-packed samples. Of the 83 samples, only three (3.6%) were found to be non-compliant. By comparison, of the 48 non-WHO-prequalified AL and A&A co-packed samples which gave conclusive testing results, 29 (60%) failed to comply with specifications (see Figure 9).

Figure 9:
Failure rates of WHO-prequalified and non-WHO-prequalified samples of relevant product types



Details about the results of these samples are presented in section 5.5. As specifically concerns the three failing samples of WHO-prequalified products, in two of the cases failures were not observed in other

samples from the same manufacturing batch tested in the survey, meaning that the problem was likely caused after manufacture:

- One AL sample failed in the related substances test (Impurity A was found to be above the limit); two other samples from the same batch were compliant, as were the remaining 61 samples of this product from 41 different batches.
- One A&A co-packed sample failed the mass uniformity test. Three tablets were found to be outside ±5% of the average mass (no tablet was found to be outside ±10%) while four other samples from the same batch were compliant.

The third failure occurred in an AL sample which was the only one tested of that particular batch. The sample contained a lower amount of artesunate (82.0%) and higher amount of artesunate-related substances. Such a failure was not observed in another four samples of three different batches from the same manufacturer.

5.5 Compliance with product specifications

5.5.1 Overview of failures in different laboratory tests

The tests performed at the laboratory included:

- appearance
- identity and content of active ingredient (tested by assay for each active ingredient)
- related substances
- dissolution, and
- uniformity of dosage units.

As mentioned in Section 5.4.1, assessment of appearance by visual inspection of the dosage form was subjective in this survey and did not give valid results. Because appearance itself has low specificity and predicative value as concerns health implications, the picture of sample quality in this survey is based on the results of laboratory testing.

Table 18 gives an overview of the numbers of samples of different product types failing the different laboratory tests.

Table 18: Failure rates for product types, and number of samples failing each laboratory test

		AL	A&A co-packed	AA FDC	SP	SPP
Total samples with conclusive results		94	37	9	119	8
Non-compliant		**14**	**18**	**9**	**33**	**2**
Overall failure rate		15%	49%	100%	28%	25%
Samples that failed in:	Assay	**9**	6	**7**	7	0
	Related substances test	4	**17**	*	*	*
	Dissolution test	6	3	4	**25**	**2**
	Mass uniformity test	1	6	0	10	0

Shaded cells indicate the most frequently failed test for each product type

* Test not included in the respective specifications

As Table 18 shows, different reasons contributed most frequently to failure for the different product types:

- Non-compliant results in assay markedly contributed to failure of AL products and AA FDC products.

- Related substances testing was performed for A&A co-packed and AL products. The test for artesunate-related substances failed in almost all non-compliant samples, especially in the case of A&A co-packed products.
- For all products, out-of-specification results were found in the dissolution test, contributing substantially to overall failures of SP products.
- The least contributing test to overall failure was the mass uniformity test, which for A&A co-packed products and SP products contributed approximately 30% of failures. Negative results in the mass uniformity test often corresponded to failure in the assay or dissolution test.

The findings for each product type are discussed in the following sections.

5.5.2 Artemether/lumefantrine tablets

Samples containing the AL combination were collected in all six countries. In all, 108 samples were subjected to QC laboratory testing, 91% of which represented the strength 20/120 mg. Testing of one sample was completed after its expiry date and this sample is not reported. Manufacturers of samples, numbers of samples and batches tested and countries of collection are listed in Table 19.

Fourteen samples (from 24 batches, produced by 10 different manufacturers) were found non-compliant in one or more tests.

Table 19: Manufacturers of tested artemether/lumefantrine samples

Manufacturer	No. of samples tested	No. of batches tested	Countries of collection
Beijing Novartis Pharma Ltd, China / Novartis Pharmaceuticals Corporation, USA	64	40	Cameroon, Ethiopia, Ghana, Kenya, Nigeria, Tanzania
Ajanta Pharma Ltd, India	10	6	Cameroon, Kenya
GVS Labs, India	6	4	Ghana, Nigeria
Jiangsu Yixing Forward Pharm. Factory, China	5	4	Nigeria
Addis pharmaceutical factory, Ethiopia	3	2	Ethiopia
Bliss GVS Pharma Ltd, India	3	1	Ghana
Ernest Chemists Ltd, Ernest, Ghana	3	2	Ghana
Naxpar Lab Ltd, India	3	2	Nigeria
Danadams Pharmaceutical Industry Ltd, Ghana	2	1	Ghana
Ecomed Pharma Ltd, Nigeria	1	1	Nigeria
Ipca Laboratories Ltd, India	1	1	Kenya
Jayson Pharmaceuticals Ltd, Bangladesh	1	1	Ghana
Kinapharma Ltd, Ghana	1	1	Ghana
Macleods Pharmaceuticals Ltd, India	1	1	Nigeria
May & Baker Nigeria Plc, Nigeria	1	1	Nigeria
Medreich Plc, India	1	1	Ghana
Mekophar Chemical Pharm. Joint-Stock Company, Viet Nam	1	1	Nigeria
Universal Corporation Ltd, Kenya	1	1	Kenya
Total	**108**	**71**	
Expired samples with inconclusive or non-compliant results	1		
Total discussed below	**107**		

Identity and content of active ingredients

Nine of 107 samples of AL products were found non-compliant in terms of content of active ingredients: For five samples assay of both active ingredients failed, for two samples only the assay of artemether failed and for two samples only the assay of lumefantrine failed. In one sample no artemether was detected both in the assay and dissolution test; however, artemether-related substances were above limits, which suggests serious manufacturing errors or substandard active ingredient used; assay and dissolution of lumefantrine were compliant in this sample. Another sample contained only 29% of the stated amount of artemether. The five remaining samples contained 82-89% of artemether. The content of lumefantrine in non-compliant samples was within the range 71-89% of the stated amount.

In GPHF-Minilab® testing of the same 107 samples, five samples failed in the TLC test:

- one sample due to contaminant spot found; in laboratory testing of this sample artemether was not detected, but artemether-related impurities were found above limits;
- four samples due to higher intensity of lumefantrine spot; higher lumefantrine content was not confirmed by laboratory testing and all four samples were found compliant in laboratory testing.

Artemether-related substances

Four of 107 samples were found non-compliant in terms of the artemether-related substances test (impurities A, B, C were found to be above the limits set in the International Pharmacopoeia). In seven samples impurity D (alpha-artemether) spot was identified, but it could not be quantitatively assessed as the reference substance was not available.

Dissolution

Five of 107 samples of AL products were found non-compliant in terms of dissolution of active ingredients (for one sample dissolution failed for both active ingredients, for one sample only dissolution of artemether failed, and for four samples only dissolution of lumefantrine failed). The two samples that failed in artemether dissolution were those that contained no, or only 29% of, artemether (the laboratory noted that the sample without artemether did not disintegrate during the dissolution test). Apart from five non-compliant samples, for 13 samples the outcome of the dissolution test could not be determined. Dissolution of either artemether or lumefantrine or both failed to comply to Stage 1 or Stage 2 criteria. However, there were not enough tablets to continue with Stage 3 and confirm the outcome of the dissolution test. Detailed results of dissolution testing are presented in Appendix 2.

In GPHF-Minilab® testing, all 107 samples except one passed the simple disintegration test. The sample failing the disintegration test was the one without artemether.

Uniformity of mass

All 107 samples except one complied with requirements of the mass uniformity test. In the non-compliant sample, one tablet was found to be outside of ±10% (89%), in all other tests this sample complied.

5.5.3 Artesunate + amodiaquine co-packed tablets/powder

Samples of A&A co-packed products were collected in Cameroon, Ghana, Kenya and Nigeria, but no sample was collected in Ethiopia or Tanzania. Fifty samples were subjected to QC laboratory testing, and several strengths from 50/150mg to 200/600mg were represented - see Table 11 (in principle the lowest strength was present in 72% of samples). Testing of 12 samples was completed after their expiry date and these samples are not reported. Manufacturers of samples, numbers of tested samples and batches and countries of collection are listed in Table 20.

Eighteen samples (from 15 batches, produced by 11 different manufacturers) were found non-compliant in one or more tests.

Table 20: Manufacturers of tested artesunate + amodiaquine co-packed samples

Manufacturer	Number of samples tested	Number of batches tested	Countries of collection
Ipca Laboratories Ltd, India	12	5	Ghana, Nigeria
Adams Pharmaceutical (ANHUI) Co Ltd, China	5	3	Cameroon, Nigeria
Cipla Ltd, India	5	3	Cameroon
Swiss Pharma Nigeria Ltd, Nigeria	5	2	Nigeria
GVS Labs, India	4	2	Ghana
Baader Schulz Lab, India	2	2	Nigeria
Danadams Pharmaceutical Industry Ltd, Ghana	2	1	Ghana
Ecomed Pharma Ltd, Nigeria	2	1	Nigeria
Madras Pharmaceuticals, India	2	2	Nigeria
Saga Laboratories Ltd, India	2	1	Nigeria
Strides Arcolab Ltd, India	2	2	Ghana
Atlantic Pharmaceutical Ltd, Ghana	1	1	Ghana
Bliss GVS Pharma Ltd, India	1	1	Ghana
Bond Chemical Ind. Ltd, Nigeria	1	1	Nigeria
Cosmos Ltd, Kenya	1	1	Kenya
Guilin Pharmaceutical Co Ltd, China	1	1	Cameroon
Mekophar Chemical Pharm. Joint-Stock Company, Viet Nam	1	1	Nigeria
Plethico Pharmaceuticals Ltd, India	1	1	Cameroon
Total	**50**	**31**	
Expired samples with inconclusive or non-compliant results	12		
Total discussed below	**38**		

Identity and content of active ingredients

Six of 38 samples of A&A co-packed products were found non-compliant in terms of content of active ingredients. For four samples, assay of artesunate failed, being in the range 76-89% of the stated amount, and for two samples assay of amodiaquine was found to be 85.1% and 115.0%, respectively (high content of amodiaquine in the latter sample was confirmed in the dissolution test by consistently high results).

In GPHF-Minilab® testing of the same 38 samples, nine samples failed in the TLC test. In one sample no artesunate spot was detected and in eight samples contaminant spots were found. In laboratory testing missing artesunate in the sample was not confirmed (artesunate assay was 99.8%), another three of these nine samples failed either in the artesunate assay (76.7 and 89.4%) or the amodiaquine assay (115.0%), eight samples failed in artesunate-related substances (however some failures were borderline) and one sample complied in all tests.

Artesunate-related substances

Seventeen of 38 samples of A&A co-packed products were found non-compliant in terms of the artemether-related substances test. Detailed results of this test are presented in Appendix 3. The International Pharmacopoeia monograph specifications used for this testing do not require identification of individual peaks. As dihydroartemisinin, artemisinin and glycan reference substances were available, the laboratory determined the approximate retention times for these impurities in the system used as follows: dihydroartemisinin approx 7 min, artemisinin approx 15 min, and glycan approx 28 min. Some mass balance relation between artesunate assay and related substances existed, e.g. for the sample with low artesunate assay (76.7%) the sum of the impurities was 33%. Apart from this extreme result, the sum of the impurities in the samples that failed this test was within the range 2.1-3.5%.

Dissolution

Of 38 samples of A&A co-packed products, 35 were tested for dissolution. Two samples could not be tested due to insufficient number of tablets collected and the dissolution test of powder form was not performed.

Three out of 35 samples were found non-compliant in terms of dissolution of artesunate (samples failed at Stage 1 to Stage 3 criteria). Apart from three non-compliant samples, one sample failed to comply with Stage 1 dissolution criteria and, due to the low content of artesunate, the dissolution test was not continued. No sample was found non-compliant for amodiaquine dissolution. For two samples, the dissolution test for amodiaquine was inconclusive. One failed in Stage 1 and, due to the low content of amodiaquine, the test

was not continued. The other sample failed in Stage 2 and the test was not continued due to insufficient tablets. In the case of the sample with high amodiaquine content and correspondingly high results for its dissolution, the dissolution test was evaluated as "out of expectation". Detailed results are presented in Appendix 3.

In GPHF-Minilab® testing of the same 35 samples, two samples failed in simple disintegration testing (one sample for disintegration of artesunate tablets, the other for disintegration of amodiaquine tablets). Laboratory testing confirmed failed dissolution of artesunate tablets in the first sample. The second sample was compliant in all laboratory tests, including amodiaquine dissolution. Disintegration testing of the sample in powder form was not performed.

Uniformity of mass

Six of 36 tested samples (two samples could not be tested for uniformity of mass due to insufficient number of collected tablets) did not comply with the requirements of the mass uniformity test. Detailed results are presented in Appendix 3.

5.5.4 Artesunate/amodiaquine fixed-dose combination tablets/powder

Samples of AA FDC products were collected in Cameroon, Ghana and Nigeria only. Twelve samples (11 in the form of tablets, one in powder form) were subjected to QC laboratory testing, and several strengths from 50/150mg to 200/600mg were evenly represented (see Table 11). Testing of three samples was completed after their expiry date and these samples are not reported. Manufacturers of samples, numbers of tested samples and batches and countries of collection are listed in Table 21.

Nine samples (from 7 batches, produced by four different manufacturers) were found non-compliant in one or more tests.

Table 21: Manufacturers of tested artesunate/amodiaquine FDC samples

Manufacturer	Number of samples tested	Number of batches tested	Countries of collection
Emzor Pharm Ind. Ltd, Nigeria	4	4	Nigeria
Kamala Overseas, India	3	1	Cameroon
Kinapharma Ltd, Ghana	1	1	Ghana
Maphar Laboratories SA	2	1	Cameroon
Mercury Laboratories Ltd, India	1	1	Nigeria
Rajat Pharmachem Ltd, India	1	1	Nigeria
Total	**12**	**9**	
Expired samples with inconclusive or non-compliant results	3		
Total discussed below	**9**		

Identity and content of active ingredients

Seven of nine samples of AA FDC products were found non-compliant in terms of content of active ingredients. Six samples failed, the assay of artesunate failed being in the range 73-88% of the stated amount, and the content of amodiaquine in one sample was 76.4%.

In GPHF-Minilab® testing of the same nine samples, eight samples failed in the TLC test:

- three samples due to low content of artesunate and the presence of an additional spot; in laboratory testing these three samples failed in the artesunate assay (72-83%), and dihydroartemisinin was found within the range of 4-12%;
- five samples due to a contaminant spot; in laboratory testing three of these five samples failed in the artesunate assay (83-88%), one sample failed in the amodiaquine assay (76.4%) and one sample complied in both artesunate and amodiaquine assays; in all these five samples dihydroartemisinin was found within the range of 2-9% and in two of them 7-8% of artemisinin was found.

Artesunate-related substances

The laboratory in-house HPLC method used for testing of artesunate-related substances in AA FDC products was specific for the products for which it was developed and did not prove to be suitable for a wider range of products. There were observed interferences from excipients and from amodiaquine, which made the determination of unknown impurities and the total sum of impurities impossible. Therefore, only dihydroartemisinin, artemisinin and glycan, which were identified using reference substances, were reported. No specifications for the limits of these related substances were available and thus no compliance statement was made.

The percentages of dihydroartemisinin, artemisinin and glycan related to the artesunate peak found in individual samples are presented in Appendix 4. In no sample was more than 0.2% of glycan found. Dihydroartemisinin was found in the range 2.0-12.2% and artemisinin in the range 0.1-8.4%. It is clear that some mass balance relationship exists between the assay of artesunate and related substances, especially dihydroartemisinin and artemisinin. The lower the assay of artesunate, the higher the content of these related substances found. As dihydroartemisinin is an active metabolite and artemisinin is an active pharmaceutical ingredient on its own, these substances should not pose any safety or efficacy risk.

Dissolution

Four of eight samples of AA FDC tablets were found non-compliant in terms of dissolution of artesunate (failed Stage 1 to Stage 3 criteria). Another three samples failed to comply with Stage 1 or Stage 2 dissolution criteria and, due to their low content of artesunate, the dissolution test was not continued. All samples complied in the dissolution test for amodiaquine. Dissolution testing of the powder form was not performed. Detailed results of dissolution testing are presented in Appendix 4.

In GPHF-Minilab® testing all eight tablet samples passed the simple disintegration test. Disintegration testing of the sample in powder form was not performed.

Uniformity of mass

All eight tablet samples complied with the requirements of the mass uniformity test. Testing was not performed for the sample in powder form.

5.5.5 Sulfadoxine/pyrimethamine tablets

Samples containing SP combination were collected in all six countries. In all, 127 samples were subjected to QC laboratory testing, all with the strength 500/25mg. Testing of one sample was completed after its expiry date and this samples is not reported. Manufacturers of samples, numbers of tested samples and batches and countries of collection are listed in Table 22.

Thirty-three samples (from 25 batches, produced by 18 different manufacturers) were found non-compliant in one or more tests.

Table 22: Manufacturers of tested sulfadoxine/pyrimethamine samples

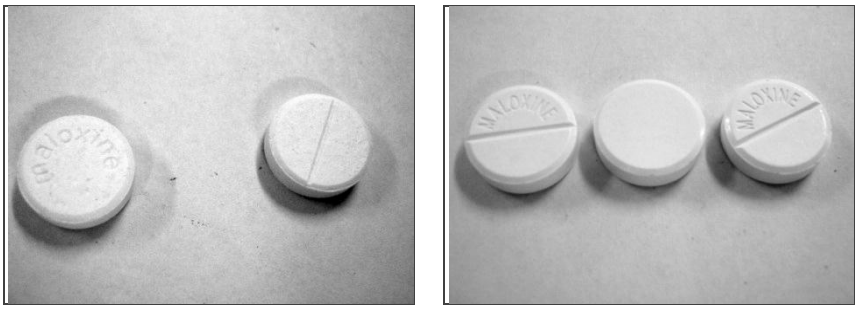
Manufacturer	No. of samples tested	No. of batches tested	Countries of collection
Addis pharmaceutical factory, Ethiopia	11	4	Ethiopia
Elys Chemical Industries Ltd, Kenya	11	4	Tanzania
Shelys Pharmaceuticals Ltd, Tanzania	11	5	Tanzania
Roche Products Pvt Ltd, South Africa	9	6	Ethiopia, Cameroon, Kenya
Ipca Laboratories Ltd, India	8	4	Ethiopia, Kenya
Cosmos Ltd, Kenya	7	3	Kenya
Swiss Pharma Nigeria Ltd, Nigeria	5	4	Cameroon, Nigeria
Universal Corporation Ltd, Kenya	5	3	Ethiopia, Kenya
Emzor Pharm Ind. Ltd, Nigeria	4	3	Nigeria
Kinapharma Ltd, Ghana	4	2	Ghana
Maneesh Pharmaceuticals Pvt Ltd, India	4	2	Cameroon
Micro Labs Ltd, India	4	3	Nigeria
Sterling Lab, India	4	2	Ethiopia
Gracure Pharmaceuticals Ltd, India	3	2	Cameroon
Neimeth International Pharmaceuticals Plc, Nigeria	3	2	Nigeria
Phyto-Riker Pharmaceuticals Ltd, Ghana	3	2	Ghana
Ally Pharma Options, India	2	2	Ghana
Bond Chemical Ind. Ltd, Nigeria	2	2	Nigeria
Britlodge Ltd, UK	2	1	Cameroon
Lupin Ltd, India	2	1	Kenya
Medreich Plc, India	2	1	Ghana
Milan Laboratories Pvt Ltd, India	2	1	Ghana
Shreechem Lab, India	2	2	Nigeria
Simrone Pharmaceuticals Industries Ltd, India	2	1	Cameroon
Uni-Med, India	2	1	Ghana
Ajanta Pharma Limited, Mauritius	1	1	Cameroon
Atlantic Pharmaceutical Ltd, Ghana	1	1	Ghana
Baader Schulz Lab, India	1	1	Nigeria
Danadams Pharmaceutical Industry Ltd, Ghana	1	1	Ghana
Evans Medical Plc, Nigeria	1	1	Nigeria
GR Industries Ltd, Ghana	1	1	Ghana
Intas Pharmaceutical Ltd, India	1	1	Tanzania
Juhel Nigeria Ltd, Nigeria	1	1	Nigeria
May & Baker Nigeria Plc, Nigeria	1	1	Nigeria
Medrel Pharmaceuticals Ltd, India	1	1	Nigeria
Mission Pharmaceuticals Ltd, India	1	1	Ghana
SKG - Pharma Ltd, Nigeria	1	1	Nigeria
Vitaphos Laboratory Nigeria Ltd, Nigeria	1	1	Nigeria
Total	**127**	**76**	
Expired samples with inconclusive or non-compliant results	1		
Total discussed below	**126**		

Identity and content of active ingredients

Seven out of 126 tested samples of SP products were found non-compliant in terms of content of active ingredients. Six samples failed in the pyrimethamine assay, being in the range 80-89% of the stated amount. In one sample no pyrimethamine was detected in the assay, related substances and dissolution test, and this sample contained 9% of the stated amount of sulfadoxine (the dissolution test confirmed this low result). Moreover, tablet appearance was different from another sample from the same manufacturer (different batch); differences were observed in imprint and score line (see Figure 10).

Figure 10:
Comparison of tablets appearance for two SP samples from the same manufacturer

The sample on the left does not contain pyrimethamine



In GPHF-Minilab® testing of the same 126 samples, two samples failed in the TLC test; one sample due to no detection of pyrimethamine (this was confirmed in laboratory testing), the other due to a contaminant spot. In laboratory testing, the related substance test was not performed as it was not required by the USP monograph used for testing. Therefore, the presence of impurity could not be confirmed, but the content of active substances was found compliant in this sample (96.2% of sulfadoxine, 92.4% of pyrimethamine).

Dissolution

Of 126 samples of SP products, 123 were tested for dissolution; three samples could not be tested due to insufficient numbers of tablets collected.

Twenty-five of these samples were found to be non-compliant in terms of dissolution of active ingredients (for 10 samples dissolution failed for both active ingredients, whereas for 15 samples only the dissolution of pyrimethamine failed). Apart from the sample that did not contain pyrimethamine, the minimum amount of pyrimethamine found in the dissolution test for these samples was in the range 2-46%; in the case of sulfadoxine it was in the range 4-44%.Apart from 25 non-compliant samples, for eight samples the outcome of dissolution testing was not decisive. Dissolution of either sulfadoxine or pyrimethamine or both failed to comply with Stage 1 or Stage 2 criteria. However, there were insufficient tablets to continue with Stage 3 and confirm the outcome of dissolution testing. Detailed results of dissolution testing are presented in Appendix 5.

In GPHF-Minilab® testing, five of the same 123 samples failed in simple disintegration tests. In laboratory testing, four of these samples failed the dissolution test, and one sample was compliant in the dissolution of both sulfadoxine and pyrimethamine.

Uniformity of mass

Two samples of 124 tested samples (two samples could not be tested for dissolution due to insufficient number of collected tablets) did not comply with the requirements of the mass uniformity test. Detailed results of this test are presented in Appendix 5.

5.5.6 Sulfamethoxypyrazine/pyrimethamine tablets

Samples containing the SPP combination were collected in Ghana, Kenya, Nigeria and Tanzania. Nine samples from Kenya, Nigeria and Tanzania were subjected to QC laboratory testing, all with the strength 500/25mg. Manufacturers of samples, numbers of tested samples and batches and countries of collection are listed in Table 23. Two samples (from two batches, produced by two different manufacturers) were found non-compliant.

Table 23: Manufacturers of tested sulfamethoxypyrazine/pyrimethamine samples

Manufacturer	No. of samples tested	No. of batches tested	Countries of collection
Elys Chemical Industries Ltd, Kenya	2	2	Tanzania
Laboratory & Allied, Kenya	2	2	Tanzania
Pharmacia&Upjohn, Italy	2	2	Tanzania
Dafra Pharma International Ltd, Belgium	1	1	Kenya
Drugfield Pharmaceuticals Ltd, Nigeria	1	1	Nigeria
Shelys Pharmaceuticals Ltd, Tanzania	1	1	Tanzania
Total	**9**	**9**	

Identity and content of active ingredients

All nine tested samples of SPP products were found compliant in terms of content of active ingredients in laboratory testing.

In GPHF-Minilab® testing, eight samples passed TLC testing, and one sample was not analysed.

Dissolution

Two of nine tested samples of SPP products were found non-compliant in terms of dissolution of pyrimethamine. Apart from two non-compliant samples, for one sample the outcome of the dissolution test was not decisive (dissolution of pyrimethamine failed to comply with Stage 2 criteria; however, there were not enough tablets to continue with Stage 3 and confirm the outcome of dissolution testing). Detailed results are presented in Appendix 6.

In GPHF-Minilab® testing all nine samples passed the simple disintegration test.

Uniformity of mass

All nine tested samples of SPP products complied with the requirements of the mass uniformity test.

5.6 Comparison of outcomes of GPHF-Minilab® screening with QC testing outcomes

Outcomes of GPHF-Minilab® screening and full QC testing results were discussed in sections 5.5.2 to 5.5.6 above for each type of product separately. This section compares the outcomes of screening and the corresponding full QC laboratory tests. Only samples with conclusive testing outcomes are included.

5.6.1 Overall failure rates

As GPHF-Minilab® is used for screening of samples in the field, it is important to understand to which extent final outcomes of GPHF-Minilab® screening correspond to quality determined by QC laboratory testing.

The outcomes of QC laboratory testing and GPHF-Minilab® screening were therefore compared (see Table 24). Results of appearance assessment were not considered in the comparison, because appearance is assessed in a similar way in both approaches, is subject to great variability depending on the assessors' experience, and its interpretation is inconsistent.

Table 24: Non-compliant samples detected by GPHF-Minilab® screening

	Number of non-compliant samples identified in laboratory testing	**Numbers of non-compliant samples detected by GPHF-Minilab® screening**
ACTs	41	**19 (46%)**
SPs	35	**5 (14%)**
Total	76	**24 (32%)**

As the table shows, GPHF-Minilab® screening only detected approximately one in three non-compliant samples.

GPHF-Minilab® screening also gave some false negative results: Six of 99 ACT samples (6%) and one of 92 SP samples (1%) failed in GPHF-Minilab® screening, but complied with all specifications in QC laboratory testing.

GPHF-Minilab® screening is designed to detect substantial deviations from specifications in the field. For the purposes of this report, extreme non-compliance was defined as a deviation of 20% or more from the declared amount of at least one active ingredient as determined by assay, and/or a percentage of active ingredient dissolved 25% or more below the pharmacopoeial limit Q in dissolution testing. Table 25 shows the detection rate for these samples in GPHF-Minilab® screening.

Table 25: Extremely non-compliant samples detected by GPHF-Minilab® screening

	Number of extremely non-compliant* samples identified in laboratory testing	**Number of extremely non-compliant* samples detected by GPHF-Minilab® screening**
ACTs	10	**6 (60%)**
SPs	21	**3 (14%)**
Total	31	**9 (29%)**

* Extremely non-compliant: Assay: deviation by 20% or more from declared amount of API, and/or dissolved amount less than pharmacopoeial limit (Q) minus 25% in dissolution test

As for non-compliant samples overall, GPHF-Minilab® screening detected only approximately one in three extremely non-compliant samples.

Details of the performance of the two approaches are shown in the next sections.

5.6.2 Detection of content problems

Table 26 shows the outcomes of GPHF-Minilab® screening by TLC, and corresponding results of assay and/or related substances testing at the QC laboratory.

Table 26: Detection of content problems by TLC screening and assay/related substances test

		Assay and/or related substances test: Passed	Failed	Total
TLC screening:	Passed	219 (97%)	***24 (59%)***	243
	Failed	**7 (3%)**	17 (41%)	24
	Total	226	41	267

	GPFH-Minilab screening falsely gave non-compliant result
	GPHF-Minilab® screening failed to detect non-compliance

Out of 41 samples that were found to be non-compliant in the assay and/or in related substances test, the GPHF-Minilab® TLC test identified only 17 (41%) correctly, indicating a limited sensitivity. On the other hand, of 226 samples that complied both in assay and related substances test, only seven samples (3%) were falsely identified as non-compliant.

Extreme non-compliances

GPHF-Minilab® uses a semi-quantitative TLC method and is designed to identify medicines with substantial quality defects. Therefore the comparison was done also for extremely non-compliant samples, i.e. in case of API content deviations by more than 20% from the declared content (see Table 27).

Table 27: Assay results and GPHF-Minilab® TLC screening outcomes for samples extremely non-compliant* in assay

	Full laboratory testing			GPHF Minilab screening	
	Assay (shaded: extremely non-compliant results)		Related substances	TLC test	
Product type	Active ingredient 1 (%)	Active ingredient 2 (%)	Impurities detected	Intensity	Contaminant spot
AL	**29.0**	81.5	**Yes**	Passed	
AL	85.5	**71.0**	No	Passed	
AL	**No artemether**	Complied	**Yes**	OK	**Yes**
A&A co-packed	**76.7**	Complied	**Yes**	OK	**Yes** (in artesunate)
AA FDC	**73.1**	Complied	**Yes**	**Lower**	**Yes**
AA FDC	**72.4**	Complied	**Yes**	**Lower**	**Yes**
AA FDC	Complied	**76.4**	**Yes**	OK	**Yes**
SP	**9.1**	**No pyrimeth-amine**	Not tested	**No pyrimeth-amine spot**	

* Extremely non-compliant: deviating by more than 20% from the declared API content

As shown in Table 27, of eight samples with an API content below 80% three were detected in GPHF-Minilab® TLC screening due to either missing API spot or lower intensity spot. In those cases where low content of artemether or artesunate was associated with presence of impurities detected in QC laboratory testing (most likely caused by degradation), GPHF-Minilab® TLC test proved to be useful to identify samples failing due to contaminant spots.

5.6.3 Detection of dissolution problems

Table 28 shows the outcomes of GPHF-Minilab® screening by simple disintegration, and corresponding results of dissolution testing.

Table 28: Detection of dissolution problems by disintegration screening and dissolution testing

		Dissolution testing		Total
		Passed	Failed	
Disintegration screening	Passed	213 (99%	***34 (85%)***	247
	Failed	**2 (1%)**	6 (15%)	8
	Total	215	40	255

GPFH-Minilab screening falsely gave non-compliant result

GPHF-Minilab® screening failed to detect non-compliance

Good agreement was achieved for samples compliant in the dissolution test, where 213 of 215 samples (99%) were correctly identified as compliant. However, out of 40 samples that failed the dissolution test, only six samples (15%) were correctly identified as non-compliant in the GPHF-Minilab® simple disintegration test, indicating a low sensitivity of GPHF-Minilab® screening.

Extreme non-compliances

To evaluate GPHF-Minilab® sensitivity to detect samples extremely non-compliant in dissolution, the extreme value was arbitrarily set as the average dissolution value lower than the pharmacopoeial Q value minus 25% (see Table 29, extreme values in bold). Substantial deviations from declared content (defined here as less than 80% of declared value present in dosage form) naturally affect also dissolution test results: In the extreme case where no active substance is present in the dosage form, no substance can be detected in dissolution medium, and dissolution results therefore do not comply. For this reason, samples with less than 80% of declared content of active ingredient (bold) were excluded from the evaluation.

Table 29: GPHF Minilab disintegration test outcomes for samples non-compliant in dissolution test

Product type	QC laboratory testing: Extreme values shown in bold: Dissolution <=Q-25% or assay <80% — Dissolution -Mean value (%)		Assay (%)		GPHF Minilab screening: Simple disintegration test
	*Active ingredient 1**	*Active ingredient 2**	*Active ingredient 1*	*Active ingredient 2*	
Samples with non-extreme dissolution problems (>= Q-25%)					
AL	Complied	42	Complied	Complied	Passed
AL	Complied	40	Complied	Complied	Passed
AL	Complied	49	Complied	Complied	Passed
A&A co-packed	65	Complied	Complied	Complied	**Failed (32 min)**
AA FDC	53	Complied	82.5	Complied	Passed
AA FDC	61	Complied	Complied	Complied	Passed
SP	Complied	48	Complied	Complied	Passed
SP	Inconclusive	35	Complied	87.2	Passed
SP	Complied	41	Complied	Complied	Passed
SP	Inconclusive	39	Complied	Complied	**Failed (>1 hour)**
SP	Complied	39	Complied	Complied	Passed
SP	Complied	35	Complied	Complied	Passed
Samples with extreme, but content-related dissolution problems (<Q-25%, less than 80% API present in tablet-shaded)					
AL	**No artemether**	38	**29.0**	81.5	**Failed (>1 hour)**
AL	Complied	45	85.5	**71.0**	Passed
AL	**No artemether**	Complied	**No artemether**	Complied	Passed
AA FDC	53	Complied	**73.1**	Complied	Passed
SP	**2**	**No pyrimeth.**	**9.1**	**No pyrimeth.**	**Failed (47 min)**
Samples with extreme dissolution problems (<Q-25%)					
A&A co-packed	**6**	Complied	89.4	Complied	Passed
A&A co-packed	**26**	Complied	Complied	Complied	Passed
AA FDC	**46**	Complied	Complied	Complied	Passed
SP	Inconclusive	**24**	Complied	Complied	Passed
SP	46	**19**	Complied	Complied	Passed
SP	Inconclusive	**29**	Complied	Complied	Passed
SP	45	**20**	Complied	Complied	Passed
SP	Inconclusive	**32**	Complied	87.2	Passed
SP	**30**	**30**	Complied	Complied	Passed
SP	Inconclusive	**23**	Complied	Complied	Passed
SP	43	**19**	Complied	Complied	Passed
SP	Inconclusive	**31**	Complied	83.9	Passed
SP	Inconclusive	**21**	Complied	Complied	Passed
SP	Inconclusive	**32**	Complied	Complied	Passed
SP	44	**32**	Complied	Complied	Passed
SP	Inconclusive	**32**	Complied	88.6	Passed
SP	**34**	**6**	Complied	80.2	Passed
SP	Complied	**27**	Complied	Complied	Passed
SP	**5**	**4**	Complied	Complied	**Failed (40 min)**
SP	35	**12**	Complied	Complied	Passed
SP	**22**	**10**	Complied	Complied	**Failed (32 min)**
SPP	Complied	**34**	100.1	98.9	Passed
SPP	Complied	**23**	95.7	96.8	Passed

***Active ingredient 1 / 2, and limits (Q) in the dissolution test were as follows for the different product types:**
AL: Artemether / Lumefantrine: Q=60%
AA: Artesunate: Q=80% (co-packed), 75% (FDC) / Amodiaquine: Q=75%
SP: Sulfadoxine: Q=60% / Pyrimethamine: Q=60%
SPP: Sulfamethoxypyrazine**:** Q=80% / Pyrimethamine**:** Q=80%

As shown in Table 29, GPHF-Minilab® screening detected none of three ACT samples extremely non-compliant in dissolution (not related to the extreme content non-compliance) and only two out of 20 such SP samples (10% sensitivity). It also detected two moderately non-compliant samples.

6. Discussion

6.1 Objectives, achievements and limitations of study

6.1.1 Objectives

The objectives of this survey were to:

1. evaluate the quality of selected antimalarials in six countries of sub-Saharan Africa;
2. estimate the proportion of ACTs and SPs meeting specific quality standards at different points of the regulated and informal distribution systems;
3. identify possible causes for any findings;
4. propose possible strategies and implementation plans to address the problems identified.

One of the objectives proposed in the survey protocol was to estimate the proportion of counterfeit ACT and SP products at different points of the regulated and informal distribution system. However, it was recognized that confirmation of substandard products as counterfeits is a very complex activity going beyond the scope of quality testing and therefore could not be fully executed. As a result, no specific steps to identify counterfeits were included in the protocol. Sampling teams were asked to pay attention to medicines suspected of being counterfeited and to report these observations. During testing two samples were identified in which one of the APIs was missing - ACT in one case and SP in the other. Data collected within the survey were insufficient for further investigation.

In addition to predefined objectives, the survey provided other useful observations, which are discussed under the relevant survey objectives.

6.1.2 Strengths and limitations of methodology

Data quality and testing methods

As demonstrated in sections 4.1 and 5.1, collection of samples was done in a way that collected samples as much as possible represented the situation in the supply chain in individual countries.

First-stage screening of collected samples was performed by GPHF-Minilab®. Verification of medicine identity, semi-quantitative estimate of content of active ingredients and simple disintegration testing for antimalarials were carried out in this survey. Because GPHF-Minilab® testing is proposed as a screening procedure only, conclusions on the quality of selected antimalarials were based on the results of QC laboratory testing. Only results of testing that was completed in accordance with pharmacopoeial criteria were considered for final evaluation.

Selection of samples for QC laboratory testing was done according to pre-defined criteria assuring the representativeness of the sub-set of selected samples (see section 5.3).

For QC laboratory testing, the methods and specifications according to established pharmacopoeias were sought as standards of acceptable quality. Testing according to official pharmacopoeial methods enables the comparison of products from different manufacturers. International Pharmacopoeia monographs were used for AL and artesunate tablets because at the time of preparation of the survey protocol no other monographs of reputable pharmacopoeias were available. These monographs did not include testing for dissolution, and therefore validated methods and specifications developed by the testing laboratory and successfully used for a range of products were used in this survey. For SP and amodiaquine tablets, the only option was the use of USP monographs.

For AA FDC tablets, no pharmacopoeial monograph was available, and the validated laboratory method and specifications were used. The method was developed for a specific product and did not prove to be suitable for the related substances test for a wider range of products. There were observed interferences of excipients and amodiaquine, which made determination of unknown impurities and the total sum of impurities

impossible. No pharmacopoeial monograph was available for SPP tablets, and in this case the methods were requested from manufacturers by the USP laboratory.

The reliability of results was assured by testing at a WHO-prequalified laboratory (97% of samples) and at an internationally respected USP laboratory (3% of samples).

Samples were collected, stored and transported in compliance with the survey protocol, which ensured that no quality deterioration occurred before laboratory testing. Conduct of the survey in compliance with rigorously defined conditions helped to eliminate those weaknesses that affected the validity of data published in some previous studies (e.g. WHO, 2003).

In retrospect, one survey limitation was a low sample size defined in the planning phase, which subsequently prevented, in some cases, rigorous conduct of complete dissolution testing. Because of that, 7% of tested samples had to be excluded from the final evaluation. The definition of optimal sampling size is always a dilemma between reliable testing results and the risk of depriving health care facilities or the users of needed medicines. In this survey, sample size probably could have been higher, with an instruction to the collectors to prevent shortage of collected medicines.

6.1.3 Overall findings

Of 306 samples tested, 267 were fully tested with conclusive results, of which 76 (28.5%) failed to comply with pre-specified internationally acceptable quality criteria. This rate indicated a high proportion of substandard products in distribution channels.

Non-compliance with pre-established criteria cannot be directly related to a risk for patients' health. Also it is not possible to deduce the degree of risk for the population treated, because the survey results were not related to consumption data. In spite of this, all substandard medicines must be considered as potentially dangerous and therefore the results of the survey are worrying.

With full respect to limitations of the applied approach, an attempt has been made to differentiate deviations which most likely impact the health of patients. For this purpose, the category of extreme deviations was defined as the content of any API deviating for more than 20% from the declared content and/or average dissolution value of tested units below pharmacopoeial Q value minus 25%. Focusing only on these extreme deviations, the total failure rate reached 11.6%.

Screening by GPHF-Minilab®

Comparison of the outcomes of dissolution testing performed in QC laboratory and simple disintegration by GPHF-Minilab® in the subset of samples tested by both GPHF-Minilab® and QC laboratory (not considering inconclusive and expired samples) suggests a low discrimination power of GPHF-Minilab® regarding dissolution characteristics. GPHF-Minilab® screening failed to identify 85.0% of samples proven to be non-compliant with specifications in the dissolution test. When looking only at samples extremely non-compliant in the dissolution test (average dissolution value lower than pharmacopoeial Q value minus 25%) and eliminating cases, in which dissolution non-compliance was related to extreme deviation in the content of API, GPHF-Minilab® failed to identify 91% samples. GPHF-Minilab® simple disintegration test therefore lacks sensitivity to detect even extreme non-compliances in dissolution. The test detects extreme situations, in which a dosage form is not disintegrating, but does not help to identify to which extent the release of active principles from a dosage form is reduced. Results of this survey, in which less than 9% of extreme dissolution non-compliances (not related to the content) were identified by Minilab, call in question the usefulness of performing disintegration test in case of ACTs and SPs.

On the other hand, only two samples compliant in the dissolution test were identified as falsely non-compliant by GPHF-Minilab® (0.9%) and when disintegration testing failed, the probability of dissolution problems was high (75%).

As regards the GPHF-Minilab® TLC test, the outcomes (taking into account any observation, either different intensity of spots or additional spots) were compared with the outcomes of the assay and related substances test performed by HPLC or UV spectrophotometry in QC laboratory. Again the comparison was done for the subset of tested samples, and inconclusive and expired samples were not considered. GPHF-Minilab® TLC testing failed to identify 58.5% of samples proven to be non-compliant with specifications either in the assay or related substances test or in both. As TLC is a semi-quantitative method, it cannot identify minor

deviations from specifications. Therefore the outcomes of GPHF-Minilab® screening were evaluated for samples, in which in the QC laboratory the content of API was found below 80% of the declared content. GPHF-Minilab® identified 75% of these samples as failing (even if it was not always due to no spot or lower intensity spot for API but sometimes only for contaminant spot).On the other hand, only 3.1% of samples compliant in the assay and/or related substances test were falsely identified as non-compliant. Failure to identify samples substantially deviating in content of artemether (sample with 29% of artemether) and lumefantrine (sample with 71% of lumefantrine) may be explained by poor performance of the test due to less experienced staff. Therefore, emphasis should be put on proper training before such a screening is performed.

Comparison of the outcomes of QC laboratory testing with the results of GPHF-Minilab® screening suggests that the sensitivity of GPHF-Minilab® in identifying non-compliant samples is low, especially for the dissolution test. For ACTs, GPHF-Minilab® failed to identify 40% samples extremely deviating from pre-defined quality parameters, in case of SPs non-detection rate of extreme deviations was 86%. In total, GPHF-Minilab® detected 32% of samples non-compliant in lab testing. Considering samples with extreme deviations, 29% of cases were detected by GPHF-Minilab®.

Based on the results of this survey, the frequency of quality defects of surveyed antimalarials identified by GPHF-Minilab® substantially underestimates non-compliant findings in comparison with laboratory testing and it cannot be concluded that GPHF-Minilab® ensures identification of extreme quality deviations. There may be various reasons for this. Subjective assessment by GPHF-Minilab® stresses the importance of standardized performance of tests and training. Low sensitivity indicates a limited usefulness of GPHF-Minilab® for final regulatory decisions. The extent to which GPHF-Minilab® as a screening tool helps to identify the most deviating cases for other categories of medicines and the extent to which results may be influenced by performing screening poorly should be further investigated.

6.2 Objective 1: Evaluate quality of selected antimalarials in six African countries

6.2.1 Countries of collection

Substantial differences in failure rates were observed in individual countries. It should be noted that because of the small numbers of samples tested from individual countries, interpretation of results must be made with caution, and the possibility of chance findings should be borne in mind. No failing sample was found in Ethiopia and relatively low failure rates were observed in Kenya and Tanzania. In the other three countries, Cameroon, Ghana and Nigeria, failure rates were substantially higher (in Cameroon and Ghana more than one-third of all tested products and in Nigeria almost two-thirds of tested samples).

Ethiopia (0% failure rate)

The zero failure rate in Ethiopia cannot be fully explained by the efficiency of the regulatory system, because 41% of collected samples were not registered by the NMRA.

Among the ACT samples collected in Ethiopia, samples of AA combination, which frequently failed in other countries, were lacking. Only AL ACTs were collected. In the subset of samples selected for testing, 80% of AL samples were produced by one established globally acting manufacturer with recognized reputation. The remaining 20% were produced by a single domestic manufacturer.

From the same manufacturer also came the largest part of SPs tested for Ethiopia (44%). Although only six batches in total were tested from this manufacturer, this indicates its good performance. As regards other tested SP samples, 24% were produced by an Indian manufacturer whose product was also collected in Kenya and all four tested batches were compliant. Despite the acceptable quality found in the survey, neither this SP product nor the above-mentioned SP product from a domestic manufacturer were registered by NMRA. The remaining few SP samples were produced by three manufacturers, one of which was an internationally acting innovative company.

Kenya (5% failure rate)

The overall failure rate in Kenya compared to other countries involved in the survey (Ethiopia excepted) was low. Only two of 24 ACT samples tested failed and all SP samples were found to be compliant.

Failure of an AL sample was due to the presence of one impurity above the limit. Two samples from the same batch collected at different sites in Kenya were compliant. Most probably the isolated non-compliant result does not indicate a problem with the quality of the particular medicine, because this was the only case of non-compliance found for this brand produced by an internationally acting innovative company from 64 samples collected in the survey. The second failing sample was of an AA product from a domestic manufacturer. The level of impurities was found to be slightly above the limit. As this was the single ACT sample tested from the particular manufacturer, further investigation of this case may be recommended. In total, samples both from two domestic and six importing manufacturers were tested with generally positive results.

All tested samples were registered by the NMRA. This suggests overall acceptable quality of registered antimalarials. However, since among all the samples collected in Kenya three unregistered brands were identified at different distribution levels, improved market supervision may be a regulatory focus in the future. Owing to the low number of failing samples, no conclusion can be reached on the situation in different regions.

Tanzania (11% failure rate)

The failure rate in Tanzania was driven completely by quality deficiencies of SPs. Overall, the positive results of QC testing for samples from Tanzania were substantially influenced by the presence of only one ACT from an established globally acting manufacturer with recognized reputation.

As regards SPs, similar failure rates were seen for tested SP samples and for SPP samples. Altogether seven brands produced by five manufacturers were tested, all of them having valid national registration. Only one domestic manufacturer was involved and all failing samples were produced by this single manufacturer. From 12 tested samples (six batches) of this manufacturer, five samples were found to be non-compliant. Each sample failed in a single test only. Three samples from a single batch collected from different sites in Mtwara region failed in tablet mass uniformity. Two samples of different batches failed in the dissolution of pyrimethamine. This indicates problems in adherence of the manufacturer to good manufacturing practices.

The results of SP testing suggest good performance of the regulatory system concerning imported products and indicate certain opportunities for improvement regarding implementation of good manufacturing practices (GMP) by local manufacturer(s). No samples from the informal market were collected, and the NMRA declares that such a retail category does not exist in Tanzania.

Cameroon (37% failure rate)

In Cameroon failures were observed both for ACTs and SPs. The medicines with the highest failure rates were AA combinations, which failed almost universally in the assay and related substances test. No SPP samples were collected in Cameroon, and almost half of the SP samples failed predominantly in dissolution.

Cameroon was the only country participating in the survey that only had samples from importing manufacturers. This could have contributed to the high failure rate. Five unregistered samples coming from two manufacturers (one batch each) were tested and all of them were non-compliant. These low numbers do not allow generalization, but they indicate the risks of substandard quality for unregistered medicines. In addition, approximately one-third of registered samples failed in QC testing. Such numbers stress the need to improve either the registration process or post-marketing surveillance (PMS). Because the incidence of failures was highest in the informal market, regulatory efforts should focus especially on this area. As no major differences were seen among four geographical regions of Cameroon, the identified problems seem to be common across the country.

Ghana (39% failure rate)

Specifically in Ghana, testing results were influenced by a relatively high proportion of inconclusive samples.

Among ACT samples tested in Ghana, both AL and AA combinations were represented. In both failing AL samples, the content of active ingredients was found to be slightly below the limit. These samples each

represented a single sample of the product brand manufactured abroad. Two failing samples of AA came from domestic and two from foreign manufacturers. In general failures were mostly found in the related substances test and tablet mass uniformity test; one sample from a domestic manufacturer additionally failed in the assay of artemether. All these findings indicate inconsistencies in the implementation of GMP, both for domestic and imported ACTs, and the potential contribution of distribution and storage conditions to the deterioration of quality.

Failing SP samples were produced by two domestic and three foreign manufacturers. As was common for SP medicines, failures consisted mostly of non-compliant dissolution. Failing quality was convincingly demonstrated for one of the domestic products, for which all four samples representing two batches were found to be out of specification in the assay or dissolution test, or both. Because failing samples were collected from different sites and levels of distribution, the findings indicate problems in GMP implementation and potentially also in the design of product formulation. Both samples collected from the informal market failed. Although this low number does not allow specific conclusions to be drawn, it indicates a risk of low-quality products being present on the informal market. The risk of substandard medicines seems to increase in the southern region of Ghana, in which the capital city Accra is situated.

A substantial proportion of unregistered medicines was present among samples collected in Ghana, especially among ACTs. Samples of 13 brands produced by foreign manufacturers were identified, but five brands of domestic manufacturers were also present among the unregistered samples. There were more ACT samples than SP samples (11), but the penetration of unregistered antimalarials on the market affects both medicines. Surprisingly, although this was influenced by low numbers, the failure rate in quality testing was approximately twice as high for registered medicines. Fifteen samples of unregistered medicines were tested, out of which three samples of different brands were non-compliant. The remaining 12 samples of five brands were compliant. In each case domestic and foreign manufacturers were included. The nature of failures among registered and unregistered medicines was similar.

Frequently only one sample from the respective manufacturer was tested. This limits the possibility to judge the overall quality of production for manufacturers included in the survey, but raises concerns that should be followed up by the NMRA. The results of the survey cannot be considered representative enough to conclude on the quality of medicines in general. However, based on the results of the survey and the nature of the antimalarials tested, Ghanaian authorities may be advised to strengthen the system of market surveillance to limit the presence of unregistered medicines in the distribution channels and to review registration processes and required GMP standards. The focus in this respect should be on both domestically produced and imported medicines. Quality assurance of antimalarials in Ghana may be comparatively more difficult than in other countries because of the relatively high number of manufacturers (the second highest after Nigeria) supplying either registered or unregistered products. In Ghana more investigation is certainly needed to reach conclusions on the quality of production for those manufacturers that participated in the survey with only a single product.

Nigeria (64% failure rate)

The failure rate in Nigeria exceeded observations from other countries in this survey and also observations from a similar study organized by USP-DQI in Madagascar, Senegal and Uganda (USP/USAID (2009). All five API combinations were represented among the tested samples from Nigeria. High failure rates were observed for both ACTs (62.5%) and SPs (66.7).

In the case of AL, the content of APIs and the dissolution were leading causes of failure. The three most outlying assay values in the survey were identified in Nigeria, including one sample not containing any artemether. In the case of AA co-packed samples the most frequent failure was the high amount of related substances. This could not be compared with AA FDC samples where interferences from excipients made it impossible to interpret the test for related substances. In AA FDC samples, a low content of API was generally seen. As for AL, dissolution was a common issue for all AA samples.

Failures of SP samples consisted typically of a low dissolution rate and, in half of cases, also in tablet mass uniformity.

Out-of-specification testing results were found in the case of both domestically produced and imported medicines. Imported AL samples showed a higher proportion of failures, the proportion of locally produced and imported AA samples was comparable, and, in the case of SPs, a substantially higher rate of failure was recorded for domestic products. Overall, the failure rate was higher for domestic than for imported samples.

This indicates the need to intensify regulatory supervision in the domestic territory and also to focus on manufacturers abroad. The issue has validity for the whole country as the survey found failing medicines at different distribution levels and in different regions. Surprisingly (this may be explained almost entirely by chance findings), the highest failure rates in the distribution system were observed at the highest distribution level (manufacturers, importers, central medical), and this indicates a minimal effect of distribution on deterioration of quality. Also, taking into account numbers of collected samples, there were no substantial differences between the regions included.

In Nigeria all collected samples represented brands that were either registered or legally supplied as donations. A high proportion of failures therefore may indicate non-compliance of manufacturers with the terms of valid registration, inconsistent follow-up of changes in production processes of registered medicines, insufficient enforcement of implementation of GMP or insufficient scrutiny of registration submissions. As shown by the survey outcomes, implications are seen across the country.

Contributing factors to the high incidence of failures in Nigeria seen in this survey may be the highest number of samples collected from all the participating countries, the highest number of manufacturers supplying products on the market, the relatively high proportion of samples from informal market, and the low proportion of prequalified products collected.

It may be useful to confirm the failure rates in similar testing at country level for other categories of products and to collect more data for the risk analysis of the pharmaceutical market. Nevertheless, considering all the limitations of the survey, the outcomes underline the need to adopt certain regulatory measures to assure better quality of medicines.

Comparison of results with the WHO study (WHO, 2003)

Comparison of the outcomes of this survey with results of the WHO study published in 2003 (WHO, 2003) can be done for two countries (Ghana and Kenya) that participated in both studies. Only data for SP tablets may be compared.

- Despite the fact that the study published in 2003 used different methodology and faced some logistical problems, the outcomes for Kenya have improved substantially from 54% failed SP samples (13 of 24[*]) in 2003 to no failed SP sample in this survey (0 of 19).
- The situation in Ghana did not visibly improve; only a small change from 60% failed SP samples (12 of 20[*]) in 2003 to 56% (9 of 16) in this survey was observed. Again, due to small numbers of samples tested, such conclusions have limited validity.

6.2.2 Countries of origin

Although the number of manufacturers of tested products in all countries is not sufficient to provide a complete picture of the supply base for individual categories of tested medicines, it may serve to develop a basic idea about the number of manufacturers from which products may be available. Of the 64 manufacturers whose medicines were tested, only one was present in all six countries. One other manufacturer was present in three countries and six manufacturers supplied two countries (mostly neighbouring). This means that 56 manufacturers each supplied only a single country. This indicates a highly fragmented manufacturing base, which may contribute positively to competition on the market and stability of supplies. On the other hand, it is difficult to supervise and ensure availability of medicines of good quality when so many manufacturers are supplying the region.

Comparison of results for medicines produced locally and imported may help regulators to better focus regulatory resources and market surveillance activities. An unfavourable trend towards inferior testing results of domestic products was seen in four countries (Ghana, Kenya, Nigeria and Tanzania). To consider these results as fully representative for market situation, more samples and sampling sites should be covered. Despite that, it may be suggested that regulatory attention be also focused on domestic manufacturers and the quality of their products.

[*] Data in tables from Annex 2C and 3C to the report from the WHO study published in 2003 (WHO, 2003) were used.

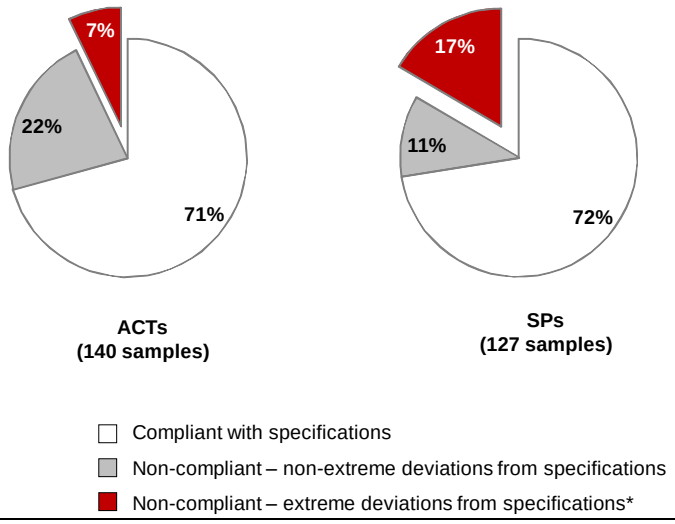
In Cameroon no domestic products were collected, and in Ethiopia no sample (either domestic or imported) failed in this survey; no conclusions on this point can therefore be reached for these two countries.

6.3 Objective 2: Estimate the proportion of ACT and SP samples meeting standards at different distribution levels

6.3.1 Proportions of ACT and SP samples meeting standards

Both ACTs and SPs were prone to quality defects to a similar extent. Focusing on deviations classified as extreme, the proportion of failing samples which had extreme deviations was lower for ACTs than SP samples (see Figure 11).

Figure 11:
ACTs and SPs: Proportions of compliant, moderately non-compliant and extremely non-compliant* samples



* In this survey, extreme deviations were defined as a deviation by at least 20% from the declared content of one or more active ingredients, and/or dissolved percentage of one or more active ingredients less than the pharmacopoeial limit (Q) minus 25%.

Content and dissolution were the predominant reasons for inferior quality; these reasons were different for ACTs and SPs.

Content

The lower content of APIs was more often a problem of ACTs (22 of 140 samples failed, see section 5.5) than SPs (7 of 127 samples failed).

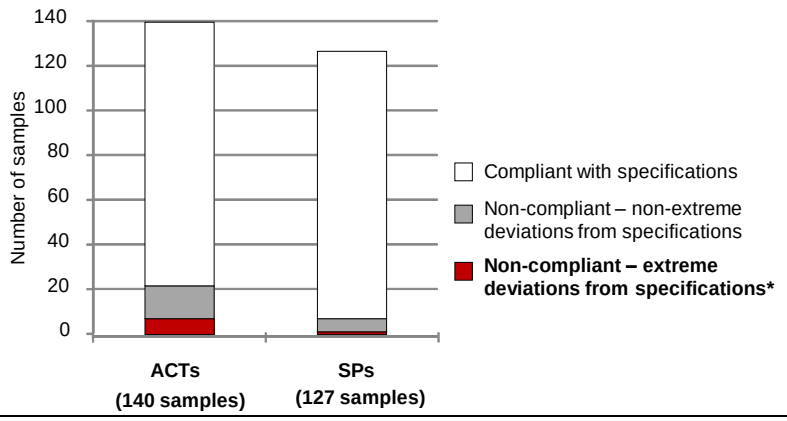
This pattern was also seen when focusing on extreme content deviations. Eight of 29 samples failing content testing (including seven of 22 ACTs) deviated from the declared content by more than 20%. Two samples in the survey were missing one of the APIs altogether (one ACT and one SP). It was not investigated whether these samples were counterfeits. However, one of them was suspicious, as it contained only 9% of the second API and tablet appearance differed from another sample from the same manufacturer. However, it can be concluded that, despite a high proportion of substandard samples collected in this survey, the proportion of medicines missing active ingredients was low.

Related substances test

The higher content of related substances seemed to be a common problem of ACTs. Even if the content of related substances in samples of AA FDC products could not be evaluated quantitatively, high levels of dihydroartemisinin, and in some cases artemisinin, were observed. Owing to the absence of a test for related

substance in the USP monograph, no information about the level of related substances in SPs was obtained from the survey.

Figure 12:
Content-related failures in ACTs and SPs

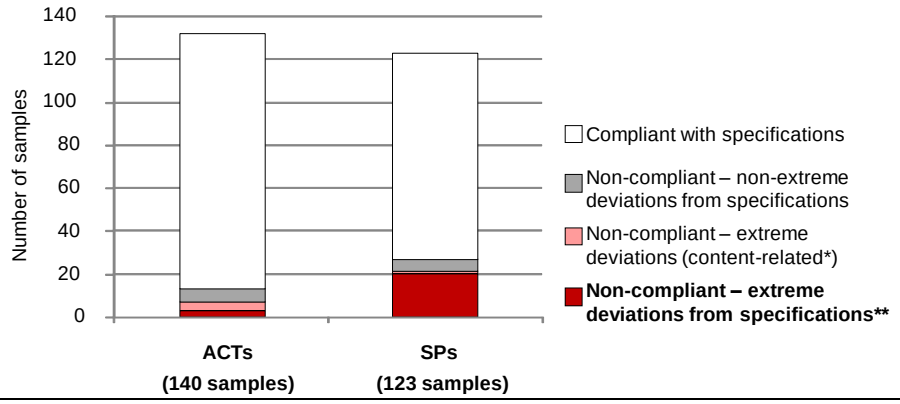


* Extreme deviations: > 20% deviation from declared content of API in dosage form

Dissolution

For all five types of products included in QC laboratory testing, cases of non-compliance were found in the dissolution test. However, for SPs the contribution of dissolution failures to total failure was higher than for ACTs and was mostly caused by low pyrimethamine dissolution. Extreme dissolution findings (<Q-25% in dissolution medium, unrelated to the lower content of APIs) were seen in 3 of 13 failing ACT samples, but 20 of 27 failing SP samples (see Figure 13).

Figure 13:
Dissolution-related failures in ACTs and SPs



* Content-related: Non-compliance in dissolution likely associated with low content of API
** Extreme deviation: Percentage of API dissolved less than pharmacopoeial limit (Q) minus 25%

Mass uniformity test

Failures in the mass uniformity test were observed in the survey, which, together with heterogeneity of testing results frequently seen inside individual batches, suggests quality problems originating from GMP non-compliance. Failing dissolutions in case of SPs might therefore be related to problems with dosage form design and manufacturing processes.

6.3.2 Quality at different distribution levels

No consistent trend in failure pattern at different distribution levels was seen. Normally the worst quality would be expected for samples collected in the informal market as no supervision or regulation is applied.

This was only true in Cameroon and Ghana. In Nigeria, on the contrary, the highest failure rate was found at level 1, i.e. for samples collected from manufacturers/importers and central medical stores.

Samples of the same batches were collected at different distribution levels and tested in the QC laboratory. In 11 such batches some failures were identified:

- In seven cases all the samples from a single batch collected at different distribution levels failed to comply with specifications, thus not indicating a problem at any particular distribution level but rather with the manufacture.
- In four cases differences in compliance status were found between different distribution levels. In three of them the problem might also have been also caused by inconsistent manufacture rather than by handling during distribution:
  - An AL sample collected in Nigeria from level 2 was non-compliant due to low lumefantrine dissolution, while the sample from the same batch collected in the informal market was compliant.
  - An A&A co-packed product sample collected in Ghana from level 1 was compliant. Out of five samples from the same batch collected at level 2, four were compliant and one sample failed in the mass uniformity test.
  - An SP sample collected in Tanzania from level 1 was non-compliant in the mass uniformity test. Three samples from the same batch were collected at level 2 and two of them also did not comply in the mass uniformity test, while one sample was compliant in all tests.
  - The single last identified case might indicate improper handling conditions during distribution and storage. It was the batch of A&A co-packed products collected in Nigeria. A sample from level 1 was compliant, while a sample collected at level 2 was non-compliant due to a higher level of related substances.

As regards the influence of distribution conditions, the collected data do not provide a consistent response. With the limited number of samples, data neither suggest nor exclude quality deterioration during distribution.

6.3.3 Quality in various geographical regions

Normally, it would be expected that the strictest supervision would be applied in large cities. This expectation has not been confirmed by the results of the survey. On average, failure rates in large cities were no lower than in other regions. If supervision was indeed more vigorous, it seems that it did not compensate for a higher consumption, more diverse supply and higher turnover of medicines.

6.3.4 Registration status

The total proportion of unregistered samples collected in the survey was relatively high (14%), and included both domestically produced and imported medicines. Samples of unregistered domestically produced medicines represented 17.8% of collected samples of domestic products, and the proportion of unregistered imported samples reached 12.2%. This surprisingly suggests that imported medicines may be subject to more intensive regulatory supervision than medicines produced by domestic manufacturers.

The rate of registered and unregistered products was similar between ACT and SPs. Lack of registration therefore was not limited to one drug category only.

The occurrence of samples of unregistered medicines was highest in the informal market and lowest at level 1 (manufacturers, importers and central medical stores). This indicates penetration of unregistered medicines by different channels into the informal market and to a lesser extent also into the approved distribution system (importers, central medical stores, wholesalers, pharmacies and dispensing facilities).

Interestingly, for imported medicines the failure rates were similar whether or not samples were registered. Even more striking is the fact that more registered than unregistered domestically produced samples failed. These findings were so surprising that confirmation of the registration status of collected samples was organized and this confirmed the results presented.

The situation in individual countries cannot be described by cumulative data. Tanzania, Nigeria and Kenya seem to have the registration situation under control, as the proportion of unregistered samples was either zero or quite low. In other countries a substantial proportion of unregistered medicines was collected.

Although the number of samples was too low to allow definitive conclusions, these findings suggest deficiencies in registration procedures, market surveillance and regulatory enforcement in some countries included in the survey. Survey results indicate that improvement of regulatory functions should cover both domestic manufacturers and importers.

6.3.5 WHO prequalification status

To facilitate global access to medicines of acceptable quality and their procurement in developing countries, the WHO Prequalification Programme evaluates pharmaceutical products according to WHO-recommended standards of safety, efficacy and quality, and compliance with good manufacturing practices and good clinical practices, focusing on HIV-, malaria- and tuberculosis-related products[2].

Although prequalification is an important tool for the assessment of medicines intended to be procured by United Nations agencies, there is a need to be assured about the quality of procured prequalified medicines by random quality control. Sampling and testing of prequalified medicines at all stages of the supply cycle is therefore an essential part of the WHO Prequalification Programme. Prequalified medicines represented a significant subset of the samples collected in this survey, and data on their quality are therefore separately presented and discussed.

As there are no WHO-prequalified SP products, and none of the WHO-prequalified AA FDC samples gave conclusive testing results in this survey, failure rates could only be compared for AL and A&A co-packed samples.

The difference between WHO-prequalified and non-WHO-prequalified products was striking. The failure rate of samples of non-prequalified AL and A&A co-packed samples was more than ten times higher than that of samples of WHO-prequalified AL and A&A co-packed samples. In total, three failures were identified. Two were not critical for patients' health, the third was a content of one API 8% below the acceptance limit. This demonstrates that medicines for which quality was confirmed by WHO prequalification have a much lower quality risk than with non-prequalified products.

Although the representativeness of these results may be affected by the fact that 64 of 83 samples tested were from one prequalified product (AL tablets, Novartis), samples of products from another five manufacturers were also tested and the difference in quality compared to non-prequalified products was still convincing.

6.4 Objective 3: Identify possible causes of findings

Generalization of findings to draw conclusions on possible causes of products' non-compliance with pre-set specifications is somewhat limited by several factors. Although the survey protocol was designed to maximize the information value of results, a certain bias cannot be excluded, resulting from the focus of the survey on selected antimalarial medicines and the relatively low number of samples and batches from individual countries subjected to laboratory testing (maximum of 75 samples of 59 batches from Nigeria),. Selection of various sampling sites was intended to give a picture of the situation at all distribution levels and different regions in countries and to be as much as possible representative for the situation in the markets in individual countries.

The data obtained in this survey suggest that the factors influencing quality of medicines in the markets of individual countries differ substantially. Although this was not observed to the same extent in all countries, the most visible factor was non-compliance of manufacturers with established GMP and quality standards, accompanied by insufficient regulatory performance and market supervision by NMRAs. This was demonstrated in several countries by the penetration of unregistered products into the market and by the poor

[2] WHO Prequalification of Medicines Programme (PQP) - Facts and figures for 2009. http://www.who.int/prequal/info_general/documents/PQ_facts_figures_2009.pdf.

quality of registered medicines. The nature of quality defects indicated non-compliance of manufacturers with GMP principles, and this problem seemed to be more common for domestic manufacturers. In the light of the observations made in the survey, problems related to the design of product formulation and distribution and storage conditions seemed to contribute to inferior quality to a lesser extent.

Best regulatory performance, which resulted in the lowest proportion of unregistered products in the market and low total failure rate, was observed in Tanzania and Kenya. In the other countries, either a relatively high proportion of unregistered products or a high failure rate was seen, which affected both registered and unregistered medicines.

In countries with high failure rates, products from a larger number of manufacturers were generally collected compared to countries with low failure rates. This suggests that increased market complexity makes the regulation of medicines and market supervision more difficult and may be one of the causes for the high failure rates observed in several countries.

Because of a substantially higher failure rate of domestically produced registered medicines, in comparison with registered imported medicines, one may hypothesize that domestic products are less strictly scrutinized during registration. Another piece of evidence for insufficient regulatory performance is the comparable failure rate of registered and unregistered imported medicines.

In countries with less mature medicines regulation, WHO prequalification or approval by a stringent regulatory authority seems to be an effective mechanism to assure acceptable quality of imported medicines. WHO prequalification has in this survey proven to be highly efficient and has contributed to reducing failure rates in countries that generally use prequalified ACTs.

Results of the survey do not support the assumption that distribution and storage conditions dramatically influence the quality of medicines available to patients.

6.5 Objective 4: Propose strategies to address the problems identified

6.5.1 National stakeholders' consultations

Three of the participating countries held national stakeholders' consultations to review the findings of this survey and address the gaps identified. The conclusions of these consultations address a broad range of recommendations and actions, which sometimes, due to a detailed knowledge of the specific situation in the respective countries, go beyond the evidence provided by the survey results.

Ghana

Following a national stakeholders' meeting, a decision was made to recall all the batches of products that were identified as non-compliant in the survey. At the stakeholders' conference, it was resolved that:

- commercial consignments of the affected brands must be sampled at the ports of entry for laboratory testing before release for distribution;
- importation of the affected finished products must be suspended until results of analysis of three batches showed them to be compliant;
- all raw materials imported for local manufacturing must be accompanied by certificates of analysis;
- it was critical to raise public awareness and consciousness on medicine quality issues.

The pharmaceutical industry was challenged to commit to GMP principles and the production of quality medicines. The meeting recommended that procurement of API by local companies should be centralized; a bioequivalence centre in Ghana should be established; the NMRA (Food and Drug Board of Ghana) should be supported to regulate the industry more effectively; and, during national procurement of medicines, quality should be evaluated critically rather than considering the price alone. Human resource development in the pharmaceutical industry was noted as a key to the growth of the industry.

Other key recommendation were: the database of medicines registered by the NMRA should be shared with the Pharmacy Council, Dental and Medical Council, National Malaria Control Program and other key stakeholders in order to ensure that only registered products are stocked at the various facilities and that prescribers prescribe using the registered product database; the private sector should be involved in the

pricing of medicines; the pharmaceutical companies should contract bioequivalence studies to outside agencies while a national bioequivalence centre is being developed; and more transparency should be shown on the part of all stakeholders.

Cameroon

The stakeholders' consultation in Cameroon identified the following problems:

- significant unsatisfactory quality of antimalarials circulating in Cameroon;
- difficulties in supply and availability of antimalarials according to population needs;
- a non-operational pharmacovigilance programme in the country;
- a multiplicity of antimalarials in circulation and its incidence on the follow-up and evaluation of treatments;
- a mismatch between products registered and recommended malaria treatment protocols;
- insufficient distribution and non-compliance with malaria treatment protocols;
- no communication strategy to reinforce therapeutic coverage for malaria.

The participants in the workshop resolved to address the antimalarial quality problems through:

- presenting the survey results to the Ministry of Health with the resolutions and recommendations of the workshop;
- proposing to the Ministry of Health to set up a working group;
- adopting the multisectoral plan for access to antimalarials of recognized quality and its presentation to the Ministry of Health;
- establishing a follow-up committee for the implementation of the plan;
- strengthening the national quality control laboratory.

Nigeria

Participants in the national stakeholders' consultation considered the findings of the survey and made the following recommendations to:

a) Government

- streamline distribution activities by forming mega-zonal stores to reduce the proliferation of importers and distributors;
- strengthen national and international collaboration on anti-counterfeiting; the Federal Taskforce on anti-counterfeiting should be supported and a state taskforce should be inaugurated;
- reduce informal markets in general and dismantle open drug markets in particular;

b) NMRA

- promote better collaboration between the NMRA (National Agency for Food and Drug Administration and Control) and the Pharmacists' Council of Nigeria and other relevant agencies;
- support capacity development of manufacturers in GMP and WHO prequalification requirements and enforce compliance with the newly drafted regulations on good distribution practice and good manufacturing practice;
- strengthen post-marketing surveillance activities;
- continue and strengthen the ongoing collaboration with countries from which finished products are procured;
- enforce contract manufacturing standards to enhance the quality of imported medicines;
- consider the rationalization of registered products in order to have better control.

c) Manufacturers

- ensure adherence to GMP;
- forge close collaboration between industry and academia in order to promote research and development and to support the capacity of manufacturers in research and development.

d) WHO

- support industries to build capacity in GMP and prequalification;
- promote inter-country experience in sharing and disseminating good practices in medicine regulation.

6.5.2 Recommendations from survey wrap-up meeting

A "wrap-up" meeting involving WHO and the national teams was held in Nairobi in July 2010. The main objectives were to enable participating countries to share 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. Participants at this meeting recommended that the following measures.

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 registration, to enable uniform assessment of quality parameters.
- NMRAs should adopt a formal protocol for post-marketing surveillance 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 should be applied sensibly so as not to decrease the availability of medicines.

GPHF-Minilab® testing

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

Post-marketing surveillance (PMS)

- All NMRAs should have a PMS strategy, based on which PMS plans should be developed.
- PMS plans should be risk–based, identifying properly products to be monitored after registration.
- Signals on substandard quality, findings from inspections and information from pharmacovigilance systems should be combined when developing PMS plans.

Pharmaceutical manufacturing companies

- In addition to obtaining the certificates of analysis, manufacturers of medicines should test the quality of purchased APIs, including for purity.
- Regulatory supervision of local manufacturers should be strengthened.

Regional collaboration

Collaboration among NMRAs should be promoted with the objectives of exchanging information on substandard/counterfeit products circulating in markets, registered products, inspection outcomes, PMS plans and outcomes of PMS activities. Furthermore, it was noted that collaboration is facilitated by harmonization of registration requirements (e.g. Common Technical Document in conformity with ICH) and regulations on GMP and PMS. Collaboration may take the form of joint inspections of facilities, evaluation of medicines under the leadership of WHO/QSM and joint operations to combat counterfeit products. Collaboration may also include a mechanism to share the services of quality control laboratories or other facilities. 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.

Existing sub-regional collaborations of NMRAs such as the West African Drug Regulatory Authorities Network (WADRAN), including Cameroon, should be sustained.

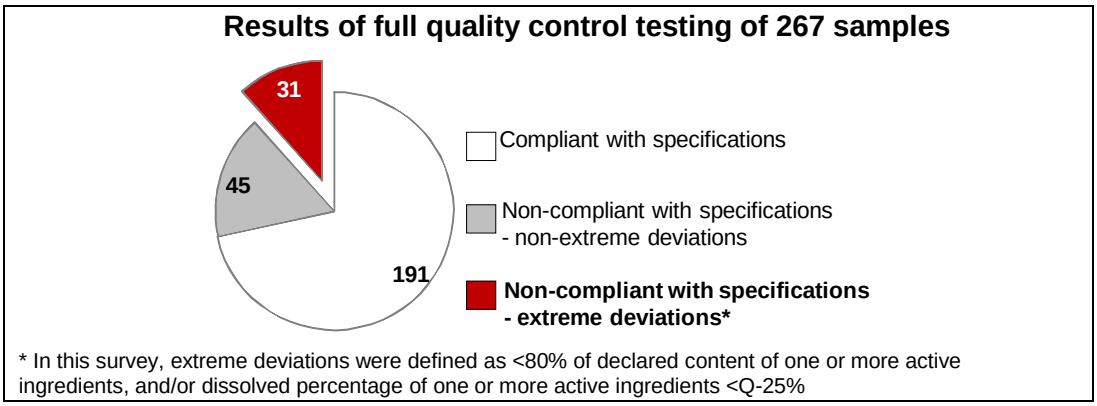
7. Conclusions

This survey, conducted in six countries of sub-Saharan Africa, focused on evaluating the quality of selected antimalarials against established international standards. Samples were collected and selected for QC laboratory testing according to the pre-defined criteria in a way, which strived to achieve a representative picture on the quality of selected antimalarials in the supply chain. Quality testing was done by reliable quality control laboratories according to specifications set up in recognized pharmacopoeias. In addition to results of quality testing of key categories of antimalarials, data were collected that made it possible to relate the results of quality testing to distribution levels, geographical regions, domestic production or import, registration status and prequalification status. Although the results cannot be considered as fully representative, as they are related to quality of samples collected in short time period (April - June 2008) and to the relatively low numbers of samples from individual countries and individual manufacturers tested in the laboratory, relevant conclusions may be drawn. We can only regret that the sample size defined in the initial planning phase did not in some cases allow rigorous conduct of complete dissolution testing and, because of that,7% of tested samples had to be excluded from the final evaluation.

The survey results indicate the presence of substantial problems in the quality of antimalarials in several sub-Saharan African countries. The situation was significantly different from country to country and this finding corresponds with that of the study supported by the USP (USP/USAID, 2009).

It is a positive observation that in some countries (Kenya, Tanzania) the quality of antimalarials seems to be reasonably under control. In other countries results are less positive, either because of the presence of a substantial proportion of samples that did not comply with pre-set specifications or because of the high proportion of unregistered products, which suggests vulnerability of the market towards penetration of products with unknown properties. An example of such a country is Ethiopia, where no failing sample was detected but a high proportion of samples of collected antimalarials were not registered (41%). In countries with the highest incidence of failing samples (Nigeria, Ghana, Cameroon) according to the survey results, the probability of being treated with an antimalarial medicine complying with international quality standards is only 36%, 60% and 63%, respectively. In these countries, strengthening of regulatory systems and market supervision seems to be of primary importance. A strong argument for the need to improve regulatory capacity may be the observation in Ghana, where the failure rate for registered medicines was higher than for unregistered ones. In countries with high failure rates, products from a larger number of manufacturers were collected, compared to countries with low failure rates. The complexity of markets, in terms of the number of products from different manufacturers, therefore seems to be one of the contributing factors in making medicines regulation more difficult and increasing the possibility of substandard medicines on the market.

The total failure rate observed in the survey for tested samples from all countries was 28.5% (29.3% for ACTs and 27.6% for SPs). Focusing only on extreme deviations as defined in this report, which are likely associated with health implications, the failure rate reaches 11.6% (7.1% for ACTs and 16.5% for SPs).



Both ACTs and SPs were prone to quality defects to a similar extent, although the reasons for inferior quality might be different. Prevailing problems of ACTs are the content of APIs and impurities; in the case of SPs it is mostly dissolution.

Failure rate concerning the content of APIs was 15.7% and 5.5% for ACTs and SPs, respectively. The substantial proportion (72%) from all samples failing in the content of API deviated from the declared content for less than 20%. Within the survey two samples were identified in which one of the APIs was missing (one ACT and one SP), however it was not investigated whether these samples were counterfeits. As regards dissolution, failure rate of ACTs was 9.3% and of SPs 21.3%. Extreme dissolution findings (average dissolution value of tested units below pharmacopoeial Q value minus 25%) unrelated to lower content of APIs were seen in 23% of failing ACTs and 74% of failing SPs. It can be concluded that, despite a high proportion of substandard samples collected in this survey, the proportion of medicines missing active ingredients was low and many detected non-compliances were not extreme.

Failures in the mass uniformity test were observed in the survey, which, together with heterogeneity of testing results frequently seen inside individual batches, suggests quality problems originating from GMP non-compliance. Failing dissolutions in case of SPs might indicate problems related to the proper design of product formulation and manufacturing process.

As regards the influence of distribution conditions, the collected data do not provide a consistent response. With a limited number of samples and no specific pattern of results, the data do not argue for systematic quality deterioration during distribution, but such a possibility cannot be excluded in individual settings.

It appears that there is a trend of higher failure rates among domestically manufactured products compared to imported ones. This indicates the need to strengthen the monitoring of domestic production in countries that have pharmaceutical manufacturers within their territory and to apply the same regulatory standards for domestically produced and imported medicines. So far medicines manufactured in the countries participating in the survey appeared in general very rarely on the market in any other than the producing country. This situation may easily change and export to neighbouring countries may become more common. The solution to prevent the movement of substandard antimalarials among countries is again competent regulatory supervision of domestic manufacturers and domestically produced medicines, together with regulatory oversight over imported medicines and cooperation between regulatory bodies. Low failure rate was specifically observed for imported products manufactured by established globally acting manufacturers and for products prequalified by WHO. The total failure rate of samples of WHO prequalified medicines collected from all six countries participating in the survey was astonishingly low (below 4%) and observed deviations were not critical. This establishes WHO prequalification as the effective mechanism for assuring the quality of procured medicines.

Comparison of results obtained during laboratory testing with the GPHF-Minilab® screening method indicated a substantially lower sensitivity of GPHF-Minilab® to detect non-compliance in dissolution and in assay/related substances (detected 15% and 42%, respectively). Especially sensitivity of the simple disintegration test to detect samples non-compliant in dissolution is low and in case disintegration testing is performed its results should be cautiously interpreted. Considering final outcome of testing, GPHF-Minilab® underestimated negative laboratory results approximately three times, irrespective of the seriousness of deviation. This stresses the usefulness of Minilab only as a simple screening method with low sensitivity for which results should be as much as possible confronted with laboratory testing. In situations requiring regulatory or forensic decisions, laboratory QC testing should always be applied.

Results of the survey were analysed on several occasions with regulators from participating countries. All countries approached the survey results in a positive spirit, and outcomes of the survey led in several countries to the adoption of regulatory actions and system measures. Recommendations were agreed about the strategies to strengthen medicines regulation, strengthen the supervision of manufacturers and improve their adherence to GMP principles, extend post-marketing surveillance, harmonize regulatory requirements, facilitate exchange of information and cooperation among countries, in a region as well as between regions, and support participation of local manufacturers in WHO prequalification and utilization of WHO-prequalified products. These changes should be reflected in updated pharmaceutical policies prepared by regulators in cooperation with all the stakeholders, such as manufacturers, importers/distributors, central medical stores and national malaria programmes.

Having available the survey results, three countries with high failure rates organized national stakeholders' consultations to review the findings of this survey and address the gaps identified. The conclusions of these consultations addressed a broad range of recommendations and actions.

Although overall survey results indicate a relatively high proportion of antimalarials that are out of specifications set up in recognized pharmacopoeias, survey outcomes should not be generalized as 'catastrophic'. In several countries results of quality testing were quite encouraging and many detected non-compliances were not extreme. Moreover, observed quality failure rates cannot be always directly related to therapeutic failures of these medicines. The relationship between quality and health implications is more complex and was not a subject investigated in this survey. Detailed interpretation of study results needs knowledge of limits set up by manufacturers for specific products and registration conditions. Nevertheless, out of specification results documented in the survey are always of concern and, if present in such rate as observed, call for fast action.

The information obtained through the survey has led to a better understanding of the quality profile of antimalarials in sub-Saharan Africa. It has also contributed towards evidence-based regulatory actions, development of regulatory systems and their enforcement capacity, advancement of post-marketing surveillance and cooperation between national drug regulatory authorities.

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Appendices

Appendix 1: Survey protocol

SURVEY OF THE QUALITY OF SELECTED ANTIMALARIAL MEDICINES CIRCULATING IN SELECTED AFRICAN COUNTRIES

Version: Final 3

1. Introduction

WHO has identified fighting malaria as a major priority for action. Antimalarial medicines are central to any strategy aimed at effectively reducing mortality caused by malaria. Quality, efficacy and safety of antimalarials are therefore essential and should be assured.

2. Objective/purpose

The present survey aims to evaluate the quality of selected antimalarials in a defined number of countries of sub-Saharan Africa. The specific objectives are to:

1. estimate the proportion[3] of artemisinin-based combination therapy (ACT) products and sulfadoxine/pyrimethamine (SP) products meeting specific quality standards in the selected countries at different points of the regulated and informal distribution systems;
2. estimate the proportion of counterfeit ACT and SP products in the selected countries at different points of the regulated and informal distribution systems;
3. identify possible causes for any findings;
4. propose possible strategies and implementation plans to address the problems identified by the survey.

3. Antimalarial products to be surveyed

This survey aims at studying oral solid preparations of ATC products (co-packed and fixed-dose combinations products) available in each participating country and products containing the SP combination[4]. In the regular sector, sampling will be based on the products most sold and/or recommended by national guidelines. In the informal sector, the Focal Person for Sampling (FPS) will ask for the "best ACT and the best SP".

4. Main activities

- Collect and test samples of selected antimalarials from selected sites of the regulated private and public sector, as well as from the informal market.
- Analyse findings and write a report describing overall results and country-specific results.
- Identify the elements of a strategy aimed at addressing the problems identified by this survey.

5. Countries participating in the survey

The first phase of the survey will be carried out in Cameroon, Ethiopia, Ghana, Kenya, Madagascar, Malawi, Nigeria, Senegal, Tanzania and Uganda.

The second phase of the survey will include Angola, Guinea, Liberia, Mali, Mozambique and Sudan.

6. Sampling

A defined amount of all branded and/or generic presentations (which means the same product name, manufacturer, dosage form, package size, packaging material and strength) of selected ACTs and SP

[3] Proportion refers to the percentage of the total sample collected.

[4] Since policies on and use of specific products vary, a separate list of products to be included in the study will be drawn up for each participating country.

products available at each sample collection site will be collected. Items collected for each presentation at the same collection site will be called a sample. All administration units (e.g. tablet, capsule) of one sample must be of the same batch or the same dispensing container in the case of loose items in the informal sector.

7. Items to sample and sample collection sites

- The selection of products and sites will be determined through a national plan. For this reason, malaria control programmes and staff from national drug registration authorities as well as national quality control laboratories should be involved in the sampling selection from different sectors (public, private and informal).
- Sampling should be practical and feasible and should reflect the reality of the geographical area. Sampling should be also balanced between the budget availability for testing and the aim of reaching all levels of drug distribution.
- Selection should take into consideration the following criteria (for the template see Annex1).

Steps to developing sampling strategy

Sampling level 1

7.1. Identify the sources of medicines in each participating country. Sources include: importers, central medical store, manufacturers, and NGO central stores. These categories are referred to as 'sources' or 'the highest level of the distribution system'.

7.2. List sample collection sites for each source. Identify the sources that, in the concerned country, provide the medicines that will be sampled (see point 7.7 below). Collect the samples from these sites.

Sampling level 2

7.3. Identify at least three survey regions of high malaria prevalence on the basis of epidemiological information drawn from the national malaria strategy and other elements, as appropriate.

7.4. Within each region: map types of facilities for each level of the distribution chain (excluding the highest level identified above at point 7.1), e.g. wholesalers (both public and private sector, including NGOs), regulated retailers (including all dispensing facilities) and informal sector[5].

7.5. List all facilities at each level within this map in order to identify potential sample collection sites for each one of the distribution chain levels identified above.

7.6. For each level, randomize a number of sampling sites on the basis of the following criteria: a) take at least three sites for the higher levels within the region (public and private medical stores, wholesalers); b) ensure that there is a larger number of sites among those facilities of the distribution system that are closer to the point where patients obtain their medicines.

7.7. The purpose of this step is to identify the products that most patients use. List all the products on the market, or potentially on the market, that contain ACTs or SP and group them by INNs. Then indicate the most sold[6] ACT (by INNs) and the most sold SP at the national level and, if feasible, at the regional level in the regions identified above (see point 7.3).

7.8. Allocate the budget in a way that the largest number of samples is drawn from the lowest levels of the distribution system. The following breakdown can be used as guidance:

[5] The actual classification of levels will be decided at the national level on the basis of what is relevant in each country.

[6] According to the best available information from central medical stores, importers, market studies, price surveys or other sources. Countries may request WHO assistance in order to improve their capacity to produce or obtain the necessary information.

- **Level 1**
  - 5% each to the most sold ACT (nationally, by INNs), recommended ACT (according to national guidelines) and the most sold SP (nationally) at the highest level of the distribution system (e.g. importer, central medical store, manufacturer, NGO central store)[7]
- **Level 2**
  - 20% to the most sold (according to region-specific information) ACT* (by INNs),
  - 20% to the recommended ACT (according to national guidelines)[8],
  - 20% to the most sold SP*
  - 25% to the informal market (buyers should ask for the 'best medicine for malaria' as recommended by the seller). At least every attempt should be made to collect both ACTs and SP in the informal market. If an expired product is found, purchase one presentation and take notes after visual identification; in this case sample only one package to fill annex 3.

    If other drugs are used instead of ACTs or SPs, take a note of the drug and ask why it is sold to treat malaria (e.g. affordable, available, better known to the public, doesn't have side effects, etc.)

* Remark: If the most sold ACT (by INNs) and the most sold SP are not available in a site, select a new site in replacement. If they are also not available in the new selected site, then sample the product available in this new selected site.

8. The Focal Person for Sampling

In every country the National Drug Regulatory Authority (NMRA) will communicate to WHO[9] the name and CV of a candidate to be designated as Focal Person for Sampling (FPS). This candidate must have a pharmacy background and, preferably, work as inspector.

The FPS will, in collaboration with other national counterparts, as appropriate:

- ensure the development of the national sampling plan, as established in point 7, and provide reasons for this choice (Annex 1);
- supervise the implementation of the sampling strategy and the completion of sample collection;
- complete or supervise the completion of Annexes 2 and 3 for each sample collected and ensure all the package leaflets are copied;
- conduct or supervise testing with the Minilab.

During August 2007 a period of time will be identified when sampling will be carried out in all countries to enable the laboratory to test samples in series. The common deadline for sending the last sample must be adhered to.

9. Sample collection techniques

- Ensure the use of sampling checklist prior to departure to the collecting site.
- Whenever possible, the technique of "Mystery client" should be adopted to collect samples. This will be essential at informal market and private collection sites. Arrangements should be made to ensure the replacement of samples collected in government and other facilities as appropriate.
- Practice key questions to be used at the informal market in order to obtain ACTs and SPs.

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7 If the most sold and the recommended are the same, 10% should be allocated to this ACT(by INNs).
8 If the most sold and the recommended are the same, 40% should be allocated to this ACT(by INNs).
9 Focal point: Dr Amor Toumi, WHO/OMS, Avenue Appia, 1211 Geneva, Switzerland, toumia@who.int.

10. Number of units per sample

The number of units/sample at level 1 will be 40. For level 2 it is fixed at 30. Ideally, for the informal sector the number of units/sample is fixed at 30.If it is not possible to obtain this amount in the informal sector, consider a sample up to a limit of 5 units.

11. Additional precautions for sample collection

11.1. Every effort must be made to collect samples and send them for testing in the original package, including the package leaflet.

11.2. When the original package cannot be collected, the sample will be collected using ad hoc packaging provided by WHO.

11.3. For each sample collected, the FPS will fill and sign the sample collection form (Annex 2) and insert samples and form in a dedicated envelope. This should be done after leaving the sampling site in order to avoid triggering unnecessary questions.

11.4. In order to avoid confusion, each sample will be identified by a unique code number (A/B/C/D/E as indicated below) consisting of the name of the country, type of product, sampling level, sampling date and a sequential number of the sample.

A: Country name - CM for Cameroon, ET for Ethiopia, GH for Ghana, KE for Kenya, MW for Malawi, MG for Madagascar, NG for Nigeria, SN for Senegal, TZ for Tanzania and UG for Uganda

B: Type of product - ACT or SP

C: Sampling level - 1 or 2

D: Sampling date DD-MM-YY

E: Sample sequential number - from 01 to 99.

11.5. When it is necessary to collect more than one original package in order to obtain the required number of units, all original packages will be marked with the appropriate sample code number.

11.6. Sample envelopes should be labelled, mentioning sample code number, INN and trade name of each product.

11.7. Packages that have been opened in order to collect units to be used for Minilab testing will be clearly indicated.

11.8. Package leaflets, where available, will be taken out of the original package, photocopied (or scanned) and reinserted in the original package. Photocopies (or electronic copies) will be marked with the appropriate sample code number and sent to WHO[9].

12. Information collected

The following product details will be indicated for each sample collected. The details are important not only for writing the final reports but also to help differentiate one sample from another:

- Sample code number
- Product name (as applicable brand/trade name, generic name)
- Names of active ingredients
- List of excipients (when available)
- Dosage form
- Strength per administration unit
- Type and packaging material of primary container
- Package size (number of administration units per package)
- Batch number
- Manufacturing date
- Expiry date
- Name of manufacturer
- Country and address of manufacturing site

- Regulatory status in the country according to the national MRA, i.e. authorized for marketing, not-authorized for marketing, other status (if authorized, provide name of marketing authorization holder and number).

At the end of sampling, the NFP informs WHO or USP. Validation of sampling will be organized in each country by WHO and/or USP.

13. Sample analysis

After validation of the sampling, each sample collected will first be tested using GPHF-Minilab®. In order to evaluate the compliance with the basic requirements on information accompanying products (on external and primary packaging, as well as in the package leaflet), the form in Annex 3 should be filled in. This form also includes a report on the results of Minilab testing. All Minilab basic tests should be performed on collected samples, i.e. visual inspection, disintegration/dissolution and TLC. Medicines that cannot be tested by Minilab will be tested by a method performed by USP DQI at phase I otherwise they will be tested in phase II.

The NFP will send the results and the filled Annex 3 to the funding organization (WHO or USP). A meeting between the teams of these two organizations will examine the results and decide what samples should be sent to the QC laboratory.

The selected samples will be sent for verification testing at a designated QC laboratory for 1) appearance, 2) identification, 3) dissolution or disintegration depending on the product and 4) assay for content of APIs. Testing will be based either on International Pharmacopoeia 4th edition (2006), USP30-NF25, Pharmacopoeia of the People's Republic of China, or validated analytical methods (in this order of preference).

Participating QC laboratories will establish communication and coordination in order to ensure comparability of results.

The Report on QC laboratory testing shall, in accordance with the *Good Practices for National Pharmaceutical Control Laboratories*[10], contain the information listed in Annex 4.

14. Sample transportation and documentation for QC laboratory testing

Adequate care and measures should be taken to ensure that samples reach the site where the tests are performed (both basic testing using the GPHF-Minilab® and QC lab) without any physical or chemical damage.

Appropriate care should be taken to provide adequate packaging to protect samples during transportation, e.g. by filling the container with cotton, foam or other suitable material. All containers should be sealed and appropriately labelled.

14.1 Samples must follow the paths presented in point 16.

14.2 All samples, envelopes and documents are placed in a box with sufficient care for travel and given to WHO/NPO.

14.3 WHO/NPO will verify that the boxes can travel without damage and send them to the designated control laboratory.

15. Payment for samples

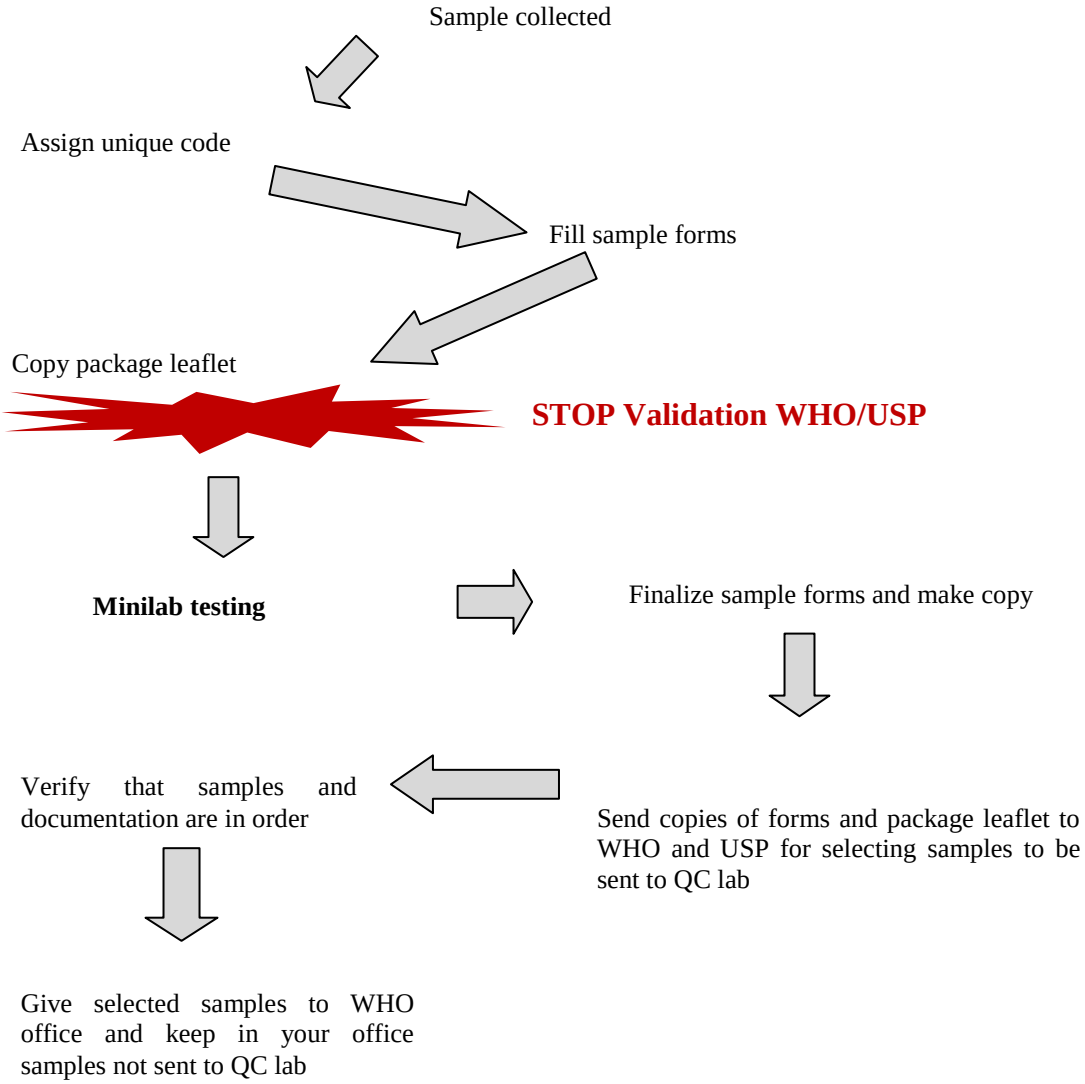
An invoice should be obtained for samples collected and immediate payment should be facilitated by the WHO representation in the country. An allotment number will be provided for all local costs associated with the sample collection, Minilab testing and transportation to designated QC laboratory.

[10] World Health Organization. WHO Technical Report Series (TRS), No. 902(2002). Annex 3: Good practices for national pharmaceutical control laboratories. http://whqlibdoc.who.int/trs/WHO_TRS_902.pdf#page=37

16. Handling and storing of samples

Samples collected are packed, transported, and stored in such a way as to prevent any deterioration, contamination or adulteration. Samples collected should be stored and transported in their original sealed containers and in accordance with storage instructions for the respective product. Closures and labels should be tamper-evident, that is, of such a type that unauthorized opening can be detected. When it is necessary to open a sample container, the analyst or the person who opens it must re-seal, date and initial the container and complement the sample documents with a note explaining the reason for opening the container. Any product purchased without the original container must be stored in a plastic bottle. All information must be indicated on the new container and a note must be inserted.

The following flowchart outlines the steps to be followed after sample collection. The flowchart needs to show the validation step by WHO and USP DQI between phase 1a and phase 1b. Also, reporting of the Minilab data should follow a template that will be prepared by USP DQI and sent to all participants.



Annex 1 to Survey Protocol

National sampling plan

Country:

Focal person for sampling:

Products to be collected	
ACTs *(oral solid preparations co-packed and/or fixed-dose combinations)*	*International Nonproprietary Names*
Most-sold ACT	
ACT recommended by national guidelines	
Sulfadoxine/pyrimethamine	*Product name and marketing authorization holder/manufacturer*
Most-sold SP	

Sample collection sites			
	Level 1 *(Highest level of distribution system, e.g. importers, central medical store, manufacturers, NGO central stores)*		
	Facility name, address, region	*Type of facility*	*Private/ Public*
1.			
2.			
3.			
	Level 2 *(e.g. wholesalers, regulated retailers, dispensing facilities, informal sector)*		
	Facility name, address, region	*Type of facility*	*Private/ Public/ Informal*
1.			
2.			
3.			
4.			
5.			
6.			

7.			
8.			
Reasons for this choice			

Allocated budget	Level 1	Level 2	
		Regulated market	Informal market
(Most-sold ACT)	*(5%)*	*(20%)*	*(25%)*
(ACT recommended according to guidelines)	*(5%)*	*(20%)*	
(Most-sold SP)	*(5%)*	*(20%)*	

Date, name and signature of the Focal Person for Sampling

Annex 2 to Survey Protocol

QAMSA Survey

Sample Collection Form

1. Country: _____

   Code given to the sample: _____

2. Name of survey site (e.g. region, city): _____

3. Price of the product: _____

4. Name, type and address of collection site/point (please specify if the site is private or public, as well as the type, e.g. hospital, clinic, public dispensary, wholesaler, pharmacy, other retail outlet, NGO facility or informal market; in the case of an informal market, please describe):

_____

_____

_____

5. Commercial name of product: _____

6. INN of active ingredients:

_____

7. List of excipients: _____

_____

_____

_____

8. Dosage form *(e.g. tablet, capsule)*: _____

9. Strength per unit dose *(e.g. mg/tablet):* _____

10. Type and packaging material (primary container):

    (e.g. strips, PVC bottle)

_____

☐ taken in original package ☐ taken from bulk container

11. Quantity collected per sample, with specification of the package size:

_____

12. Batch number: _____

13. Manufacturing date: _____

14. Expiry date: _____

15. Name of manufacturer: _____

16. Country and postal address of manufacturer:

17. Regulatory status of the product in the country (on the basis of NMRA records), i.e. registered, unregistered or other and, if registered, marketing authorization holder and number:

18. Any other comment

Besides any comments on the above-mentioned collected sample, list drugs that are not ACTs or SPs and are sold at this site for malaria treatment.

Date of sample collection, name(s) and signature(s) of the person(s) who collected the sample and of the Focal Person for Sampling

Note: ***Samples collected to be sent to QC laboratory must be in their original containers, intact and unopened. Package leaflet must be included. Packages that have been opened for Minilab testing will be clearly indicated and the sample placed into a plastic package as indicated previously.***

Annex 3 to Survey Protocol

Compliance with the basic requirements for information accompanying the product and report on Minilab testing

Product name:_____

INNs:_____

Code given to the sample (from Sample Collection Form):_____

1- External packaging	**Information present on the label**	
Product name	YES ☐	NO ☐
INN	YES ☐	NO ☐
Strength	YES ☐	NO ☐
Batch number	YES ☐	NO ☐
Expiry date	YES ☐	NO ☐
Manufacturer/Marketing authorization holder (MAH) - name/address	…… ……	
Storage conditions	……	

2- Primary packaging	**Information present on the label**	
Product name	YES ☐	NO ☐
Strength	YES ☐	NO ☐
Unit dose per blister or container stated	YES ☐	NO ☐
Batch number	YES ☐	NO ☐
Expiry date	YES ☐	NO ☐
Manufacturer/MAH name	YES ☐	NO ☐
(specify only if different from the external packaging under point 1)	……	
Inviolability system present	YES ☐	NO ☐

3- Package leaflet		
Presence of the leaflet	YES ☐	NO ☐
Language(s) of the leaflet	……	
Composition	YES ☐	NO ☐
Manufacturer/MAH name/address	YES ☐	NO ☐
(specify only if different from the external packaging under point 1)	…… ……	

Storage conditions YES ☐ NO ☐

(specify only if different from the external packaging under point 1) ……

……

4- Observation on any discrepancy between the above points 1, 2 or 3 or non-compliance, if any

_____

_____

5- Report on Minilab testing:

PHYSICAL/VISUAL INSPECTION TEST	
Description of dosage form	
Shape (circular, oval, flat sides, other)	
Uniformity of shape	
Uniformity of colour	
No physical damage (cracks, breaks, erosion, abrasion, sticky)	
Other observations (no foreign contaminant, dirty marks, proper seal - for capsule)	

DISINTEGRATION TEST		
Time of complete disintegration expected (30 minutes for uncoated tablet)	Time in minutes of complete disintegration observed	Did the drug pass disintegration test?
	----------	☐ Yes ☐ No

RESULT OF TLC TEST (see Appendix 2 for TLC result interpretation)		
Rf Standard (---): ---------- Rf Standard (---): ---------- Rf Standard (---): ---------- Rf Standard (---): ---------- Rf Sample (1): ---------- Rf Sample (2): ---------- Rf Sample (3): ---------- Rf Sample (4): ----------	Did the drug and the standard spots have the same intensity? ---------- Was there any contaminant spot on TLC? ----------	Did the sample pass quality by using the TLC Test? ☐ Yes ☐ No

FINAL COMMENTS

☐ The sample conformed with basic testing specifications

☐ The sample did not conform with basic quality testing (Reason:……..…….…)	
☐ The sample is doubtful for its basic quality testing (Reason:…….……..……..……..……)	
REPORT PREPARED BY: Date: …….... Name: …….……. Signature: ……	REPORT REVIEWED BY: Date: …….. Name: …… Signature:……..……
ACTION TO BE TAKEN BY THE PROVINCIAL FIELD DRUG TESTING FACILITY[11]	
Report the result to national disease programme Date of report …….. Signature…….……	Send the remaining sample units together with this Form to the national laboratory for further testing Date……Signature……
Reasons given for the chosen action: ---------- ----------	

Date, name and signature of the Focal Person for Sampling

[11] Action to be taken and communication between key agencies in the country should be dependent on country's rules and regulations.

Annex 4 to Survey Protocol

Content of the Report on QC laboratory testing

The Report on QC laboratory testing shall, in accordance with the Good Practices for National Pharmaceutical Control Laboratories, provide the following information:

1. name and address of the QC laboratory performing the sample testing;
2. number/code of the Report on QC laboratory testing;
3. name and address of the originator of the request for testing;
4. code given to the sample (from Sample Collection Form);
5. date on which the sample was received;
6. name of the country where the sample was collected;
7. sample product name, dosage form, active ingredients, strength, package size, type and packaging material of primary container;
8. description of the sample;
9. batch number of the sample, expiry date and manufacturing date, if available;
10. name and address of the manufacturer;
11. reference to the specifications used for testing the sample, including the limits;
12. results of all the tests performed, or the numerical results of all the tests performed (if applicable);
13. conclusion on whether or not the sample was found to be within the limits of the specifications used,
14. date on which the test was performed;
15. signature of the head of the laboratory or authorized person.

Appendix 2: Artemether/lumefantrine samples – test results

Sample code and country of collection*	Strength (mg)	Manu-facturer	Batch num-ber	Exp. Date	Samp-ling level	Sample collection site	Region	MINILAB SCREENING				LABORATORY TESTING								
								Phys/ Vis inspec-tion (excl. label and leaflet)	**Disintegr ation**	**TLC**	**Conclusion** (label and leaflet defects not taken into account)	**Appearance**	**Identity**	**Assay 90.0 - 110.0%**		**Artemether-related substances**	**Dissolution**		**Uniformity of mass**	**Conclusion** (appearance not taken into account)
														Assay - artemether %	**Assay - lumefan-trine %**	Impurity A ≤ 1.5% Impurity B ≤ 1.0% Impurity C ≤ 0.5% Impurity D ≤ 0.3% Any other spot ≤ 0.2%	**Artemether NLT 40%(Q) in 60min NLT 60%(Q) in 180min**	**Lumefantrine NLT 60%(Q) in 45min**		
Cm/ACT/1/2 2.05.08/20	20/120	Ajanta Pharma Ltd, India	P0657J	2009 Sep	1	LABOREX (GROSSIST E PRIVE)	Centre	Passed	Passed	Passed	OK	Tablets heavily mottled, powder on surface, traces of powder in blisters	Complies	99.8	95.9	Complies	60min: Does not comply at S1 mean (n=6): 38% min:36%; max:43%-not continued 120min: Complies at S1 mean (n=6): 72%	Complies at S1 mean (n=6): 82%	Complies	In-conclusive
Cm/ACT/1/1 4.05.08/22	20/120	Ajanta Pharma Ltd, India	P0957H	2009 Jul	1	PHARMAC AM (GROSSIST E PRIVE)	Centre	Passed	Passed	Passed	OK	Tablets mottled, spots, powder on surface, uneven surface	Complies	91.6	93.2	Complies	60min: Does not comply at S1 mean (n=6): 40%-not enough sample to continue 120min: Complies at S1 mean (n=6): 64%	Complies at S1 mean (n=6): 83%	Complies	In-conclusive
Cm/ACT/2/2 4.05-08/30	20/120	Ajanta Pharma Ltd, India	P0957H	2009 Jul	3	Marché informel, MOKOLO YDE Sous un grand hangar	Centre	**Failed**	Passed	Passed	**Not OK**	Tablets mottled, spots, powder on surface, uneven coating	Complies	91.3	94.7	Complies	60min: Complies at S1 mean (n=6): 43% 120min: Complies at S1 mean (n=6): 71%	Complies at S1 mean (n=6): 83%	Complies	Compliant
Cm/ACT/2/2 1.05.08/51	40/240	Ajanta Pharma Ltd, India	P0137F	2009 May	2	OFFICINE PRIVEE YDE	Centre	**Failed**	Passed	Passed	**Not OK**	Tablets mottled, spots, crystals and powder on surface, uneven surface, traces of powder in blisters	Complies	91.4	90.3	Complies	60min: Complies at S1 mean (n=6): 55% 120min: Complies at S1 mean (n=6): 75%	Complies at S1 mean (n=6): 82%	Complies	Compliant (Testing completed 1 month after expiry)
Cm/ACT/2/1 6.05.08/66	20/120	Ajanta Pharma Ltd, India	P0957H	2009 Jul	3	Marché, informel MBOUDA, abri de fortune exposé aux intempéries	West	**Failed**	Passed	Passed	**Not OK**	Tablets mottled, crystals on surface, uneven surface, faint scoreline	Complies	94.2	95.3	Complies	60min: Does not comply at S1 mean (n=6): 42% min:39%; max:44%-not continued 120min: Complies at S1 mean (n=6): 67%	Complies at S1 mean (n=6): 81%	Complies	In-conclusive
Cm/ACT/2/2 7.05.08/123	20/120	Ajanta Pharma Ltd, India	P0297H	2009 Jul	2	OFFICINE PRIVEE DLA	Coast	**Failed**	Passed	Passed	**Not OK**	Tablets heavily mottled, powder on surface, uneven coating, traces of powder in blisters	Complies	**Does not comply 82.0**	91.4	**Does not comply** - Impurity A, impurity B (Dihydro-artemisinin) and impurity C above limits	60min: Complies at S1 mean (n=6): 46% 120min: Complies at S1 mean (n=6): 72%	Complies at S1 mean (n=6): 81%	Complies	**Non-com-pliant**
Cm/ACT/2/2 7.05.08/146	20/120	Ajanta Pharma Ltd, India	P0657J	2009 Sep	2	LIMBE PHARMAC Y	South-West	Passed	Passed	Passed	OK	Tablets mottled, crystals and powder on surface, uneven surface	Complies	94.0	95.5	Complies	60min: Complies at S1 mean (n=6): 44% 120min: Complies at S1 mean (n=6): 78%	Complies at S1 mean (n=6): 89%	Complies	Compliant
Cm/ACT/1/1 4.05.08/11	20/120	Beijing Novartis Pharma Ltd, China	X1143	2009 Jul	1	U.C. PHARM (GROSSIST E PRIVE)	Centre	Passed	Passed	Passed	OK	Tablets faintly mottled - minority affected	Complies	96.1	96.9	Complies	60min: Complies at S1 mean (n=6): 62% 120min: Complies at S1 mean (n=6): 86%	Complies at S1 mean (n=6): 78%	Complies	Compliant

*Cm=Cameroon, Et=Ethiopia, Gh=Ghana, Ke=Kenya, Ng=Nigeria, Tz=Tanzania

Sample code and country of collection*	Strength (mg)	Manu-facturer	Batch num-ber	Exp. Date	Samp-ling level	Sample collection site	Region	MINILAB SCREENING				LABORATORY TESTING								
								Phys/ Vis inspec-tion (excl. label and leaflet)	Disintegr ation	TLC	Conclusion (label and leaflet defects not taken into account)	Appearance	Identity	Assay 90.0 - 110.0%		Artemether-related substances	Dissolution		Uniformity of mass	Conclusion (appearance not taken into account)
														Assay - artemether %	Assay - lumefan-trine %	Impurity A ≤ 1.5% Impurity B ≤ 1.0% Impurity C ≤ 0.5% Impurity D ≤ 0.3% Any other spot ≤ 0.2%	Artemether NLT 40%(Q) in 60min NLT 60%(Q) in 180min	Lumefantrine NLT 60%(Q) in 45min		
Cm/ACT/2/15.05.08/84	20/120	Beijing Novartis Pharma Ltd, China	X1142	2009 Jul	2	PHCIE D'OFFICINE PRIVEE DSCHANG	West	Passed	Passed	Passed	OK	Tablets mottled, crystals on surface - minority affected	Complies	99.0	99.4	Complies	60min: Complies at S1 mean (n=6): 62% 120min: Complies at S1 mean (n=6): 86%	Complies at S1 mean (n=6): 78%	Complies	Compliant
Cm/ACT/2/27.05.08/122	20/120	Beijing Novartis Pharma Ltd, China	X1142	2009 Jul	2	OFFICINE PRIVEE DLA	Coast	Passed	Passed	Passed	OK	Tablets faintly mottled, crystals on surface - minority affected	Complies	95.1	95.8	Complies	60min: Complies at S1 mean (n=6): 62% 120min: Complies at S1 mean (n=6): 86%	Complies at S1 mean (n=6): 83%	Complies	Compliant
Cm/ACT/1/13.05.08/02	20/120	Novartis Pharma-ceuticals Corporation, USA	F0727	2009 Jul	1	CENAME (CENTRALE NATIONALE D'ACHAT)	Centre	Passed	Passed	Passed	OK	Crystals on surface - minority affected	Complies	95.5	95.3	Complies	60min: Complies at S1 mean (n=6): 55% 120min: Complies at S1 mean (n=6): 83%	Complies at S1 mean (n=6): 85%	Complies	Compliant
Cm/ACT/2/22.05.08/45	20/120	Novartis Pharma-ceuticals Corporation, USA	F0727	2009 Jul	2	HOP CENTRAL YDE PUBLIC	Centre	Passed	Passed	Passed	OK	Tablets mottled, crystals on surface - majority affected, 1 tabl in blister broken	Complies	95.8	96.9	Complies	60min: Complies at S1 mean (n=6): 55% 120min: Complies at S1 mean (n=6): 81%	Complies at S1 mean (n=6): 72%	Complies	Compliant
Cm/ACT/2/15.05.08/65	20/120	Novartis Pharma-ceuticals Corporation, USA	F0743	2009 Jul	3	Marché informel DSCHANG, abri de fortune exposé aux intempéries	West	**Failed**	Passed	Passed	**Not OK**	Tablets mottled, crystals on surface, packaging dirty, looks like wetted	Complies	92.5	94.2	Complies	60min: Complies at S1mean (n=6): 57% 120min: Complies at S1 mean (n=6): 81%	Complies at S1mean (n=6): 80%	Complies	Compliant
Cm/ACT/2/27.05.08/117	20/120	Novartis Pharma-ceuticals Corporation, USA	F0743	2009 Jul	2	CAPP LITTORAL DLA	Coast	Passed	Passed	Passed	OK	Tablets faintly mottled, crystals on surface - minority affected	Complies	93.7	93.6	Complies	60min: Complies at S1 mean (n=6): 57% 120min: Complies at S1 mean (n=6): 81%	Complies at S1 mean (n=6): 89%	Complies	Compliant
Cm/ACT/2/26.05.08/137	20/120	Novartis Pharma-ceuticals Corporation, USA	F0727	2009 Jul	2	HOP.PUBLIC DIST. BUEA	South-West	Passed	Passed	Passed	OK	Tablets faintly mottled, crystals on surface - minority affected	Complies	96.8	96.9	Complies	60min: Complies at S1 mean (n=6): 56% 120min: Complies at S1 mean (n=6): 82%	Complies at S1 mean (n=6): 91%	Complies	Compliant
Et/Act/1/11/06/08/06	20/120	Addis pharma-ceutical factory, Ethiopia	2719	2009 Jul	1	Addis pharmaceutical factory - manufacturer /wholesaler	Central	Passed	Passed	Passed	OK	No inscription (should be), scoreline on 1 side (should not be), powdery tablets, light yellow spots on some tablets-major	Complies	101.8	94.1	Complies	60min: Complies at S1 mean (n=6): 99% 120min: Complies at S1 mean (n=6): 102%	Complies at S1 mean (n=6): 69%	Complies	Compliant
Et/Act/1/29/06/08/41	20/120	Addis pharma-ceutical factory, Ethiopia	2712	2009 Jul	1	Addis pharmaceutical factory - manufacturer /wholesaler	Southern	Passed	Passed	**Failed -** LUM spot inten-sity higher than standard	**Not OK**	No inscription (should be), scoreline on 1 side (should not be), sharp odour, prominently mottled, crystals on tablet surface, 8 of 20 tablets edges not neatly formed	Complies	97.7	99.0	Complies Impurity D (Alfa-artemether) spot identified, but cannot be quantitatively assessed	60min: Complies at S1 mean (n=6): 99% 120min: Complies at S1 mean (n=6): 99%	Complies at S2 mean (n=12): 68%	Complies	Compliant

*Cm=Cameroon, Et=Ethiopia, Gh=Ghana, Ke=Kenya, Ng=Nigeria, Tz=Tanzania

Sample code and country of collection*	Strength (mg)	Manu-facturer	Batch num-ber	Exp. Date	Samp-ling level	Sample collection site	Region	MINILAB SCREENING				LABORATORY TESTING								
								Phys/ Vis inspec-tion (excl. label and leaflet)	**Disintegr ation**	**TLC**	**Conclusion** (label and leaflet defects not taken into account)	**Appearance**	**Identity**	**Assay 90.0 - 110.0%**		**Artemether-related substances**	**Dissolution**		**Uniformity of mass**	**Conclusion** (appearance not taken into account)
														Assay - artemether %	**Assay - lumefan-trine %**	Impurity A ≤ 1.5% Impurity B ≤ 1.0% Impurity C ≤ 0.5% Impurity D ≤ 0.3% Any other spot ≤ 0.2%	**Artemether NLT 40%(Q) in 60min NLT 60%(Q) in 180min**	**Lumefantrine NLT 60%(Q) in 45min**		
Et/Act/2/29/ 06/08/44	20/120	Addis pharma-ceutical factory, Ethiopia	2712	2009 Jul	2	Private drugstore - Amanuel	Southern	Passed	Passed	Passed	OK	No inscription (should be), scoreline on 1 side (should not be), crystals on tablet surface	Complies	101.4	94.9	Complies Impurity D (Alfa-artemether) spot identified, but cannot be quantitatively assessed	60min: Complies at S1 mean (n=6): 101% 120min: Complies at S1 mean (n=6): 104%	Does not comply S1 to S1 criteria mean (n=6): 58% min:57%; max:61%; not enough sample to continue	Complies	In-conclusive
Et/Act/1/10/ 06/08/02	20/120	Beijing Novartis Pharma Ltd, China	X1193	2009 Oct	1	Private - Amba pharmaceuti cal plc	Central	Passed	Passed	Passed	OK	Minority of tablets are faintly mottled	Complies	98.7	98.9	Complies	60min: Complies at S1 mean (n=6): 65% 120min: Complies at S1 mean (n=6): 91%	Complies at S1 mean (n=6): 88%	Complies	Compliant
Et/Act/2/29/ 06/08/43	20/120	Beijing Novartis Pharma Ltd, China	X1193	2009 Oct	2	Private pharmacy - Kiklu	Southern	Passed	Passed	Passed	OK	Minority of tablets are faintly mottled	Complies	96.9	94.9	Complies Impurity D (Alfa-artemether) spot identified, but cannot be quantitatively assessed	60min: Complies at S1 mean (n=6): 61% 120min: Complies at S1 mean (n=6): 84%	Complies at S1 mean (n=6): 74%	Complies	Compliant
Et/Act/1/11/ 06/08/03	20/120	Novartis Pharma-ceuticals Corporat ion, USA	F0772	2009 Aug	1	NGO - MSF	Central	Passed	Passed	Passed	OK	Tablets faintly mottled, with light yellow spots	Complies	93.8	94.7	Complies	60min: Complies at S1 mean (n=6): 61% 120min: Complies at S1 mean (n=6): 87%	Complies at S1 mean (n=6): 74%	Complies	Compliant
Et/Act/2/17/ 06/08/12	20/120	Novartis Pharma-ceuticals Corporat ion, USA	F0828	2009 Oct	3	Informal market - Airisi	Eastern	Passed	Passed	Passed	OK	Tablets faintly mottled, with light yellow spots	Complies	93.7	94.5	Complies	60min: Complies at S1 mean (n=6): 73% 120min: Complies at S1 mean (n=6): 87%	Complies at S1 mean (n=6): 79%	Complies	Compliant
Et/Act/2/17/ 06/08/13	20/120	Novartis Pharma-ceuticals Corporat ion, USA	F0511	2009 Feb	3	Informal market - Puntland	Eastern	Passed	Passed	Passed	OK	Tablets faintly mottled, with light yellow spots	Complies	94.5	95.4	Complies	60min: Complies at S1 mean (n=6): 62% 120min: Complies at S1 mean (n=6): 86%	Complies at S1 mean (n=6): 79%	Complies	Compliant
Et/Act/2/25/ 06/08/28	20/120	Novartis Pharma-ceuticals Corporat ion, USA	F0704	2009 Jun	2	Private drugstore - Kidus Giorgis	Northern	Passed	Passed	Passed	OK	Tablets are faintly mottled	Complies	93.6	94.1	Complies	60min: Complies at S1 mean (n=6): 60% 120min: Complies at S1 mean (n=6): 82%	Complies at S1 mean (n=6): 76%	Complies	Compliant
Et/Act/2/26/ 06/08/31	20/120	Novartis Pharma-ceuticals Corporat ion, USA	F0819	2009 Sep	2	Public hospital - Gondar	Northern	Passed	Passed	Passed	OK	Tablets faintly mottled, with light yellow spots	Complies	92.1	94.7	Complies	60min: Complies at S1mean (n=6): 55%120min: Complies at S1 mean (n=6): 82%	Complies at S1 mean (n=6): 80%	Complies	Compliant
Et/Act/2/27/ 06/08/34	20/120	Novartis Pharma-ceuticals Corporat ion, USA	F0798	2009 Sep	2	Private drug vendor - Makisegnit rural	Northern	Passed	Passed	Passed	OK	Minority of tablets with yellow spots	Complies	92.7	94.2	Complies	60min: Complies at S1 mean (n=6): 60% 120min: Complies at S1 mean (n=6): 80%	Complies at S1 mean (n=6): 79%	Complies	Compliant

Sample code and country of collection*	Strength (mg)	Manu-facturer	Batch num-ber	Exp. Date	Samp-ling level	Sample collection site	Region	MINILAB SCREENING				LABORATORY TESTING								
								Phys/ Vis inspec-tion (excl. label and leaflet)	Disintegr ation	TLC	Conclusion (label and leaflet defects not taken into account)	Appearance	Identity	Assay 90.0 - 110.0%		Artemether-related substances	Dissolution		Uniformity of mass	Conclusion (appearance not taken into account)
														Assay - artemether %	Assay - lumefan-trine %	Impurity A ≤ 1.5% Impurity B ≤ 1.0% Impurity C ≤ 0.5% Impurity D ≤ 0.3% Any other spot ≤ 0.2%	Artemether NLT 40%(Q) in 60min NLT 60%(Q) in 180min	Lumefantrine NLT 60%(Q) in 45min		
Et/Act/2/27/ 06/08/36	20/120	Novartis Pharma-ceuticals Corporat ion, USA	F0819	2009 Sep	2	Public health center - Addis Zemen	Northern	Passed	Passed	**Failed -** LUM spot intensity higher than standard	**Not OK**	Minority of tablets with yellow spots	Complies	95.0	94.2	Complies Impurity D (Alfa-artemether) spot identified, but cannot be quantitatively assessed	60min: Complies at S1 mean (n=6): 55% 120min: Complies at S1 mean (n=6): 80%	Complies at S1 mean (n=6): 91%	Complies	Compliant
Et/Act/2/29/ 06/08/45	20/120	Novartis Pharma-ceuticals Corporat ion, USA	F0828	2009 Oct	2	Public, store - Southern Nations, Nationalities and People's Regional Health Bureau	Southern	Passed	Passed	Passed	OK	Tablets slightly mottled	Complies	92.0	94.0	Complies	60min: Complies at S1 mean (n=6): 76% 120min: Complies at S1 mean (n=6): 92%	Complies at S1 mean (n=6): 93%	Complies	Compliant
Et/Act/2/30/ 06/08/46	20/120	Novartis Pharma-ceuticals Corporat ion, USA	F0798	2009 Sep	2	Private retail outlet - Amanuel	Central	Passed	Passed	**Failed -** LUM spot intensity higher than standard	**Not OK**	1 tbl with crystals on surface	Complies	91.9	93.8	Complies	60min: Complies at S1 mean (n=6): 58% 120min: Complies at S1 mean (n=6): 86%	Complies at S1 mean (n=6): 94%	Complies	Compliant
Et/Act/1/06/ 07/08/47	20/120	Novartis Pharma-ceuticals Corporat ion, USA	F0819	2009 Sep	1	Public medical store (MoH)	Central	Passed	Passed	**Failed -** LUM spot intensity higher than standard	**Not OK**	3 tbl misformed on engraving, 1 tbl with a spot, small crystals on tablet surface	Complies	96.2	93.2	Complies	60min: Complies at S1 mean (n=6): 60% 120min: Complies at S1 mean (n=6): 82%	Complies at S1 mean (n=6): 100%	Complies	Compliant
Gh/ACT/1/1 3-05-08/02	20/120	Beijing Novartis Pharma Ltd, China	X1185	2009 Oct	1	Importer-Private (Osons Chemist, Accra)	Southern	Passed	Passed	Passed	OK	Tablets mottled	Complies	97.7	97.3	Complies	60min: Complies at S1 mean (n=6): 60% 120min: Complies at S1 mean (n=6): 86%	Complies at S1 mean (n=6): 84%	Complies	Compliant
Gh/ACT/2/1 7-05-08/51/S	20/120	Beijing Novartis Pharma Ltd, China	X1185	2009 Oct	2	Retail Pharmacy (W.Link chemist, Tarkwa)	Southern	Passed	Passed	Passed	OK	OK	Complies	100.0	101.1	Complies	60min: Complies at S1 mean (n=6): 63% 120min: Complies at S1 mean (n=6): 88%	Complies at S1 mean (n=6): 81%	Complies	Compliant
Gh/ACT/2/1 3-05-08/03/M	20/120	Beijing Novartis Pharma Ltd, China	X 1090	2009 May	2	Polyclinic OPD -Public (Komfo Anokye-Kumasi)	Middle	Passed	Passed	Passed	OK	OK	Complies	98.4	96.0	Complies	60min: Complies at S1 mean (n=6): 65% 120min: Complies at S1 mean (n=6): 81%	Complies at S1 mean (n=6): 82%	Complies	Compliant
Gh/ACT/2/1 6-05-08/49/M	20/120	Beijing Novartis Pharma Ltd, China	X 1069	2009 Mar	2	Licensed Chemical Seller (Onyame Asem Chemicals)	Middle	Passed	Passed	Passed	OK	OK	Complies	100.9	96.5	Complies	60min: Complies at S1 mean (n=6): 61% 120min: Complies at S1 mean (n=6): 81%	Complies at S1 mean (n=6): 81%	Complies	Compliant
Gh/ACT/2/1 6-05-08/40/M	20/120	Beijing Novartis Pharma Ltd, China	X1185	2009 Oct	2	Private Clinic (Healthlane Hospital, Sunyani)	Middle	Passed	Passed	Passed	OK	OK	Complies	99.4	96.4	Complies	60min: Complies at S1 mean (n=6): 62% 120min: Complies at S1 mean (n=6): 87%	Complies at S1 mean (n=6): 83%	Complies	Compliant

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Sample code and country of collection*	Strength (mg)	Manu-facturer	Batch num-ber	Exp. Date	Samp-ling level	Sample collection site	Region	MINILAB SCREENING				LABORATORY TESTING								
								Phys/ Vis inspec-tion (excl. label and leaflet)	Disintegr ation	TLC	Conclusion (label and leaflet defects not taken into account)	Appearance	Identity	Assay 90.0 - 110.0%		Artemether-related substances	Dissolution		Uniformity of mass	Conclusion (appearance not taken into account)
														Assay - artemether %	Assay - lumefan-trine %	Impurity A ≤ 1.5% Impurity B ≤ 1.0% Impurity C ≤ 0.5% Impurity D ≤ 0.3% Any other spot ≤ 0.2%	Artemether NLT 40%(Q) in 60min NLT 60%(Q) in 180min	Lumefantrine NLT 60%(Q) in 45min		
Gh/ACT/2/14-05-08/14/N/UE	20/120	Beijing Novartis Pharma Ltd, China	X 1068	2009 Mar	2	Retail Pharmacy (Valdi Pharmacy, Bolgatanga)	Northern	Passed	Passed	Passed	OK	OK	Complies	99.7	95.6	Complies	60min: Complies at S1 mean (n=6): 66% 120min: Complies at S1 mean (n=6): 90%	Complies at S1 mean (n=6): 81%	Complies	Compliant
Gh/ACT/2/14-05-08/19/S	40/240	Bliss GVS Pharma Ltd, India	LF-12	2009 Nov	2	Wholesale Pharmacy(G &E Health Services, Hoi)	Southern	Passed	Passed	Passed	OK	Scoreline and logo faint on some tablets	Complies	100.8	99.9	Complies	60min: Complies at S1mean (n=6): 92% 120min: Complies at S1 mean (n=6): 97%	Complies at S1 mean (n=6): 75%	Complies	Compliant
Gh/ACT/2/14-05/08/M	40/240	Bliss GVS Pharma Ltd, India	LF-12	2009 Nov	2	Private Clinic (Paradise Clinic, Ejisu)	Middle	Passed	Passed	Passed	OK	Scoreline and logo faint on some tablets	Complies	100.9	98.5	Complies	60min: Complies at S1 mean (n=6): 93% 120min: Complies at S1 mean (n=6): 96%	Does not comply at S1 to S1 criteria mean (n=6): 54% min:49%; max:57%; not enough sample to continue	Complies	In-conclusive
Gh/ACT/2/13-O5-08/04/N/UW	40/240	Bliss GVS Pharma Ltd, India	LF-12	2009 Nov	2	Retail Pharmacy (Green Beam Chemis,Wa)	Northern	Passed	Passed	Passed	OK	Scoreline and logo faint on some tablets	Complies	99.4	96.7	Complies	60min: Complies at S1 mean (n=6): 96% 120min: Complies at S1 mean (n=6): 96%	Does not comply at S1 to S1 criteria mean (n=6): 60% min:58%; max:63%; not enough sample to continue	Complies	In-conclusive
Gh/ACT/1/22-05-08/61	20/120	Danadams pharma-ceutical Industry Ltd, Ghana	803010	2010 Mar	1	Manufacturer-Private (Danadams Pharm. Industry Ltd, Accra)	Southern	Passed	Passed	Passed	OK	Tablets mottled, with large spots and chipped embossing	Complies	103.5	94.2	Complies	60min: Complies at S1 mean (n=6): 70% 120min: Complies at S1 mean (n=6): 90%	Does not comply at S2 to S2 criteria mean (n=12): 48% min:45%; max:50%; not continued	Complies	In-conclusive
Gh/ACT/2/17-05-08/49/S	20/120	Danadams pharma-ceutical Industry Ltd, Ghana	803010	2010 Mar	2	Quasi-Govt Hospital (ABL Hospital, Tarkwa)	Southern	**Failed**	Passed	Passed	**Not OK**	Tablets mottled, 1 misformed	Complies	100.5	94.3	Complies	60min: Complies at S1 mean (n=6): 69% 120min: Complies at S1 mean (n=6): 92%	Does not comply at S2 to S2 criteria mean (n=12): 47% min:45%; max:50%; not enough sample to continue	Complies	In-conclusive
Gh/ACT/2/16-O5-08/27/N/NR	20/120	Ernest Chemists Ltd, Ghana	0101H	2011 Jan	2	Teaching Hospital-Public (TamaleTeaching Hospital)	Northern	Passed	Passed	Passed	OK	Tablets with uneven surface	Complies	94.5	91.9	Complies Impurity D (Alfa-artemether) spot identified, but cannot be quantitatively assessed	60min: Does not comply at S2 to S2 criteria mean (n=12): 31% min:17%; max: 40% 120min: Does not comply at S2 to S2 criteria mean (n=12): 45% min:21%; max: 63%; not enough sample to continue	Complies at S1 mean (n=6): 74%	Complies	In-conclusive

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Sample code and country of collection*	Strength (mg)	Manu-facturer	Batch num-ber	Exp. Date	Samp-ling level	Sample collection site	Region	MINILAB SCREENING				LABORATORY TESTING								
								Phys/ Vis inspec-tion (excl. label and leaflet)	Disintegr ation	TLC	Conclusion (label and leaflet defects not taken into account)	Appearance	Identity	Assay 90.0 - 110.0%		Artemether-related substances	Dissolution		Uniformity of mass	Conclusion (appearance not taken into account)
														Assay - artemether %	Assay - lumefan-trine %	Impurity A ≤ 1.5% Impurity B ≤ 1.0% Impurity C ≤ 0.5% Impurity D ≤ 0.3% Any other spot ≤ 0.2%	Artemether NLT 40%(Q) in 60min NLT 60%(Q) in 180min	Lumefantrine NLT 60%(Q) in 45min		
Gh/ACT/2/16-O5-08/32/N/NR	20/120	Ernest Chemists Ltd, Ghana	0101H	2011 Jan	2	Wholesale Pharm (Ernest Chemist,Tamale)	Northern	**Failed**	Passed	Passed	**Not OK**	Tablets with uneven surface, red spot	Complies	95.8	92.9	Complies Impurity D (Alfa-artemether) spot identified, but cannot be quantitatively assessed	60min: Does not comply at S1 to S1 criteria mean (n=6): 42% min:40%; max: 50% 120min: Does not comply at S1 to S1 criteria mean (n=6): 60% min:58%; max: 62%; not continued; not enough sample to continue	Complies at S1 mean (n=6): 73%	Complies	In-conclusive
Gh/ACT/1/15-05-08/32	40/240	Ernest Chemists Ltd, Ghana	0101H	2011 Jan	1	Manufacture r-Private (Ernest Chemist, Accra}	Southern	Passed	Passed	Passed	OK	Tablets misformed/chipped, embossing fontsize differences observed	Complies	104.6	96.0	Complies	60min: Does not comply at S2 to S2 criteria mean (n=12): 27% min:23%; max: 31% 120min: Does not comply at S2 to S2 criteria mean (n=12): 45% min:42%; max: 49%; not enough sample to continue	Complies at S2 mean (n=12): 69%	Complies	In-conclusive
Gh/ACT/2/14-05-08/20/S	40/240	GVS Labs, India	LF-12	2009 Nov	2	Retail Pharmacy (Victorious Mt Zion Pharmacy, Ho)	Southern	Passed	Passed	Passed	OK	Scoreline and logo faint on some tablets	Complies	94.5	94.0	Complies	60min: Complies at S1 mean (n=6): 91% 120min: Complies at S1 mean (n=6): 93%	Does not comply at S1 to S1 criteria mean (n=6): 63% min:61%; max:63%; not enough sample to continue	Complies	In-conclusive
Gh/ACT/2/30-05-08/75/S	20/120	Jiangsu Yixing Forward Pharm. Factory, China	005	2009 Dec	2	Retail Pharmacy(JAK Pharmacy, Accra)	Southern	Passed	Passed	Passed	OK	OK	Complies	**Does not comply 87.6**	**Does not comply 84.6**	Complies	60min: Does not comply at S1 to S1 criteria mean (n=6): 37% min:33%; max: 42% 120min: Does not comply at S1 to S1 criteria mean (n=6): 66% min:60%; max: 75%; not continued	Complies at S1 mean (n=6): 76%	Complies	**Non-com-pliant**
Gh/ACT/1/23-05-08/65	80/480	Kinapharma Ltd, Ghana	003	2010 Jan	1	Manufacture r-Private (Kinapharma Ltd Accra)	Southern	Passed	Passed	Passed	OK	Mottled, with spots, breakable tablets	Complies	Assay inconclusive due to problems in sample preparation causing large variance in assay results: Artemether 87-114%, Lumefantrine 85-109%; further samples and manufacturer's method were requested but analytical problem continued also with the manufacturer's method		Complies	60min: Does not comply at S1 to S1 criteria mean (n=6): 46% min:41%; max: 53% 120min: Does not comply at S1 to S1 criteria mean (n=6): 66% min:63%; max: 68%; not continued	Does not comply at S1 to S1 criteria mean (n=6): 51% min:50%; max:53%; not continued	Complies	In-conclusive
Gh/ACT/1/22-05-08/59	20/120	Medreich Plc, India	370402	2010 Nov	1	Importer-Private (Ernest Chemist, Accra)	Southern	Passed	Passed	Passed	OK	Tablets mottled with very small dots	Complies	93.5	**Does not comply 89.2**	Complies	60min: Complies at S1 mean (n=6): 71% 120min: Complies at S1 mean (n=6): 88%	Complies at S1 mean (n=6): 82%	Complies	**Non-com-pliant**
Gh/ACT/2/16-05-08/33/N/NR	20/120	Novartis Pharma-ceuticals Corporation, USA	F0731	2009 Jul	2	Retail Pharmacy (Ricky Pharmacy)	Northern	Passed	Passed	Passed	OK	OK	Complies	99.7	93.6	Complies	60min: Complies at S1 mean (n=6): 57% 120min: Complies at S1 mean (n=6): 88%	Complies at S1 mean (n=6): 89%	Complies	Compliant

*Cm=Cameroon, Et=Ethiopia, Gh=Ghana, Ke=Kenya, Ng=Nigeria, Tz=Tanzania

Sample code and country of collection*	Strength (mg)	Manu-facturer	Batch num-ber	Exp. Date	Samp-ling level	Sample collection site	Region	MINILAB SCREENING				LABORATORY TESTING								
								Phys/ Vis inspec-tion (excl. label and leaflet)	**Disintegr ation**	**TLC**	**Conclusion** (label and leaflet defects not taken into account)	**Appearance**	**Identity**	**Assay 90.0 - 110.0%**		**Artemether-related substances**	**Dissolution**		**Uniformity of mass**	**Conclusion** (appearance not taken into account)
														Assay - artemether %	**Assay - lumefan-trine %**	Impurity A ≤ 1.5% Impurity B ≤ 1.0% Impurity C ≤ 0.5% Impurity D ≤ 0.3% Any other spot ≤ 0.2%	**Artemether NLT 40%(Q) in 60min NLT 60%(Q) in 180min**	**Lumefantrine NLT 60%(Q) in 45min**		
Ke/ACT/1/1 7.06.08/21	20/120	Ajanta Pharma Ltd, India	P0657J	2009 Sep	1	PRIVATE/ IMPORTER - Harleys Pharmaceuti cals	Central	Passed	Passed	Passed	OK	Tablets mottled, uneven surface with crystals	Complies	97.2	96.8	Complies	60min: Complies at S1 mean (n=6): 45% 120min: Complies at S1 mean (n=6): 76%	Complies at S1 mean (n=6): 88%	Complies	Compliant
Ke/ACT/1/1 7.06.08/22	40/240	Ajanta Pharma Ltd, India	P0478B	2010 Jan	1	PRIVATE/ IMPORTER - Harleys Pharmaceuti cals	Central	Passed	Passed	Passed	OK	Tablets mottled, uneven surface	Complies	95.8	91.7	Complies	60min: Complies at S1 mean (n=6): 48% 120min: Complies at S1 mean (n=6): 83%	Complies at S1 mean (n=6): 88%	Complies	Compliant
Ke/ACT/11/ 24.06.08/85	20/120	Ajanta Pharma Ltd, India	P1057G	2009 Jun	2	PRIVATE/ WHOLESA LER - Harleys Pharmaceuti cals	Nyanza	Passed	Passed	Passed	OK	Tablets heavily mottled, uneven surface	Complies	90.3	95.9	Complies	60min: Complies at S1 mean (n=6): 49% 120min: Complies at S1 mean (n=6): 74%	Complies at S1 mean (n=6): 87%	Complies	Compliant
Ke/ACT/1/1 3.06.08/01	20/120	Beijing Novartis Pharma Ltd, China	X1171	2009 Sep	1	MISSION FACILITY/ CMS - MEDS	Central	Passed	Passed	Passed	OK	OK	Complies	96.5	97.4	Complies	60min: Complies at S1 mean (n=6): 61% 120min: Complies at S1 mean (n=6): 86%	Complies at S1 mean (n=6): 86%	Complies	Compliant
Ke/ACT/11/ 19.06.08/52	20/120	Beijing Novartis Pharma Ltd, China	X1126	2009 Jun	2	PRIVATE/ WHOLESA LER - Riddhi Pharmaceuti cals	Western	Passed	Passed	Passed	OK	Tablets faintly mottled - minority affected	Complies	96.5	99.4	Complies	60min: Complies at S1 mean (n=6): 59% 120min: Complies at S1 mean (n=6): 84%	Complies at S1 mean (n=6): 76%	Complies	Compliant
Ke/ACT/11/ 24.06.08/93	20/120	Beijing Novartis Pharma Ltd, China	X1126	2009 Jun	2	PRIVATE/ WHOLESA LER - Kentons	Nyanza	Passed	Passed	Passed	OK	Crystals on tablets surface - minority affected	Complies	98.0	97.4	Complies	60min: Complies at S1 mean (n=6): 58% 120min: Complies at S1 mean (n=6): 83%	Complies at S1 mean (n=6): 77%	Complies	Compliant
Ke/ACT/11/ 25.06.08/102	20/120	Beijing Novartis Pharma Ltd, China	X1126	2009 Jun	2	PHARMAC Y-RETAIL OUTLET - Borabu Medicals	Nyanza	Passed	Passed	Passed	OK	OK	Complies	96.8	98.3	Complies	60min: Complies at S1 mean (n=6): 57% 120min: Complies at S1 mean (n=6): 84%	Complies at S1 mean (n=6): 78%	Complies	Compliant
Ke/ACT/11/ 01.07.08/131	20/120	Beijing Novartis Pharma Ltd, China	X1059	2009 Feb	2	PHARMAC Y-RETAIL OUTLET - Palmland Pharmaceuti cals	Coast	Passed	Passed	Passed	OK	Crystals on tablets surface - minority affected	Complies	95.2	95.3	Complies	60min: Complies at S1 mean (n=6): 63% 120min: Complies at S1 mean (n=6): 86%	Complies at S1 mean (n=6): 75%	Complies	Compliant (Testing completed 4 months after expiry)
Ke/ACT/11/ 01.07.08/132	20/120	Beijing Novartis Pharma Ltd, China	X1059	2009 Feb	2	PRIVATE/ WHOLESA LER - Oceanview Pharmaceuti cals	Coast	Passed	Passed	Passed	OK	Crystals on tablets surface - minority affected	Complies	97.0	96.5	Complies	60min: Complies at S1 mean (n=6): 60% 120min: Complies at S1 mean (n=6): 87%	Complies at S1 mean (n=6): 74%	Complies	Compliant (Testing completed 4 months after expiry)
Ke/ACT/1/1 3.06.08/09	20/120	Novartis Pharma-ceuticals Corporat ion, USA	F0807	2009 Sep	1	MISSION FACILITY/ CMS - MEDS	Central	Passed	Passed	Passed	OK	OK	Complies	94.0	94.1	Complies	60min: Complies at S1 mean (n=6): 59% 120min: Complies at S1 mean (n=6): 85%	Complies at S1 mean (n=6): 93%	Complies	Compliant

Sample code and country of collection*	Strength (mg)	Manu-facturer	Batch num-ber	Exp. Date	Samp-ling level	Sample collection site	Region	MINILAB SCREENING				LABORATORY TESTING								
								Phys/ Vis inspec-tion (excl. label and leaflet)	Disintegr ation	TLC	Conclusion (label and leaflet defects not taken into account)	Appearance	Identity	Assay 90.0 - 110.0%		Artemether-related substances	Dissolution		Uniformity of mass	Conclusion (appearance not taken into account)
														Assay - artemether %	Assay - lumefan-trine %	Impurity A ≤ 1.5% Impurity B ≤ 1.0% Impurity C ≤ 0.5% Impurity D ≤ 0.3% Any other spot ≤ 0.2%	Artemether NLT 40%(Q) in 60min NLT 60%(Q) in 180min	Lumefantrine NLT 60%(Q) in 45min		
Ke/ACT/1/16.06.08/17	20/120	Novartis Pharma-ceuticals Corporation, USA	F0789	2009 Aug	1	PUBLIC/ CMS - KEMSA	Central	Passed	Passed	Passed	OK	Crystals on tablets surface - minority affected	Complies	95.5	97.4	Complies	60min: Complies at S1 mean (n=6): 63%120min: Complies at S1 mean (n=6): 90%	Complies at S1 mean (n=6): 92%	Complies	Compliant
Ke/ACT/11/19.06.08/23	20/120	Novartis Pharma-ceuticals Corporation, USA	F0808	2009 Sep	2	PUBLIC FACILITY/ HOSPITAL - Western Provincial General Hospital	Western	Passed	Passed	Passed	OK	Crystals on tablets surface - minority affected	Complies	93.4	96.1	Complies	60min: Complies at S1 mean (n=6): 63% 120min: Complies at S1 mean (n=6): 87%	Complies at S1 mean (n=6): 91%	Complies	Compliant
Ke/ACT/11/19.06.08/24	20/120	Novartis Pharma-ceuticals Corporation, USA	F0759	2009 Aug	2	PUBLIC FACILITY/ HOSPITAL - Western Provincial General Hospital	Western	Passed	Passed	Passed	OK	Crystals on tablets surface - minority affected	Complies	95.8	96.3	Complies	60min: Complies at S1 mean (n=6): 63% 120min: Complies at S1 mean (n=6): 90%	Complies at S1 mean (n=6): 100%	Complies	Compliant
Ke/ACT/11/23.06.08/57	20/120	Novartis Pharma-ceuticals Corporation, USA	F0759	2009 Aug	2	PUBLIC FACILITY/ HOSPITAL - Nyanza Provincial General Hospital	Nyanza	Passed	Passed	Passed	OK	Tablets faintly mottled - minority affected	Complies	94.6	98.7	Complies	60min: Complies at S1 mean (n=6): 61% 120min: Complies at S1 mean (n=6): 87%	Complies at S1 mean (n=6): 90%	Complies	Compliant
Ke/ACT/11/23.06.08/63	20/120	Novartis Pharma-ceuticals Corporation, USA	F0763	2009 Aug	2	PUBLIC/ CMS - KEMSA Depot Kisumu	Nyanza	Passed	Passed	Passed	OK	Crystals on tablets surface - minority affected	Complies	93.7	95.2	Complies	60min: Complies at S1 mean (n=6): 60% 120min: Complies at S1 mean (n=6): 82%	Complies at S1 mean (n=6): 86%	Complies	Compliant
Ke/ACT/11/25.06.08/109	20/120	Novartis Pharma-ceuticals Corporation, USA	F0762	2009 Aug	2	PUBLIC FACILITY/ HOSPITAL - Keumbu District Hospital	Nyanza	Passed	Passed	Passed	OK	Crystals on tablets surface - minority affected	Complies	95.9	96.1	Complies	60min: Complies at S1 mean (n=6): 62% 120min: Complies at S1 mean (n=6): 83%	Complies at S1 mean (n=6): 88%	Complies	Compliant
Ke/ACT/11/25.06.08/110	20/120	Novartis Pharma-ceuticals Corporation, USA	F0768	2009 Aug	2	PUBLIC FACILITY/ HOSPITAL - Kisii District Hospital	Nyanza	Passed	Passed	Passed	OK	Crystals on tablets surface - minority affected	Complies	94.3	95.1	Complies	60min: Complies at S1 mean (n=6): 62% 120min: Complies at S1 mean (n=6): 84%	Complies at S1 mean (n=6): 92%	Complies	Compliant
Ke/ACT/11/01.07.08/118	20/120	Novartis Pharma-ceuticals Corporation, USA	F0756	2009 Aug	2	PUBLIC FACILITY/ HOSPITAL - Coast Provincial General Hospital	Coast	Passed	Passed	Passed	OK	Crystals on tablets surface - minority affected	Complies	93.9	94.4	Complies	60min: Complies at S1 mean (n=6): 57% 120min: Complies at S1 mean (n=6): 82%	Complies at S1 mean (n=6): 91%	Complies	Compliant

*Cm=Cameroon, Et=Ethiopia, Gh=Ghana, Ke=Kenya, Ng=Nigeria, Tz=Tanzania

Sample code and country of collection*	Strength (mg)	Manu-facturer	Batch num-ber	Exp. Date	Samp-ling level	Sample collection site	Region	MINILAB SCREENING				LABORATORY TESTING								
								Phys/ Vis inspec-tion (excl. label and leaflet)	**Disintegr ation**	**TLC**	**Conclusion** (label and leaflet defects not taken into account)	**Appearance**	**Identity**	**Assay 90.0 - 110.0%**		**Artemether-related substances**	**Dissolution**		**Uniformity of mass**	**Conclusion** (appearance not taken into account)
														Assay - artemether %	**Assay - lumefan-trine %**	Impurity A ≤ 1.5% Impurity B ≤ 1.0% Impurity C ≤ 0.5% Impurity D ≤ 0.3% Any other spot ≤ 0.2%	**Artemether NLT 40%(Q) in 60min NLT 60%(Q) in 180min**	**Lumefantrine NLT 60%(Q) in 45min**		
Ke/ACT/11/01.07.08/121	20/120	Novartis Pharma-ceuticals Corporation, USA	F0768	2009 Aug	2	PUBLIC FACILITY/ HOSPITAL - Port Reitz District Hospital	Coast	Passed	Passed	Passed	OK	Crystals on tablets surface - minority affected	Complies	94.1	93.3	Complies	60min: Complies at S1 mean (n=6): 52% 120min: Complies at S1 mean (n=6): 78%	Complies at S1 mean (n=6): 91%	Complies	Compliant
Ke/ACT/11/02.07.08/141	20/120	Novartis Pharma-ceuticals Corporation, USA	F0759	2009 Aug	2	PUBLIC FACILITY/ HOSPITAL - Kilifi District Hospital	Coast	Passed	Passed	Passed	OK	Crystals on tablets surface - majority affected, spots	Complies	96.5	95.2	Complies	60min: Complies at S1 mean (n=6): 60% 120min: Complies at S1 mean (n=6): 84%	Complies at S1 mean (n=6): 91%	Complies	Compliant
Ke/ACT/11/03.07.08/145	20/120	Novartis Pharma-ceuticals Corporation, USA	F0768	2009 Aug	2	PUBLIC FACILITY/ HOSPITAL - Manakani District Hospital	Coast	Passed	Passed	Passed	OK	OK	Complies	95.2	94.8	**Does not comply** Impurity A above limit	60min: Complies at S1 mean (n=6): 57% 120min: Complies at S1 mean (n=6): 85%	Complies at S1 mean (n=6): 92%	Complies	**Non-com-pliant**
Ke/ACT/11/01.07.08/136	20/120	Ipca Laboratories Ltd, India	BXN8002R	2009 Dec	2	PRIVATE/ WHOLESALER - Badar Pharmacy	Coast	Passed	Passed	Passed	OK	Tablets heavily mottled	Complies	96.7	93.5	Complies	60min: Complies at S1 mean (n=6): 96% 120min: Complies at S1 mean (n=6): 98%	Complies at S1 mean (n=6): 91%	Complies	Compliant
Ke/ACT/1/17.06.08/18	20/120	Universal Corporation Ltd, Kenya	820270	2010 Jan	1	PRIVATE/ MANUFACTURER - Universal Corporation	Central	Passed	Passed	Passed	OK	Tablets mottled, with crystals on surface, 1 with brown spot	Complies	100.6	97.2	Complies	60min: Complies at S1 mean (n=6): 71% 120min: Complies at S1 mean (n=6): 92%	Complies at S1 mean (n=6): 65%	Complies	Compliant
Ng/ACT/2/23-05-08/61	20/120	Beijing Novartis Pharma Ltd, China	X1127	2009 Jun	2	Private pharmacy, retail/ dispensing outlet - Lamco	North-West	Passed	Passed	passed	OK	Tablets faintly mottled, with crystals on surface-minority affected	Complies	93.8	97.5	Complies	60min: Complies at S1 mean (n=6): 58% 120min: Complies at S1 mean (n=6): 82%	Complies at S1 mean (n=6): 82%	Complies	Compliant
Ng/ACT/2/30—05-08/166	20/120	Beijing Novartis Pharma Ltd, China	X1152	2009 Aug	3	Informal - Man T. Group	South-East	Passed	Passed	Passed	OK	Tablets faintly mottled, with crystals on surface-minority affected	Complies	91.3	94.9	Complies	60min: Complies at S1 mean (n=6): 45% 120min: Complies at S1 mean (n=6): 73%	Complies at S1 mean (n=6): 77%	Complies	Compliant
Ng/ACT/2/28—05-08/138	20/120	Beijing Novartis Pharma Ltd, China	X1153	2009 Aug	3	Informal - Chris&Chris	South-West	Passed	Passed	Passed	OK	Tablets faintly mottled, with crystals on surface-minority affected	Complies	92.2	94.0	Complies	60min: Complies at S1 mean (n=6): 56% 120min: Complies at S1 mean (n=6): 83%	Complies at S1 mean (n=6): 73%	Complies	Compliant
Ng/ACT/2/29—05-08/185	20/120	Novartis Pharma-ceuticals Corporation, USA	F0650	2009 May	2	Ministry of Health	South-South	Passed	Passed	Passed	OK	Tablets faintly mottled, with crystals on surface-minority affected	Complies	91.3	94.4	Complies	60min: Complies at S1 mean (n=6): 58% 120min: Complies at S1 mean (n=6): 87%	Complies at S1 mean (n=6): 90%	Complies	Compliant (Testing completed 1 month after expiry)
Ng/ACT/1/27 – 05 – 08/98	20/120	Ecomed Pharma Ltd, Nigeria	83003001	2010 Feb	1	Manufacturer - Ecomed Pharma	South-West	Passed	Passed	Passed	OK	Tablets heavily mottled, with many crystals on surface	Complies	93.9	**Does not comply 85.9**	Complies	60min: Complies at S1 mean (n=6): 64% 120min: Complies at S1 mean (n=6): 74%	Complies at S1 mean (n=6): 88%	Complies	**Non-com-pliant**

*Cm=Cameroon, Et=Ethiopia, Gh=Ghana, Ke=Kenya, Ng=Nigeria, Tz=Tanzania

Sample code and country of collection*	Strength (mg)	Manu-facturer	Batch num-ber	Exp. Date	Samp-ling level	Sample collection site	Region	MINILAB SCREENING				LABORATORY TESTING								
								Phys/ Vis inspec-tion (excl. label and leaflet)	Disintegr ation	TLC	Conclusion (label and leaflet defects not taken into account)	Appearance	Identity	Assay 90.0 - 110.0%		Artemether-related substances	Dissolution		Uniformity of mass	Conclusion (appearance not taken into account)
														Assay - artemether %	Assay - lumefan-trine %	Impurity A ≤ 1.5% Impurity B ≤ 1.0% Impurity C ≤ 0.5% Impurity D ≤ 0.3% Any other spot ≤ 0.2%	Artemether NLT 40%(Q) in 60min NLT 60%(Q) in 180min	Lumefantrine NLT 60%(Q) in 45min		
Ng/ACT/1/27 – 05 – 08/91	20/120	GVS Labs, India	GO-10	2009 Jun	1	Importer - Greenlife Pharmaceuticals	South-West	Passed	Passed	Passed	OK	Tablets with uneven surface	Complies	93.9	94.6	Complies	60min: Complies at S1 mean (n=6): 47% 120min: Complies at S1 mean (n=6): 74%	Complies at S1 mean (n=6): 68%	Complies	Compliant
Ng/ACT/2/23—05-08/63	20/120	GVS Labs, India	GO-10	2009 Jun	2	Private pharmacy, retail/ dispensing outlet - Lamco	North-West	Passed	Passed	Passed	OK	Tablets with uneven surface, blisters dirty	Complies	92.4	93.0	Complies	60min: Complies at S1 mean (n=6): 44% 120min: Complies at S1 mean (n=6): 74%	Complies at S1 mean (n=6): 72%	Complies	Compliant
Ng/ACT/2/27—05-08/38	20/120	GVS Labs, India	GO-12	2009 Jun	2	Private wholesale/ retail outlet	South-West	Passed	Passed	Passed	OK	Tablets with uneven surface	Complies	97.3	95.1	Complies	60min: Complies at S1 mean (n=6): 47% 120min: Complies at S1 mean (n=6): 78%	Complies at S1 mean (n=6): 65%	Complies	Compliant
Ng/ACT/2/27—05-08/124	20/120	GVS Labs, India	GO-12	2009 Jun	2	Private retail/ dispensing outlet - Bolar	South-West	Passed	Passed	Passed	OK	Tablets with uneven surface	Complies	94.6	91.0	Complies	60min: Complies at S1 mean (n=6): 46% 120min: Complies at S1 mean (n=6): 78%	Complies at S2 mean (n=12): 61%	Complies	Compliant (Testing completed 1 month after expiry)
Ng/ACT/1/27 – 05 – 08/50	20/120	Jiangsu Yixing Forward Pharm. Factory, China	70910	2010 Sep	1	Importer - Geneith Pharmaceuticals	South-West	Passed	Passed	Passed	OK	Tablets with spots, uneven surface and crystals on surface - majority affected	Complies	**Does not comply 89.7**	**Does not comply 82.0**	Complies	60min: Complies at S1 mean (n=6): 69% 120min: Complies at S1 mean (n=6): 71%	Does not comply at S1 to S1 criteria mean (n=6): 56% min:54%; max:58%; not continued	Complies	**Non-compliant**
Ng/ACT/2/27—05-08/39	20/120	Jiangsu Yixing Forward Pharm. Factory, China	71217	2010 Dec	2	Private wholesale/ retail dispensing outlet - OSBud	South-West	Passed	Passed	Passed	OK	Tablets faintly mottled with crystals on surface	Complies	91.8	93.2	Complies	60min: Complies at S1 mean (n=6): 79% 120min: Complies at S1 mean (n=6): 94%	**Does not comply at S2 to S3 criteria** mean (n=12): 49% min:33%; max:70%	Complies	**Non-compliant**
Ng/ACT/2/24—05-08/22	20/120	Jiangsu Yixing Forward Pharm. Factory, China	71217	2010 Dec	3	Informal - Prince	North-Central	Passed	Passed	Passed	OK	Tablets mottled, with crystals-minority affected	Complies	92.4	91.7	Complies	60min: Complies at S1 mean (n=6): 76% 120min: Complies at S1 mean (n=6): 90%	Complies at S1 mean (n=6): 62%	Complies	Compliant
Ng/ACT/2/30-05-08/150	20/120	Jiangsu Yixing Forward Pharm. Factory, China	70320	2010 Mar	2	Private pharmacy, retail/ dispensing outlet - XL	South-East	Passed	Passed	Passed	OK	Tablets faintly mottled, with spots and crystals on surface	Complies	**Does not comply 85.5**	**Does not comply 71.0**	Complies	60min: Complies at S1 mean (n=6): 44% 120min: Complies at S1 mean (n=6): 74%	**Does not comply at S1 to S3 criteria** mean (n=6): 45% min:44%; max:46%	Complies	**Non-compliant**
Ng/ACT/2/29—05-08/107	20/120	Jiangsu Yixing Forward Pharm. Factory, China	70702	2010 Jul	2	Private retail/ dispensing outlet - Alpha	South-West	Passed	Passed	Passed	OK	Tablets mottled, with spots and crystals on surface	Complies	**Does not comply 89.1**	**Does not comply 87.3**	Complies	60min: Complies at S1 mean (n=6): 61% 120min: Complies at S1 mean (n=6): 83%	Complies at S1 mean (n=6): 73%	Complies	**Non-compliant**
Ng/ACT/2/27—05-08/36	20/120	Mac-leods pharma-ceuticals Ltd, India	LL702	2009 Aug	2	Private wholesale/ retail dispensing outlet	South-West	Passed	Passed	**Failed - Contaminant spot**	**Not OK**	Tablets mottled, with spots	**Does not comply** Artemether not detected	**Does not comply** Artemether not detected	92.2	**Does not comply -** Impurity A and impurity B (Dihydroartemisinin) above limits	**Does not comply at S1 to S3 criteria** Artemether not detected	Complies at S1 mean (n=6): 80%	Complies	**Non-compliant**

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Sample code and country of collection*	Strength (mg)	Manu-facturer	Batch num-ber	Exp. Date	Samp-ling level	Sample collection site	Region	MINILAB SCREENING				LABORATORY TESTING								
								Phys/ Vis inspec-tion (excl. label and leaflet)	Disintegr ation	TLC	Conclusion (label and leaflet defects not taken into account)	Appearance	Identity	Assay 90.0 - 110.0%		Artemether-related substances	Dissolution		Uniformity of mass	Conclusion (appearance not taken into account)
														Assay - artemether %	Assay - lumefan-trine %	Impurity A ≤ 1.5% Impurity B ≤ 1.0% Impurity C ≤ 0.5% Impurity D ≤ 0.3% Any other spot ≤ 0.2%	Artemether NLT 40%(Q) in 60min NLT 60%(Q) in 180min	Lumefantrine NLT 60%(Q) in 45min		
Ng/ACT/1/28 – 05 – 08/191	40/240	May & Baker Nigeria Plc; Nigeria	IY 415	2010 Mar	1	Private manufacturer / wholesaler - May & Baker	South-West	Passed	Passed	Passed	OK	Tablets mottled, one crushed in blister	Complies	99.3	96.3	Complies	60min: Complies at S1 mean (n=6): 44% 120min: Complies at S1 mean (n=6): 64%	**Does not comply at S2 to S3 criteria** mean (n=12): 42% min:40%; max:44%	Complies	**Non-com-pliant**
Ng/ACT/1/27 – 05 – 08/87	80/480	Mekophar Chemical pharma-ceutical Joint-Stock Company, Viet Nam	07001FX	2010 Aug	1	Importer - Neros Pharmaceuticals	South-West	Passed	Passed	Passed	OK	Tablets faintly mottled with chips	Complies	93.6	94.5	Complies	60min: Complies at S1 mean (n=6): 61% 120min: Complies at S1 mean (n=6): 78%	**Does not comply at S1 to S3 criteria** mean (n=6): 40% min:35%; max:55%	Complies	**Non-com-pliant**
Ng/ACT/2/27—05-08/32	20/120	Naxpar Lab Ltd, India	NA001	2010 Aug	2	Private wholesale/ retail dispensing outlet - OSBud	South-West	Passed	Passed	Passed	OK	Tablets mottled with faulty engraving	Complies	99.2	93.1	Complies	60min: Complies at S1 mean (n=6): 45% 120min: Complies at S1 mean (n=6): 76%	Complies at S2 mean (n=12): 60%	Complies	Compliant
Ng/ACT/2/27—05-08/122	20/120	Naxpar Lab Ltd, India	NA001	2010 Aug	2	Private retail/ dispensing outlet - Bolar	South-West	Passed	Passed	Passed	OK	Tablets mottled with faulty engraving	Complies	97.5	90.6	Complies	60min: Complies at S1 mean (n=6): 44% 120min: Complies at S1 mean (n=6): 74%	Complies at S1 mean (n=6): 82%	**Does not comply:** mean: 298.8mg min: 89.0%; max:102.4% 2 tabl outside ±5% **1 tabl outside ±10%**	**Non-com-pliant**
Ng/ACT/2/24—05-08/02	20/120	Naxpar Lab Ltd, India	NP001	2010 Jul	2	Private retail/ dispensing outlet - Pariflac	North-Central	Passed	**Failed (>1 hour)**	Passed	**Not OK**	Tablets extremely mottled, non-uniform colour yellow/light brown/yellowish brown, chipped	Complies	**Does not comply 29.0**	**Does not comply 81.5**	**Does not comply** impurity B (Dihydroartemisinin), impurity C above limits, impurity D (Alfa-artemether) spot identified, but cannot be quantitatively assessed	**60min: Does not comply at S1 to S3 criteria** no peak detected 120min: Does not comply at S1 to S3 criteria no peak detected	**Does not comply at S1 to S3 criteria** mean (n=6): 38% min:20%; max:67%	Complies	**Non-com-pliant**
Tz/ACT/1/13.05.08/02	20/120	Beijing Novartis Pharma Ltd, China	X1113	2009 May	1	Heko Pharmacy-Wholesale Pharmacy	Dar es Salaam	Passed	Passed	Passed	OK	OK	Complies	98.2	99.1	Complies	60min: Complies at S1 mean (n=6): 65% 120min: Complies at S1 mean (n=6): 87%	Complies at S1 mean (n=6): 94%	Complies	Compliant
Tz/ACT/2/15.05.08/05	20/120	Beijing Novartis Pharma Ltd, China	X1113	2009 May	2	MHS-MASAMA Hospital Kinondoni	Dar es Salaam	Passed	Passed	Passed	OK	OK	Complies	95.9	98.2	Complies	60min: Complies at S1 mean (n=6): 60% 120min: Complies at S1 mean (n=6): 85%	Complies at S1 mean (n=6): 95%	Complies	Compliant

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Sample code and country of collection*	Strength (mg)	Manu-facturer	Batch num-ber	Exp. Date	Samp-ling level	Sample collection site	Region	MINILAB SCREENING				LABORATORY TESTING								
								Phys/ Vis inspec-tion (excl. label and leaflet)	Disintegr ation	TLC	Conclusion (label and leaflet defects not taken into account)	Appearance	Identity	Assay 90.0 - 110.0%		Artemether-related substances	Dissolution		Uniformity of mass	Conclusion (appearance not taken into account)
														Assay - artemether %	Assay - lumefan-trine %	Impurity A ≤ 1.5% Impurity B ≤ 1.0% Impurity C ≤ 0.5% Impurity D ≤ 0.3% Any other spot ≤ 0.2%	Artemether NLT 40%(Q) in 60min NLT 60%(Q) in 180min	Lumefantrine NLT 60%(Q) in 45min		
Tz/ACT/2/28 .05.08/20	20/120	Beijing Novartis Pharma Ltd, China	X1112	2009 Jun	2	Arafa Pharmacy	Dar es Salaam	Passed	Passed	Passed	OK	OK	Complies	96.2	97.0	Complies	60min: Complies at S1 mean (n=6): 65% 120min: Complies at S1 mean (n=6): 89%	Complies at S1 mean (n=6): 81%	Complies	Compliant
Tz/ACT/2/19 .05.08/28	20/120	Beijing Novartis Pharma Ltd, China	X1113	2009 May	2	Kigoma Pharmacy	Kigoma	Passed	Passed	Passed	OK	OK	Complies	97.0	98.8	Complies	60min: Complies at S1 mean (n=6): 67% 120min: Complies at S1 mean (n=6): 87%	Complies at S1 mean (n=6): 80%	Complies	Compliant
Tz/ACT/2/26 .05.08/36	20/120	Beijing Novartis Pharma Ltd, China	X1113	2009 May	2	Agha Khan Medical Centre	Mwanza	Passed	Passed	Passed	OK	OK	Complies	95.0	95.7	Complies	60min: Complies at S1 mean (n=6): 63% 120min: Complies at S1 mean (n=6): 87%	Complies at S1 mean (n=6): 95%	Complies	Compliant
Tz/ACT/2/21 .05.08/38	20/120	Beijing Novartis Pharma Ltd, China	X1112	2009 May	2	Kayonza Enterprises ltd (Wholesale & Retail Pharmacy)	Mwanza	Passed	Passed	Passed	OK	OK	Complies	95.5	96.4	Complies	60min: Complies at S1 mean (n=6): 64% 120min: Complies at S1 mean (n=6): 88%	Complies at S1 mean (n=6): 83%	Complies	Compliant
Tz/ACT/2/20 .05.08/39	20/120	Beijing Novartis Pharma Ltd, China	X1041	2009 Jun	2	Pamba Pharmaceuti cals Co. ltd (Wholesale & Retail Pharmacy)	Mwanza	Passed	Passed	Passed	OK	OK	Complies	99.7	99.9	Complies	60min: Complies at S1 mean (n=6): 69% 120min: Complies at S1 mean (n=6): 87%	Complies at S1 mean (n=6): 79%	Complies	Compliant
Tz/ACT/1/19 .05.08/11	20/120	Novartis Pharma-ceuticals Corporat ion, USA	F0524	2009 Feb	1	Medical Stores Department (MSD)	Mtwara	Passed	Passed	Passed	OK	OK	Complies	96.1	97.7	Complies	60min: Complies at S1mean (n=6): 65% 120min: Complies at S1 mean (n=6): 88%	Complies at S1 mean (n=6): 104%	Complies	Compliant
Tz/ACT/2/13 .05.08/03	20/120	Novartis Pharma-ceuticals Corporat ion, USA	F0548	2009 Mar	2	Temeke District Hospital	Dar es Salaam	Passed	Passed	Passed	OK	OK	Complies	94.0	95.9	Complies	60min: Complies at S1 mean (n=6): 60% 120min: Complies at S1 mean (n=6): 85%	Complies at S1 mean (n=6): 104%	Complies	Compliant
Tz/ACT/2/20 .05.08/12	20/120	Novartis Pharma-ceuticals Corporat ion, USA	F0524	2009 Feb	2	Ligula Regional Hospital	Mtwara	Passed	Passed	Passed	OK	OK	Complies	95.1	96.4	Complies	60min: Complies at S1 mean (n=6): 62% 120min: Complies at S1 mean (n=6): 88%	Complies at S1 mean (n=6): 92%	Complies	Compliant
Tz/ACT/2/16 .05.08/24	20/120	Novartis Pharma-ceuticals Corporat ion, USA	F0597	2009 Apr	2	Matyazo Health Centre (FBO)	Kigoma	Passed	Passed	Passed	OK	OK	Complies	95.2	96.4	Complies	60min: Complies at S1 mean (n=6): 66% 120min: Complies at S1 mean (n=6): 89%	Complies at S1 mean (n=6): 90%	Complies	Compliant
Tz/ACT/2/21 .05.08/32	20/120	Novartis Pharma-ceuticals Corporat ion, USA	F0842	2009 Oct	2	Magu District Hospital	Mwanza	Passed	Passed	Passed	OK	OK	Complies	95.6	94.9	Complies	60min: Complies at S1 mean (n=6): 61% 120min: Complies at S1 mean (n=6): 88%	Complies at S1 mean (n=6): 90%	Complies	Compliant

*Cm=Cameroon, Et=Ethiopia, Gh=Ghana, Ke=Kenya, Ng=Nigeria, Tz=Tanzania

Sample code and country of collection*	Strength (mg)	Manu-facturer	Batch num-ber	Exp. Date	Samp-ling level	Sample collection site	Region	MINILAB SCREENING				LABORATORY TESTING								
								Phys/ Vis inspec-tion (excl. label and leaflet)	Disintegr ation	TLC	Conclusion (label and leaflet defects not taken into account)	Appearance	Identity	Assay 90.0 - 110.0%		Artemether-related substances	Dissolution		Uniformity of mass	Conclusion (appearance not taken into account)
														Assay - artemether %	Assay - lumefan-trine %	Impurity A ≤ 1.5% Impurity B ≤ 1.0% Impurity C ≤ 0.5% Impurity D ≤ 0.3% Any other spot ≤ 0.2%	Artemether NLT 40%(Q) in 60min NLT 60%(Q) in 180min	Lumefantrine NLT 60%(Q) in 45min		
Tz/ACT/2/20.05.08/34	20/120	Novartis Pharma-ceuticals Corporat ion, USA	F0548	2009 Mar	2	Bugando Medical Centre	Mwanza	Passed	Passed	Passed	OK	OK	Complies	94.9	95.0	Complies	60min: Complies at S1 mean (n=6): 66% 120min: Complies at S1 mean (n=6): 92%	Complies at S1 mean (n=6): 91%	Complies	Compliant
Tz/ACT/2/28.05.08/41	20/120	Novartis Pharma-ceuticals Corporat ion, USA	F0531	2009 Feb	2	Nzega District Hospital	Tabora	Passed	Passed	Passed	OK	OK	Complies	95.9	96.9	Complies	60min: Complies at S1 mean (n=6): 66% 120min: Complies at S1 mean (n=6): 87%	Complies at S1 mean (n=6): 71%	Complies	Compliant
Tz/ACT/2/28.05.08/46	20/120	Novartis Pharma-ceuticals Corporat ion, USA	F0624	2009 Apr	2	Nkinga Mission Hospital	Tabora	Passed	Passed	Passed	OK	OK	Complies	99.0	97.9	Complies	60min: Complies at S1 mean (n=6): 59% 120min: Complies at S1 mean (n=6): 81%	Complies at S1 mean (n=6): 95%	Complies	Compliant

*Cm=Cameroon, Et=Ethiopia, Gh=Ghana, Ke=Kenya, Ng=Nigeria, Tz=Tanzania

Appendix 3: Artesunate + amodiaquine co-packed samples - test results

Sample code and country of collection*	Strength (mg)	Manu-facturer	Batch number	Exp. Date	Samp-ling level	Sample collection site	Region	MINILAB SCREENING				LABORATORY TESTING								
								Phys/ Vis inspec-tion (excluding label and leaflet)	Disintegra-tion	TLC	Conclusion (label and leaflet defects not taken into account)	Appearance	Identity	Assay		Artesunate related substances No peak >1.0% Only 1 peak >0.5% Sum ≤2.0%	Dissolution		Uniformity of mass	Conclusion (appearance not taken into account)
														Arte-sunate 90.0 - 110.0 %	Amo-diaquine 93.0 - 107.0 %		Artesunate Not less than 80%(Q) in 45 min	Amodiaquine Not less than 75%(Q) in 30 min		
Cm/ACT/1/2 2.05.08/19	Tablets 100/300	Adams Pharmaceuti cal (ANHUI) Co Ltd, China	040906	2009 Aug	1	LABOREX (GROSSISTE PRIVE)	Centre	Passed	Passed	Passed	OK	OK	Complies	**Does not comply 89.4**	98.2	**Does not comply - 1 peak>1.0%; sum>2.0%** (6.7 min = 0.1%, 7.0 min = 1.8%, 26.7 min = 0.2%, sum = 2.1%)	Complies at S1 mean (n=6): 90%	Complies at S1 mean (n=6): 96%	Complies	**Non-compliant**
Cm/ACT/2/2 1.05.08/47	Tablets 100/300	Adams Pharmaceuti cal (ANHUI) Co Ltd, China	040906	2009 Aug	2	OFFICINE PRIVEE YDE	Centre	Passed	Passed	Passed	OK	Artesunate: minority of tablets with spots Amodiaquine: minority of tablets chipped	Complies	90.1	99.5	**Does not comply - 1 peak>1.0%; sum>2.0%** (7 min = 1.5%, 8.8 min = 0.3%, 21.5 min = 0.5%, 26.7 min = 0.2%, sum = 2.5%)	Complies at S1 mean (n=6): 90%	Complies at S1 mean (n=6): 99%	Complies	**Non-compliant**
Cm/ACT/2/2 7.05.08/126	Tablets 100/300	Adams Pharmaceuti cal (ANHUI) Co Ltd, China	040906	2009 Aug	2	OFFICINE PRIVEE DLA	Coast	Passed	Passed	Passed	OK	Artesunate: minority of tablets with spots Amodiaquine: minority of tablets chipped	Complies	**Does not comply 88.2**	98.0	**Does not comply - 1 peak>1.0%; sum>2.0%** (5.9 min = 0.2%, 7 min = 0.1%, 7.4 min = 2.0%, 15.9 min = 0.1%, 28.7 min = 0.2%, sum = 2.6%)	Complies at S1 mean (n=6): 86%	Complies at S1 mean (n=6): 99%	Complies	**Non-compliant**
Cm/ACT/1/1 3.05.08/04	Tablets 50/153	Cipla Ltd, India	G84425	2009 Nov	1	CENAME (CENTRALE NATIONALE D'ACHAT)	Centre	Passed	Passed	Passed	OK	OK	Complies	101.2	96.8	Complies (7.3 min = 0.6%)	Complies at S1 mean (n=6): 98%	Complies at S2 mean (n=12): 80%	Complies	Compliant
Cm/ACT/2/2 1.05.08/54	Tablets 50/153	Cipla Ltd, India	G84425	2009 Nov	2	OFFICINE PRIVEE YDE	Centre	Passed	Passed	Passed	OK	Artesunate: black spot on tablet Amodiaquine: chipped tablet	Complies	101.4	96.4	Complies (7 min = 0.5%, 21.5 min = 0.2% sum = 0.8%)	Complies at S1 mean (n=6): 96%	Complies at S1 mean (n=6): 92%	Complies	Compliant
Cm/ACT/2/2 1.05.08/55	Tablets 50/153	Cipla Ltd, India	G86565	2009 Jul	2	HOP. AD LUCEM YDE	Centre	Passed	Passed	Passed	OK	OK	Complies	98.5	96.3	Complies (7.3 min = 0.6%, 9.4 min = 0.4%, sum = 1.0%)	Complies at S1 mean (n=6): 95%	Complies at S1 mean (n=6): 95%	Complies	Compliant
Cm/ACT/2/2 4.05.08/106	Tablets 50/153	Cipla Ltd, India	G84424	2009 Nov	2	HOP. PUBLIC DE NEW BELL	Coast	Passed	Passed	Passed	OK	OK	Complies	99.0	96.9	Complies (7.4 min = 0.5%)	Complies at S1 mean (n=6): 99%	Complies at S1 mean (n=6): 92%	Complies	Compliant
Cm/ACT/2/2 6.05.08/136	Tablets 50/153	Cipla Ltd, India	G86565	2009 Jul	2	HOP.PUBLIC DIST. BUEA	South-West	Passed	Passed	Passed	OK	OK	Complies	98.1	96.3	Complies (7.4 min = 0.6%)	Complies at S1 mean (n=6): 94%	Complies at S1 mean (n=6): 90%	Complies	Compliant
Cm/ACT/1/1 4.05.08/12	Tablets 50/150	Guilin Pharmaceuti cal Co Ltd, China	LQ080302	2010 Feb	1	U.C. PHARM (GROSSISTE PRIVE)	Centre	Passed	Passed	Passed	OK	Artesunate: faint engraving on tablets Amodiaquine: OK	Complies	106.1	98.5	Complies (7.3 min = 0.2%)	Complies at S1 mean (n=6): 95%	Complies at S2 mean (n=12): 82%	Complies	Compliant

*Cm=Cameroon, Et=Ethiopia, Gh=Ghana, Ke=Kenya, Ng=Nigeria, Tz=Tanzania

Sample code and country of collection*	Strength (mg)	Manu-facturer	Batch number	Exp. Date	Samp-ling level	Sample collection site	Region	MINILAB SCREENING				LABORATORY TESTING								
								Phys/ Vis inspec-tion (excluding label and leaflet)	Disintegra-tion	TLC	Conclusion (label and leaflet defects not taken into account)	Appearance	Identity	Assay		Artesunate related substances No peak >1.0% Only 1 peak >0.5% Sum ≤2.0%	Dissolution		Uniformity of mass	Conclusion (appearance not taken into account)
														Arte-sunate 90.0 - 110.0 %	Amo-diaquine 93.0 - 107.0 %		Artesunate Not less than 80%(Q) in 45 min	Amodiaquine Not less than 75%(Q) in 30 min		
Cm/ACT/1/14.05.08/15	Tablets 50/153.1	Plethico Pharmaceuticals Ltd, India	6337	2009 Jul	1	U.C. PHARM (GROSSISTE PRIVE)	Centre	Passed	Passed	Passed	OK	Artesunate: tablets faintly mottled, with black spots Amodiaquine: tablets with faint engraving	Complies	95.1	**Does not comply 85.1**	**Does not comply - 4 peaks>0.5%; sum>2.0%** (5.9 min = 0.6%, 7 min = 0.3%, 7.4 min = 0.6%, 9.4 min = 0.7%, 10 min = 0.1%, 13.7 min = 0.3%, 15.3 min = 0.2%, 16.4 min = 0.8%, sum = 3.6%)	Complies at S1 mean (n=6): 91%	Does not comply at S1 to S1 criteria mean (n=6): 76% min:73%; max: 80%; not continued	Complies	**Non-compliant**
Gh/ACT/2/25-05-08/73/S	Tablets 100/300	Atlantic Pharmaceutical Ltd, Ghana	7005	2010 Dec	3	Informal Market (Agbogloshie market, Accra)	Southern	Passed	Passed	**Failed - Contaminant spot in ART**	**Not OK**	Artesunate: tablets with uneven coating, slight yellow spots, flaws Amodiaquine: Tablets with dark spots, foreign particles embedded, 1 tablet broke on opening blister	Complies	**Does not comply 76.7**	96.4	**Does not comply - 3 peaks>1.0%; 4 peaks>0.5%; sum>2.0%** (6 min = 27.7%, 7 min = 2.3%, 12.7 min = 0.8%, 15.3 min = 2.3%, sum = 33.1%)	Does not comply at S1 to S1 criteria mean (n=6): 70% min:66%; max: 78%; not continued	Complies at S1 mean (n=6): 89%	Artesunate: Complies **Amodiaquine: Does not comply** mean: 518.0mg min: 90.1%; max:109.7% **3 tabl outside ±5%** no tabl outside ±10%	**Non-compliant**
Gh/ACT/2/14-05-08/17/S	Tablets 50/153.1	Bliss GVS Pharma Ltd, India	KF-03	2010 Nov	2	Regional Medical Stores (Volta Region, Ho)	Southern	Passed	Passed	Passed	OK	Artesunate: tablets surface not smooth, with flaws Amodiaquine: tablets with spots, flaws	Complies	95.1	100.0	**Does not comply - 1 peak>1.0%; sum>2.0%** (7 min = 1.6%, 13.6 min = 0.1%, 14.7 min = 0.2%, 21.8 min = 0.2%, 26 min = 0.2%, sum = 2.3%)	Complies at S1 mean (n=6): 95%	Complies at S1 mean (n=6): 105%	Complies	**Non-compliant**
Gh/ACT/2/15-05-08/28/S	Tablets 100/300	Danadams Pharmaceutical Industry Ltd, Ghana	0704019	2010 Apr	2	Private Hospital (Miracle Life, Ho)	Southern	Passed	Passed	Passed	OK	Artesunate: uneven coating, foreign particles embedded in tablets, dark particles on surface, flaws Amodiaquine: uneven coating, tablets with dark spots, flaws, stick to blister	Complies	95.0	99.2	**Does not comply - 1 peak >1.0%** (7 min = 1.3%, 26 min = 0.2%, sum = 1.5%)	Complies at S1 mean (n=6): 87%	Complies at S1 mean (n=6): 92%	**Artesunate: Does not comply** mean: 289.7mg min: 94.9%; max:105.9% **3 tabl outside ±5%** no tabl outside ±10% Amodiaquine: Complies	**Non-compliant**
Gh/ACT/2/16-05-08/43/M	Tablets 100/300	Danadams Pharmaceutical Industry Ltd, Ghana	0704019	2010 Apr	2	Quasi-Govt Hospital (Holy Family Hospital, Tekyiman)	Middle	Passed	Passed	Passed	OK	Artesunate: tablets with uneven coating, flaws Amodiaquine: tablets with uneven coating, flaws, stick to blister	Complies	91.4	97.4	Complies (6 min = 0.2%, 7.4 min = 0.8%, 29.2 min = 0.1%, sum = 1.1%)	Does not comply at S1 to S1 criteria mean (n=6): 83% min:81%; max: 85%; not continued	Complies at S1 mean (n=6): 89%	Complies	Inconclusive
Gh/ACT/1/15-05-08/30	Tablets 50/153.1	Ipca Laboratories Ltd, India	ARS 7020F	2010 Nov	1	Medical Store-public (Central medical store, Tema)	Southern	Passed	Passed	Passed	OK	Artesunate: Tablets with yellow spots, flaws Amodiaquine: spots, tablets chipped, with spots, flaws	Complies	95.8	96.0	Complies (7.4min = 0.5%, 9.6min=0.1%, 13min=0.1%, 13.9min=0.7%, 15.7min=0.4%, 29.2 min =0.1%, sum = 1.9%)	Complies at S1 mean (n=6): 95%	Complies at S1 mean (n=6): 99%	Complies	Compliant

*Cm=Cameroon, Et=Ethiopia, Gh=Ghana, Ke=Kenya, Ng=Nigeria, Tz=Tanzania

Sample code and country of collection*	Strength (mg)	Manu-facturer	Batch number	Exp. Date	Samp-ling level	Sample collection site	Region	MINILAB SCREENING				LABORATORY TESTING								
								Phys/ Vis inspec-tion (excluding label and leaflet)	Disintegra-tion	TLC	Conclusion (label and leaflet defects not taken into account)	Appearance	Identity	Assay		Artesunate related substances No peak >1.0% Only 1 peak >0.5% Sum ≤2.0%	Dissolution		Uniformity of mass	Conclusion (appearance not taken into account)
														Arte-sunate 90.0 - 110.0 %	Amo-diaquine 93.0 - 107.0 %		Artesunate Not less than 80%(Q) in 45 min	Amodiaquine Not less than 75%(Q) in 30 min		
Gh/ACT/2/14-05-08/10/S	Tablets 50/153.1	Ipca Laboratories Ltd, India	ARS 7012F	2010 Oct	2	Regional Medical Store-public (Eastern Region, Koforiduai)	Southern	Passed	Passed	Passed	OK	Artesunate: tablets with dark spots, flaws Amodiaquine: tablets with flaws, spots	Complies	95.0	102.5	Complies (7min = 0.5%, 12.6min = 0.3%, 26min = 0.1%, sum = 0.9%)	Complies at S1 mean (n=6): 105%	Complies at S1 mean (n=6): 96%	Complies	Compliant
Gh/ACT/2/13-05-08/04B/M	Tablets 50/153.1	Ipca Laboratories Ltd, India	ARS 7020F	2010 Nov	2	Regional Medical Store-public (Ashanti Region, Adum-Kumasi)	Middle	Passed	Passed	Passed	OK	Artesunate: tablets with small yellow spots, foreign particles, flaws Amodiaquine: tablets chipped, faintly mottled, with flaws	Complies	97.9	98.5	Complies (7 min = 0.4%, 12.7 min = 0.4%, 14.8 min = 0.5%, 26 min = 0.5%, sum=1.8%)	Complies at S1 mean (n=6): 99%	Complies at S1 mean (n=6): 91%	Complies	Compliant
Gh/ACT/2/13-05-08/04C/M	Tablets 50/153.1	Ipca Laboratories Ltd, India	ARS 7020F	2010 Nov	2	Regional Medical Store-public (Ashanti Region, Adum-Kumasi)	Middle	Passed	Passed	Passed	OK	Artesunate: tablets with small yellow spots, flaws Amodiaquine: tablets with very small spots, flaws	Complies	99.0	97.3	Complies (7 min = 0.4%, 12.7 min = 0.4%, 14.8 min = 0.5%, 26 min = 0.5%, sum = 1.8%)	Complies at S1 mean (n=6): 95%	Complies at S1 mean (n=6): 91%	**Artesunate: Does not comply** mean: 276.2mg min: 94.3%; max:105.8% **3 tabl outside ±5%** no tabl outside ±10% Amodiaquine: Complies	**Non-compliant**
Gh/ACT/2/15-05-08/17/N/UE	Tablets 50/153.1	Ipca Laboratories Ltd, India	ARS 7020F	2010 Nov	2	Regional Medical Store-public(Upper East, Bolgatanga)	Northern	Passed	Passed	Passed	OK	Artesunate: tablets with small yellow spots, flawsAmodiaquine: tablets with very small spots, flaws	Complies	94.2	98.1	Complies (7 min = 0.5%, 8.7 min = 0.1%, 12.7 min = 0.4%, 14.8 min = 0.6%, 26 min = 0.2%, sum = 1.8%)	Complies at S1 mean (n=6): 93%	Complies at S1mean (n=6): 99%	Complies	Compliant
Gh/ACT/2/15-05-08/22/N/NR	Tablets 50/153.1	Ipca Laboratories Ltd, India	ARS 7020F	2010 Nov	2	Quasi Govt/Mission (Baptist Medical Centre, Nerilegu)	Northern	Passed	Passed	Passed	OK	Artesunate: tablets with small yellow spots, flaws Amodiaquine: tablets with flaws	Complies	99.0	99.8	Complies (7 min = 0.4%, 12.7 min = 0.4%, 14.8 min = 0.5%, 26 min = 0.1%, sum = 1.4%)	Complies at S1 mean (n=6): 101%	Complies at S1 mean (n=6): 98%	Complies	Compliant
Gh/ACT/2/15-O5-08/19/N/UE	Tablets 50/153.1	Ipca Laboratories Ltd, India	ARS 7022F	2010 Nov	2	Quasi Govt/Mission (Bawku Presby Hospital)	Northern	Passed	Passed	Passed	OK	Artesunate: tablets with small yellow spots, flaws Amodiaquine: tablets with flaws	Complies	96.5	94.8	Complies (7 min = 0.5%, 8.8 min = 0.1%, 12.8 min = 0.3%, 14.8 min = 0.6%, 26 min = 0.2%, sum = 1.7%)	Complies at S1 mean (n=6): 89%	Complies at S1 mean (n=6): 91%	Complies	Compliant
Gh/ACT/2/13-05-08/04A/M	Tablets 50/153	Strides Arcolab Ltd, India	ART-7205024 AMO-7204871	2009 Nov	2	Regional Medical Store-public (Ashanti Region, Adum-Kumasi)	Middle	Passed	Passed	Passed	OK	Artesunate: tablets faintly mottled, with small spots and flaws Amodiaquine: tablets faintly mottled, with small spots and flaws	Complies	100.4	97.6	Complies (7 min = 0.3%)	Complies at S1 mean (n=6): 99%	Complies at S1 mean (n=6): 93%	Complies	Compliant

*Cm=Cameroon, Et=Ethiopia, Gh=Ghana, Ke=Kenya, Ng=Nigeria, Tz=Tanzania

Sample code and country of collection*	Strength (mg)	Manu-facturer	Batch number	Exp. Date	Samp-ling level	Sample collection site	Region	MINILAB SCREENING				LABORATORY TESTING								
								Phys/ Vis inspec-tion (excluding label and leaflet)	Disintegra-tion	TLC	Conclusion (label and leaflet defects not taken into account)	Appearance	Identity	Assay		Artesunate related substances No peak >1.0% Only 1 peak >0.5% Sum ≤2.0%	Dissolution		Uniformity of mass	Conclusion (appearance not taken into account)
														Arte-sunate 90.0 - 110.0 %	Amo-diaquine 93.0 - 107.0 %		Artesunate Not less than 80%(Q) in 45 min	Amodiaquine Not less than 75%(Q) in 30 min		
Gh/ACT/2/14-05-08/22M	Tablets 50/153	Strides Arcolab Ltd, India	ART-7204967 AMQ-7204870	2009 Oct	2	Govt. Health Centre-Public (Offinso Health Centre)	Middle	Passed	Passed	Passed	OK	Artesunate: tablets faintly mottled, with very small spots, flaws Amodiaquine: tablets faintly mottled, with small spots, flaws	Complies	98.4	97.3	Complies (7 min = 0.3%, 18.5 min = 0.2%, 21.0 min = 0.1%, sum = 0.6%)	Complies at S1 mean (n=6): 93%	Complies at S1 mean (n=6): 94%	Complies	Compliant
Ke/ACT/1/16.06.08/12	Tablets 50/150	Cosmos Ltd, Kenya	72452	2009 Dec	1	PRIVATE/ MANUFACTURER - Cosmos	Central	Passed	Passed	Passed	OK	OK	Complies	100.0	99.7	**Does not comply - 2 peaks>1.0%; sum>2.0%** (7.4 min = 1.1%, 10.2 min = 0.2%, 15.7 min = 1.1%, sum = 2.4%)	Complies at S1 mean (n=6): 91%	Does not comply at S2 to S2 criteria mean (n=12): 71% min:60%; max: 79%; not enough sample to continue	Complies	**Non-compliant**
Ng/ACT/1/27 – 05 – 08/89	Tablets 200/600	Adams Pharmaceutical (ANHUI) Co Ltd, China	11006	2010 Dec	1	Importer - Geneith Pharmaceuticals	South-West	Passed	Passed	**Failed - Contaminant spot**	**Not OK**	Artesunate: OK Amodiaquine tablets with black spots	Complies	**Does not comply 89.4**	95.9	**Does not comply - 2 peaks>1.0%; sum>2.0%** (7.45 min = 2.6%, 15.7 min = 0.1%, 20.8 min = 1.5%, sum = 4.2%)	**Does not comply at S1 to S3 criteria** mean (n=6): 6% min:6%; max: 7%	Complies at S1 mean (n=6): 92%	**Artesunate: Does not comply** mean: 287.0mg min: 93.8%; max:106.6% **4 tabl outside ±5%** no tabl outside ±10% **Amodiaquine: Does not comply** mean: 970.0mg min: 92.5%; max:110.5% **11 tabl outside ±5%** **2 tabl outside ±10%**	**Non-compliant**
Ng/ACT/1/27 – 05 – 08/90	Powder 50/150	Adams Pharmaceutical (ANHUI) Co Ltd, China	40108	2010 Dec	1	Importer - Geneith Pharmaceuticals	South-West	Passed	Not applicable	**Failed - Contaminant spot**	**Not OK**	OK	Complies	92.7	106.1	**Does not comply - 2 peaks>1.0%; sum>2.0%** (6.8min=2.8%, 13.5min=0.3%, sum = 3.1%)	Not performed for powder	Not performed for powder	Complies	**Non-compliant**
Ng/ACT/1/27-05-08/102	Tablets 100/300	Baader Schulz Lab, India	PL-701	2010 Sep	1	Federal medical store	South-West	Passed	Passed	**Failed - No ART spot**	**Not OK**	Artesunate: tablets with faulty engraving, off-white colour Amodiaquine: tablets heavily mottled, with chips	Complies	99.8	106.7	**Does not comply - 2 peaks>1.0%; sum>2.0%** (6 min = 0.2%, 7.4 min = 1.3%, 9.5 min = 1.2%, 12 min = 0.3%, 14 min = 0.2%, 16.6 min = 0.1%, 29 min = 0.2%, sum = 3.5%)	Complies at S1 mean (n=6): 99%	Complies at S1 mean (n=6): 102%	Artesunate: Complies **Amodiaquine: Does not comply** mean: 477.8mg min: 92.8%; max:103.3% **5 tabl outside ±5%** no tabl outside ±10%	**Non-compliant**

*Cm=Cameroon, Et=Ethiopia, Gh=Ghana, Ke=Kenya, Ng=Nigeria, Tz=Tanzania

Sample code and country of collection*	Strength (mg)	Manu-facturer	Batch number	Exp. Date	Samp-ling level	Sample collection site	Region	MINILAB SCREENING				LABORATORY TESTING								
								Phys/ Vis inspec-tion (excluding label and leaflet)	Disintegra-tion	TLC	Conclusion (label and leaflet defects not taken into account)	Appearance	Identity	Assay		Artesunate related substances No peak >1.0% Only 1 peak >0.5% Sum ≤2.0%	Dissolution		Uniformity of mass	Conclusion (appearance not taken into account)
														Arte-sunate 90.0 - 110.0 %	Amo-diaquine 93.0 - 107.0 %		Artesunate Not less than 80%(Q) in 45 min	Amodiaquine Not less than 75%(Q) in 30 min		
Ng/ACT/1/27—05-08/103	Tablets 50/153.1	Baader Schulz Lab, India	PK-701	2010 Sep	1	Federal medical store	South-West	Passed	Passed	**Failed - Contaminant spot**	**Not OK**	Artesunate: tablets with uneven surface, chips Amodiaquine: tablets with powder on surface	Complies	100.0	**Does not comply 115.0**	**Does not comply - 2 peaks>1.0%; sum>2.0%** (6 min = 0.2%, 7.4 min = 2.3%, 12 min = 0.5%, 14 min = 0.1%, 29 min = 0.4%, sum = 3.5%)	Complies at S1 mean (n=6): 92%	**Result out of expectation, corresponding to assay** mean (n=6): 120% min:117%; max: 122%; not continued	**Artesunate: Does not comply** mean: 248.2mg min: 83.3%; max:102.9% **1 tabl outside ±10%** Amodiaquine: Complies	**Non-compliant**
Ng/ACT/1/27 – 05 – 08/101	Tablets 50/150	Madras Pharmaceuticals, India	MD 616	2009 Sep	1	Federal medical store	South-West	Passed	Passed	**Failed - Contaminant spot**	**Not OK**	Artesunate: tablets uneven surface, heavily mottled, off-white colour Amodiaquine: tablets with spots	Complies	93.7	94.1	**Does not comply - 2 peaks>1.0%; sum>2.0%** (7.4 min = 1.1%, 8.9 min = 0.2%, 14.5 min = 1.2%, 15.8 min = 0.1%, 18 min = 0.1%, 20.7 min = 0.2%, sum = 2.9%)	Complies at S1 mean (n=6): 90%	Complies at S2 mean (n=12): 83%	Complies	**Non-compliant**
Ng/ACT/2/30—05-08/172	Tablets 50/150	Madras Pharmaceuticals, India	MD 615	2009 Sep	3	Informal - Man T. Group	South-East	Passed	Passed	**Failed - Contaminant spot**	**Not OK**	Artesunate: tablets with uneven surface, non-consistent colour Amodiaquine: tablets mottled	Complies	97.2	96.9	**Does not comply - 1 peak>1.0%; sum>2.0%** (7.3 min = 1.6%, 8.6 min = 0.2%, 9.4 min = 0.3%, 13.9 min = 0.6%, 15.7 min = 0.1%, 16.7 min = 0.2%, 21.5 min = 0.1%, sum = 3.1%)	Complies at S1 mean (n=6): 92%	Complies at S1 mean (n=6): 102%	Complies	**Non-compliant**
Ng/ACT/1/27 – 05 – 08/86	Tablets 50/153	Mekophar Chemical Pharmaceutical Joint-Stock Company, Viet Nam	06002FX	2009 Oct	1	Importer - Neros Pharmaceuticals	South-West	Passed	Passed	**Failed - Contaminant spots**	**Not OK**	Artesunate: tablets with faulty engraving and small chip Amodiaquine: tablets with faulty engraving	Complies	100.6	105.0	Complies (7.4 min = 0.6%, 9.6 min = 0.1%, sum = 0.7%)	Complies at S1 mean (n=6): 97%	Complies at S1 mean (n=6): 101%	Complies	Compliant
Ng/ACT/2/23—05-08/62	Tablets 50/153.1	Saga Laboratories Ltd, India	1006	2009 Sep	2	Private pharmacy, retail/ dispensing outlet - Lamco	North-West	Passed	**Failed (ART 32 min)**	Passed	**Not OK**	Both tablets mottled, with spots	Complies	95.0	95.1	**Does not comply - 2 peaks>0.5%; sum>2.0%** (7 min = 0.1%, 7.4 min = 0.9%, 7.8 min = 0.2%, 15.2 min = 0.1%, 15.8 min = 1.0%, 29.3 min = 0.2%, sum = 2.4%)	**Does not comply at S1 to S3 criteria** mean (n=6): 65% min:38%; max:86%	Complies at S1 mean (n=6): 98%	Complies	**Non-compliant**
Ng/ACT/2/21—05-08/20	Tablets 50/153.1	Saga Laboratories Ltd, India	1006	2009 Sep	2	Private wholesale/retail dispensing outlet - IG Medical Complex	North-Central	Passed	Passed	Passed	OK	Both tablets mottled	Complies	96.4	94.0	**Does not comply - 2 peaks>0.5%; sum>2.0%**(7.3 min = 1.0%, 7.9 min = 0.2%, 15.7 min = 0.9%, 30 min = 0.2%, sum = 2.3%)	**Does not comply at S1 to S3 criteria** mean (n=6): 26% min:24%; max:28%	Complies at S1 mean (n=6): 98%	Complies	**Non-compliant**

*Cm=Cameroon, Et=Ethiopia, Gh=Ghana, Ke=Kenya, Ng=Nigeria, Tz=Tanzania

Sample code and country of collection*	Strength (mg)	Manu-facturer	Batch number	Exp. Date	Samp-ling level	Sample collection site	Region	MINILAB SCREENING				LABORATORY TESTING								
								Phys/ Vis inspec-tion (excluding label and leaflet)	Disintegra-tion	TLC	Conclusion (label and leaflet defects not taken into account)	Appearance	Identity	Assay		Artesunate related substances No peak >1.0% Only 1 peak >0.5% Sum ≤2.0%	Dissolution		Uniformity of mass	Conclusion (appearance not taken into account)
														Arte-sunate 90.0 - 110.0 %	Amo-diaquine 93.0 - 107.0 %		Artesunate Not less than 80%(Q) in 45 min	Amodiaquine Not less than 75%(Q) in 30 min		
Ng/ACT/2/23-05-08/76	Tablets 200/600	Swiss Pharma Nigeria Ltd, Nigeria	L27150	2010 Sep	2	Public hospital/ retail outlet - Aminu Kano Teaching	North-West	Passed	Passed	Passed	OK	Artesunate: tablets heavily mottled, with faulty engraving, non-uniform colour Amodiaquine: tablets heavily mottled	Complies	100.4	97.5	Complies (7.4 min = 0.7%, 13 min = 0.2%, sum = 0.9%)	Not performed; not enough sample	Not performed; not enough sample	Not performed; not enough sample	Compliant
Ng/ACT/2/27—05-08/114	Tablets 200/600	Swiss Pharma Nigeria Ltd, Nigeria	L27150	2010 Sep	2	Private pharmacy, retail outlet - Juli	South-West	Passed	Passed	Passed	OK	Artesunate: tablets mottled, with faulty engraving Amodiaquine: tablets heavily mottled	Complies	105.5	94.3	Complies (7 min = 0.9%, 9.7 min = 0.1%, 16.9 min = 0.1%, sum = 1.1%)	Not performed; not enough sample	Not performed; not enough sample	Not performed; not enough sample	Compliant
Ng/ACT/2/28—05-08/134	Tablets 200/600	Swiss Pharma Nigeria Ltd, Nigeria	L27150	2010 Sep	3	Informal - Namtex	South-West	Passed	**Failed (AMO 40 min)**	Passed	**Not OK**	Artesunate: tablets mottled, with faulty engraving, chipped Amodiaquine: tablets heavily mottled, with spots, chipped	Complies	102.2	98.1	Complies (7.2 min = 0.7%, 12.4 min = 0.4%, sum = 1.1%)	Complies at S1 mean (n=6): 106%	Complies at S1 mean (n=6): 101%	Complies	Compliant
Ng/ACT/1/28 – 05 – 08/195	Tablets 50/200	Swiss Pharma Nigeria Ltd, Nigeria	L27108	2010 Jun	1	Private manufacturer/ wholesaler - Swiss Pharma	South-West	Passed	Passed	Passed	OK	Artesunate: tablets mottled, with faulty engraving Amodiaquine: tablets with spots	Complies	102.8	96.4	Complies (7.4 min = 0.8%, 15.8min = 0.2%, sum = 1.0%)	Complies at S1 mean (n=6): 100%	Complies at S1 mean (n=6): 100%	Complies	Compliant
Ng/ACT/2/28—05-08/136	Tablets 50/200	Swiss Pharma Nigeria Ltd, Nigeria	L27108	2010 Jun	3	Informal - Namtex	South-West	Passed	Passed	**Failed - Contaminant spot**	**Not OK**	Artesunate: tablets heavily mottled Amodiaquine: OK	Complies	100.0	94.5	**Does not comply - 2 peaks>0.5%** (7.3 min = 0.7%, 12.3 min = 0.6%, 15.3 min = 0.1%, sum = 1.4%)	Complies at S1 mean (n=6): 102%	Complies at S1 mean (n=6): 98%	Complies	**Non-compliant**

*Cm=Cameroon, Et=Ethiopia, Gh=Ghana, Ke=Kenya, Ng=Nigeria, Tz=Tanzania

Appendix 4: Artesunate/amodiaquine fixed dose combination samples – test results

Sample code and country of collection*	Product Type and Strength (mg)	Manu-facturer	Batch number	Exp. Date	Sampling level	Sample collection site	Region	MINILAB SCREENING				LABORATORY TESTING								
								Phys/Vis inspection	Dis-integration	TLC	Conclusion of Minilab testing (label and leaflet defects not taken into account)	Appearance	Identity	Assay 90.0 - 110.0 %		Artesunate related substances (tested without specifications)	Dissolution Not less than 75% (Q) in 30 min		Uniformity of mass	Conclusion (appearance not taken into account)
														Arte-sunate %	Amodia-quine %		Artesunate	Amodiaquine		
Cm/ACT/2/2 1.05.08/28	Tablets 50/200	Kamala Overseas, India	VYA1-02	2009 Dec	3	Marché informel NSAM EFOULAN YDE	Centre	Passed	Passed	**Failed Artesunate** - lower content and second spot	**Not OK**	Tablets faintly mottled	Complies	**Does not comply 82.5**	97.0	Dihydroartemisinin: 3.8% Artemisinin:0.1% Glycan: n.d.	**Does not comply at S1 to S3 criteria** mean (n=6): 53% min:37%; max: 66%	Complies at S1 mean (n=6): 93%	Complies	**Non-compliant**
Cm/ACT/2/2 4.05.08/99	Tablets 50/200	Kamala Overseas, India	VYA1-02	2009 Dec	3	Marché informel NEWBEL sous parasoleil	Coast	Passed	Passed	**Failed Artesunate** - 80% content and second spot	**Not OK**	Tablets chipped, mottled, with spots and crystals on the surface	Complies	**Does not comply 73.1**	97.2	Dihydroartemisinin: 11.6% Artemisinin:0.2% Glycan: 0.1%	**Does not comply at S1 to S3 criteria** mean (n=6): 53% min:50%; max: 56%	Complies at S1 mean (n=6): 97%	Complies	**Non-compliant**
Cm/ACT/2/2 7.05.08/152	Tablets 50/200	Kamala Overseas, India	VYA1-02	2009 Dec	3	LIMBE INFORMAL M.	South-West	Passed	Passed	**Failed** - Amount not satis-factory, additional spot	**Not OK**	Tablets with spots and crystals on the surface	Complies	**Does not comply 72.4**	97.4	Dihydroartemisinin: 12.2% Artemisinin:0.2% Glycan: 0.1%	Not performed - not enough sample	Not performed - not enough sample	Complies	**Non-compliant**
Ng/ACT/1/28 – 05 – 08/200	Caplets 100/306.2	Emzor Pharm Ind. Ltd, Nigeria	1064M	2011 Mar	1	Private manufacturer / wholesaler - Emzor Pharm	South-West	Passed	Passed	**Failed** - Contaminant spot	**Not OK**	Chipped engraving, powder on caplets and in blister	Complies	**Does not comply 87.2**	99.6	Dihydroartemisinin: 8.5% Artemisinin:0.1% Glycan: 0.2%	Does not comply at S1 to S1 criteria mean (n=6): 64% min:64%; max: 65%; not continued	Complies at S1 mean (n=6): 101%	Complies	**Non-compliant**
Ng/ACT/2/23 —05-08/80	Caplets 100/306.2	Emzor Pharm Ind. Ltd, Nigeria	305K	2010 Jan	2	Private hospital/ dispensing outlet - International Clinics&Hospitals	North-West	Passed	Passed	**Failed** - Contaminant spot	**Not OK**	Caplets heavily mottled with spots	Complies	94.1	92.9	Dihydroartemisinin: 2.5% Artemisinin:0.1% Glycan: n.d.	**Does not comply at S1 to S3 criteria** mean (n=6): 46% min:35%; max: 57%	Complies at S1 mean (n=6): 93%	Complies	**Non-compliant**
Ng/ACT/2/29 —05-08/108	Caplets 100/306.2	Emzor Pharm Ind. Ltd, Nigeria	3134K	2010 Jul	2	Private retail/ dispensing outlet - Alpha	South-West	Passed	Passed	**Failed** - Contaminant spot	**Not OK**	Spots and powder on caplets, powder in blister	Complies	**Does not comply 82.5**	98.6	Dihydroartemisinin: 2.0% Artemisinin:8.4% Glycan: n.d.	Does not comply at S1 to S2 criteria mean (n=6): 62% min:59%; max: 70%; not continued	Complies at S1 mean (n=6): 105%	Complies	**Non-compliant**
Ng/ACT/2/24 —05-08/08	Tablets 50/150	Emzor Pharm Ind. Ltd, Nigeria	5324K	2010 Sep	2	Private pharmacy, retail/ dispensing outlet - Noro	North-Central	Passed	Passed	**Failed** - Contaminant spot	**Not OK**	Tablets faintly mottled with spots	Complies	**Does not comply 87.8**	101.5	Dihydroartemisinin: 2.0% Artemisinin:8.4% Glycan: n.d.	Does not comply at S1 to S1 criteria mean (n=6): 67% min:64%; max: 68%; not continued	Complies at S1 mean (n=6): 105%	Complies	**Non-compliant**
Ng/ACT/1/27 – 05 – 08/88	Tablets 200/600	Mercury Laboratories Ltd, India	815901	2011 Feb	1	Importer - Diamond Remedie	South-West	Passed	Passed	Passed	OK	Tablets with spots and chipped	Complies	94.4	105.6	Dihydroartemisinin: 2.0% Artemisinin:0.1% Glycan: n.d.	**Does not comply at S1 to S3 criteria** mean (n=6): 61% min:28%; max: 87%	Complies at S1 mean (n=6): 93%	Complies	**Non-compliant**
Ng/ACT/2/27 —05-08/99	Powder 50/150	Rajat Pharmachem Ltd, India	RA70001	2010 Jun	2	Federal medical store	South-West	Passed	Not applicable	**Failed - Contaminant spot**	**Not OK**	OK	Complies	92.7	**Does not comply 76.4**	Dihydroartemisinin: 2.1% Artemisinin:6.9% Glycan: n.d.	Not performed for powder	Not performed for powder	Not performed	**Non-compliant**

*Cm=Cameroon, Et=Ethiopia, Gh=Ghana, Ke=Kenya, Ng=Nigeria, Tz=Tanzania

Appendix 5: Sulfadoxine/pyrimethamine samples – test results

Sample code and country of collection*	Manufacturer	Batch number	Exp. Date	Sampling level	Sample collection site	Region	MINILAB SCREENING				LABORATORY TESTING							
							Phys/ Vis inspec-tion	Disintegra-tion	TLC	Conclusion (label and leaflet defects not taken into account)	Appearance	Identity	Assay 90.0 - 110.0 %		Dissolution Not less than 60% (Q) in 30 min		Uniformity of mass	Conclusion (appear-ance not taken into account)
													Sulfa-doxine %	Pyri-methamine %	Sulfadoxine	Pyrimethamine		
Cm/SP/1/22.0 5.08/16	Ajanta Pharma Limited, Mauritius	AG0136	2010 Mar	1	LABOREX (GROSSISTE PRIVE)	Centre	Passed	Passed	Passed	OK	Powder on surface of tablets, 2 with faint spots- minority affected	Complies	100.5	97.0	Complies at S1 mean (n=6): 99%	Complies at S1 mean (n=6): 89%	**Does not comply:** mean: 663.7mg min: 87.1%; max: 106.4% **4 tabl outside ±5% 1 tabl outside ±10%**	**Non-compliant**
Cm/SP/2/16.0 5.08/59	Britlodge Ltd, UK	W-25	2012 Jul	3	Marché, informel MBOUDA, abri de fortune exposé aux intempéries	West	Passed	Passed	Passed	OK	Cracks in the engraving on tablets - majority of sample affected	Complies	97.8	95.3	**Does not comply at S1 to S3 criteria** mean (n=6): 46% min:38%; max: 54%	**Does not comply at S1 to S3 criteria** mean (n=6): 19% min:16%; max:23%	Complies	**Non-compliant**
Cm/SP/2/27.0 5.08/144	Britlodge Ltd, UK	W-25	2012 Jul	2	PHCIE D'OFFICINE PRIVEE DONANGU	South-West	Passed	Passed	Passed	OK	Traces of powder in blister, uneven coating, tablets chipped/broken - majority affected	Complies	99.9	96.6	**Does not comply at S1 to S3 criteria** mean (n=5): 45% min:33%; max: 57%	**Does not comply at S1 to S3 criteria** mean (n=5): 20% min:16%; max:25%	Complies	**Non-compliant**
Cm/SP/1/14.0 5.08/08	Gracure Pharmaceuticals Ltd, India	TE-1942	2010 Oct	1	U.C. PHARM (GROSSISTE PRIVE)	Centre	Passed	Passed	Passed	OK	1 tabl broken and has a spot	Complies	98.5	94.1	Complies at S1 mean (n=6): 96%	Complies at S1 mean (n=6): 88%	Complies	Compliant
Cm/SP/2/15.0 5.08/80	Gracure Pharmaceuticals Ltd, India	TE-1830	2010 Jul	2	PHCIE D'OFFINE PRIVEE DSCHANG	West	Passed	Passed	Passed	OK	Powder on surface of tablets, 1 tabl with faint engraving	Complies	96.8	93.3	Complies at S1 mean (n=5): 91%	Complies at S1 mean (n=5): 77%	Complies	Compliant
Cm/SP/2/27.0 5.08/147	Gracure Pharmaceuticals Ltd, India	TE-1830	2010 Jul	2	LIMBE PHARMACY	South-West	Passed	Passed	Passed	OK	Traces of powder in blister, 2 tablets chipped - minority affected	Complies	96.8	93.3	Complies at S1 mean (n=6): 90%	Complies at S1 mean (n=6): 77%	Complies	Compliant
Cm/SP/1/13.0 5.08/05	Maneesh Pharmaceuticals Pvt Ltd, India	C42	2009 Nov	1	CENAME (CENTRALE NATIONALE D'ACHAT)	Centre	Passed	Passed	Passed	OK	Blisters dirty, trace of powder in blisters, tablets with faint spots - majority affected	Complies	97.6	91.4	Complies at S1 mean (n=6): 97%	Complies at S1 mean (n=6): 74%	Complies	Compliant
Cm/SP/2/16.0 5.08/79	Maneesh Pharmaceuticals Pvt Ltd, India	C38	2009 Jun	2	CAPP OUEST BFSSAM	West	Passed	Passed	Passed	OK	2 tabl with chipped edges, 1 with spot, minority affected	Complies	99.6	91.5	Complies at S1 mean (n=6): 97%	Complies at S2 mean (n=12): 66%	Complies	Compliant
Cm/SP/2/24.0 5.08/107	Maneesh Pharmaceuticals Pvt Ltd, India	C42	2009 Nov	2	HOP. PUBLIC DE NEW BELL	Coast	**Failed**	Passed	Passed	**Not OK**	Powder on surface of tablets, 2 tabl with chipped edges, 1 with spot, minority affected	Complies	96.4	92.5	Complies at S1 mean (n=6): 97%	Complies at S1 mean (n=6): 77%	Complies	Compliant
Cm/SP/2/26.0 5.08/133	Maneesh Pharmaceuticals Pvt Ltd, India	C38	2009 Jun	2	CAPP SUD - OUEST	South-West	**Failed**	Passed	Passed	**Not OK**	Powder on surface of tablets, 2 tabl with chipped edges, minority affected	Complies	99.7	93.1	Complies at S1 mean (n=6): 101%	Complies at S1 mean (n=6): 69%	Complies	Compliant
Cm/SP/1/14.0 5.08/14	Roche Products Pvt Ltd, South Africa	Z7028	2011 Nov	1	U.C. PHARM (GROSSISTE PRIVE)	Centre	Passed	Passed	Passed	OK	OK	Complies	101.5	97.1	Not performed - not enough sample	Not performed - not enough sample	Not performed - not enough sample	Compliant
Cm/SP/2/17.0 5.08/60	Roche Products Pvt Ltd, South Africa	Z7028	2011 Nov	3	Marché informel Bafoussam, abri de fortune contenant le produit	West	Passed	Passed	Passed	OK	Packaging damaged, 1 tabl with chips	Complies	100.9	96.6	Complies at S1 mean (n=6): 91%	Complies at S1 mean (n=6): 79%	Complies	Compliant

*Cm=Cameroon, Et=Ethiopia, Gh=Ghana, Ke=Kenya, Ng=Nigeria, Tz=Tanzania

Sample code and country of collection*	Manufacturer	Batch number	Exp. Date	Sampling level	Sample collection site	Region	MINILAB SCREENING				LABORATORY TESTING							
							Phys/ Vis inspec-tion	Disintegra-tion	TLC	Conclusion (label and leaflet defects not taken into account)	Appearance	Identity	Assay 90.0 - 110.0 %		Dissolution Not less than 60% (Q) in 30 min		Uniformity of mass	Conclusion (appear-ance not taken into account)
													Sulfa-doxine %	Pyri-methamine %	Sulfadoxine	Pyrimethamine		
Cm/SP/2/27.0 5.08/145	Simrone Pharmaceuticals Industries Ltd, India	SPIL 202 M8/7	2010 Mar	2	PHCIE D'OFFICINE PRIVEE DONANGU	South-West	**Failed**	Passed	Passed	**Not OK**	Tablets with chips - majority affected	Complies	95.8	**Does not comply 87.2**	Does not comply at S1 to S1 criteria mean (n=6): 64% min:61%; max: 67%; not continued	**Does not comply at S1 to S3 criteria** mean (n=6): 32% min:31%; max:33%	Complies	**Non-compliant**
Cm/SP/2/26.0 5.08/158	Simrone Pharmaceuticals Industries Ltd, India	SPIL 202 M8/7	2010 Mar	3	KUMBA INFORMEL M.	South-West	**Failed**	Passed	Passed	**Not OK**	Blisters dirty, 1 tabl chipped, 1 with black spot - majority affected	Complies	95.8	**Does not comply 87.2**	Does not comply at S1 to S1 criteria mean (n=6): 68% min:63%; max: 70%; not continued	**Does not comply at S1 to S3 criteria** mean (n=6): 35% min:34%; max:36%	Complies	**Non-compliant**
Cm/SP/2/24.0 5.08/31	Swiss Pharma Nigeria Ltd, Nigeria	L23077 (pack) DNH-AS-174 (blister)	2009 Jul 2008 Dec	3	Marché informel, ESSOS YDE, étalage en plein air au soleil	Centre	Passed	Passed	Passed	OK	Packaging damaged, blisters dirty, 1 tabl cracked, 2 tabl with faulty engraving, 2 with small chips (Different batch no on blister and box, only part of PIL in each box)	Complies	100.5	98.9	Does not comply at S1 to S2 criteria mean (n=6): 50% min:44%; max: 52%; not continued	**Does not comply at S1 to S3 criteria** mean (n=6): 24% min:22%; max:26%	Complies	**Non-compliant**
Cm/SP/2/15.0 5.08/67	Swiss Pharma Nigeria Ltd, Nigeria	L23077	2009 Jul	3	Marché informel DSCHANG, abri de fortune exposé aux intempéries	West	Passed	Passed	Passed	OK	Packaging damaged, blisters dirty, 3 tabl with faulty engraving, 2 with small chips	Complies	99.2	96.7	Does not comply at S1 to S1 criteria mean (n=6): 58% min:54%; max: 64%; not continued	**Does not comply at S1 to S3 criteria** mean (n=6): 29% min:27%; max:31%	Complies	**Non-compliant**
Et/sp/1/11/06/ 08/03	Addis pharmaceutical factory, Ethiopia	1682	2009 Dec	1	Addis pharmaceutical factory - manufacturer/wholesaler	Central	Passed	Passed	Passed	OK	Tablets faintly mottled with rough edges, 1 with spot - minority affected	Complies	99.2	101.1	Complies at S1 mean (n=6): 92%	Complies at S1 mean (n=6): 87%	Complies	Compliant
Et/sp/2/22/06/ 08/31	Addis pharmaceutical factory, Ethiopia	1649	2009 Dec	2	Private drugstore - Bahir Dar	Northern	Passed	Passed	Passed	OK	1 tabl with spot, 3 with small chips on surface	Complies	100.0	100.9	Complies at S1 mean (n=6): 91%	Complies at S1 mean (n=6): 89%	Complies	Compliant
Et/sp/2/25/06/ 08/33	Addis pharmaceutical factory, Ethiopia	1686	2009 Dec	2	Private drug vendor - Kidus Giorgis	Central	Passed	Passed	Passed	OK	Tablets mottled, 1 with spot, minority affected	Complies	99.8	101.7	Complies at S1 mean (n=6): 91%	Complies at S1 mean (n=6): 88%	Complies	Compliant
Et/sp/2/25/06/ 08/35	Addis pharmaceutical factory, Ethiopia	1682	2009 Dec	2	Private drug vendor - Gabriel	Northern	Passed	Passed	Passed	OK	Tablets mottled, minority affected	Complies	100.5	102.2	Complies at S1 mean (n=6): 89%	Complies at S1 mean (n=6): 86%	Complies	Compliant
Et/sp/2/25/06/ 08/38	Addis pharmaceutical factory, Ethiopia	1682	2009 Dec	2	Private drugstore - Aykel	Northern	Passed	Passed	Passed	OK	Tablets mottled, with rough edges, minority affected	Complies	100.4	102.3	Complies at S1 mean (n=6): 90%	Complies at S1 mean (n=6): 89%	Complies	Compliant
Et/sp/2/26/06/ 08/40	Addis pharmaceutical factory, Ethiopia	1686	2009 Dec	2	Private wholesaler - Star millenium	Northern	Passed	Passed	Passed	OK	Tablets mottled, with rough edges, minority affected	Complies	99.8	100.1	Complies at S1 mean (n=6): 90%	Complies at S1 mean (n=6): 88%	Complies	Compliant
Et/sp/2/26/06/ 08/44	Addis pharmaceutical factory, Ethiopia	1649	2009 Dec	2	Private pharmacy - Goha	Northern	Passed	Passed	Passed	OK	3 tabl with uneven coating and edges, 1 with spot	Complies	99.3	100.8	Complies at S1 mean (n=6): 91%	Complies at S1 mean (n=6): 91%	Complies	Compliant
Et/sp/1/30/06/ 08/48	Addis pharmaceutical factory, Ethiopia	1659	2009 Dec	1	Addis pharmaceutical factory - manufacturer/wholesaler	Southern	Passed	Passed	Passed	OK	3 tabl with rough edges, 1 empty blister pocket	Complies	99.1	100.0	Complies at S1 mean (n=6): 98%	Complies at S1 mean (n=6): 96%	Complies	Compliant

*Cm=Cameroon, Et=Ethiopia, Gh=Ghana, Ke=Kenya, Ng=Nigeria, Tz=Tanzania

Sample code and country of collection*	Manufacturer	Batch number	Exp. Date	Sampling level	Sample collection site	Region	MINILAB SCREENING				LABORATORY TESTING							
							Phys/ Vis inspec-tion	Disintegra-tion	TLC	Conclusion (label and leaflet defects not taken into account)	Appearance	Identity	Assay 90.0 - 110.0 %		Dissolution Not less than 60% (Q) in 30 min		Uniformity of mass	Conclusion (appear-ance not taken into account)
													Sulfa-doxine %	Pyri-methamine %	Sulfadoxine	Pyrimethamine		
Et/sp/2/26/06/08/53	Addis pharmaceutical factory, Ethiopia	1649	2009 Dec	2	Public, store - Southern Nations, Nationalities and People's Regional Health Bureau	Southern	Passed	Passed	Passed	OK	Tablets with uneven surface, 1 with spot, minority affected	Complies	101.2	102.1	Complies at S1 mean (n=6): 93%	Complies at S1 mean (n=6): 92%	Complies	Compliant
Et/sp/2/30/06/08/54	Addis pharmaceutical factory, Ethiopia	1659	2009 Dec	2	Private drugstore - Shashemene	Southern	Passed	Passed	Passed	OK	1 tabl with spot	Complies	100.5	101.2	Complies at S1 mean (n=6): 97%	Complies at S1 mean (n=6): 94%	Complies	Compliant
Et/sp/2/30/06/08/55	Addis pharmaceutical factory, Ethiopia	1659	2009 Dec	2	Private drugstore - Gabriel	Central	Passed	Passed	Passed	OK	3 tabl with spots	Complies	100.3	101.0	Complies at S1 mean (n=6): 98%	Complies at S1 mean (n=6): 98%	Complies	Compliant
Et/sp/1/10/06/08/01	Ipca Laboratories Ltd, India	PP6017R	2009 Nov	1	Private - importer, distributor - Sakon Pharmachemie	Central	Passed	Passed	Passed	OK	3 tabl with a faint spot	Complies	98.5	95.3	Complies at S1 mean (n=6): 98%	Complies at S1 mean (n=6): 91%	Complies	Compliant
Et/sp/2/14/06/08/08	Ipca Laboratories Ltd, India	PP6016R	2009 Nov	2	Private drugstore - Hakim	Eastern	Passed	Passed	Passed	OK	1 tabl with dark spot	Complies	98.4	96.3	Not performed - not enough sample	Not performed - not enough sample	Complies	Compliant
Et/sp/2/25/06/08/32	Ipca Laboratories Ltd, India	PP6017R	2009 Nov	2	Private drugstore - Africa	Northern	Passed	Passed	Passed	OK	1 tabl with spot	Complies	98.6	96.5	Complies at S1 mean (n=6): 95%	Complies at S1 mean (n=6): 90%	Complies	Compliant
Et/sp/2/26/06/08/41	Ipca Laboratories Ltd, India	PP6015R	2009 Nov	2	Private drugstore - Abiy	Northern	Passed	Passed	Passed	OK	1 tabl with small spot	Complies	98.1	97.1	Complies at S1 mean (n=6): 92%	Complies at S1 mean (n=6): 89%	Complies	Compliant
Et/sp/2/29/06/08/49	Ipca Laboratories Ltd, India	PP6015R	2009 Nov	2	Private pharmacy - Shiferaw	Southern	Passed	Passed	Passed	OK	1 tabl has a chip and 1 with spot	Complies	97.1	94.4	Complies at S1 mean (n=6): 94%	Complies at S1 mean (n=6): 92%	Complies	Compliant
Et/sp/2/29/06/08/52	Ipca Laboratories Ltd, India	PP6016R	2009 Nov	2	Private drugstore - Amanuel	Southern	Passed	Passed	Passed	OK	OK	Complies	98.1	96.7	Complies at S1 mean (n=6): 97%	Complies at S1 mean (n=6): 94%	Complies	Compliant
Et/sp/2/21/06/08/20	Roche Products Pvt Ltd, South Africa	Z5401	2010 Apr	2	Private drugstore - Kidane-Mihiret	Northern	Passed	Passed	Passed	OK	2 tabl chipped	Complies	100.0	96.9	Complies at S1 mean (n=6): 94%	Complies at S1 mean (n=6): 81%	Complies	Compliant
Et/sp/2/29/06/08/47	Roche Products Pvt Ltd, South Africa	Z5400	2010 Feb	2	Private pharmacy - Addis Hiwot	Southern	Passed	Passed	Passed	OK	1 tabl with spot, 1 with chip	Complies	100.1	96.9	Complies at S1 mean (n=6): 91%	Complies at S1 mean (n=6): 84%	Complies	Compliant
Et/sp/2/14/06/08/04	Sterling lab, India	SGM005	2010 Jan	2	Private drugstore - A Gersa Guaro	Eastern	Passed	Passed	Passed	OK	1 table with spot, 3 with rough edges, traces of powder in blister	Complies	99.2	96.9	Complies at S1 mean (n=6): 97%	Complies at S1 mean (n=6): 89%	Complies	Compliant
Et/sp/2/15/06/08/09	Sterling lab, India	SGM006	2010 Jan	2	Private pharmacy - Africa	Eastern	Passed	Passed	Passed	OK	2 tabl with rough edges and chips, 1 with big chip on edge, 1 with spot, traces of powder in blister	Complies	97.5	95.6	Complies at S1 mean (n=6): 97%	Complies at S1 mean (n=6): 87%	Complies	Compliant
Et/sp/2/29/06/08/50	Sterling lab, India	SGM006	2010 Jan	2	Private pharmacy - Alpha	Southern	Passed	Passed	Passed	OK	1 tabl with spot	Complies	98.3	95.2	Complies at S1 mean (n=6): 95%	Complies at S1 mean (n=6): 86%	Complies	Compliant
Et/sp/2/29/06/08/51	Sterling lab, India	SGM005	2010 Jan	2	Private pharmacy - Asheh	Southern	Passed	Passed	Passed	OK	1 tabl with spot, 3 with rough edges	Complies	99.1	97.8	Complies at S1 mean (n=6): 98%	Complies at S1 mean (n=6): 91%	Complies	Compliant
Et/sp/2/17/06/08/16	Universal Corporation Ltd, Kenya	721334	2010 Sep	3	Informal market - Puntland	Eastern	Passed	Passed	Passed	OK	OK	Complies	100.6	98.2	Complies at S1 mean (n=6): 81%	Complies at S1 mean (n=6): 73%	Complies	Compliant
Et/sp/2/17/06/08/17	Universal Corporation Ltd, Kenya	721334	2010 Sep	3	Informal market - Almedina	Eastern	Passed	Passed	Passed	OK	1 tabl with small spot	Complies	99.1	97.1	Complies at S1 mean (n=6): 82%	Complies at S1 mean (n=6): 75%	Complies	Compliant

Sample code and country of collection*	Manufacturer	Batch number	Exp. Date	Sampling level	Sample collection site	Region	MINILAB SCREENING				LABORATORY TESTING							
							Phys/ Vis inspec-tion	Disintegra-tion	TLC	Conclusion (label and leaflet defects not taken into account)	Appearance	Identity	Assay 90.0 - 110.0 %		Dissolution Not less than 60% (Q) in 30 min		Uniformity of mass	Conclusion (appear-ance not taken into account)
													Sulfa-doxine %	Pyri-methamine %	Sulfadoxine	Pyrimethamine		
Gh/SP/2/14-05-08/12/S	Ally Pharma Options, India	SP-04	2010 Jan	2	Retail Pharmacy (Bennol Co. Ltd , Koforidua)	Southern	Passed	Passed	**Failed - Contaminant spot**	**Not OK**	OK	Complies	96.2	92.4	Complies at S1 mean (n=6): 73%	**Does not comply at S1 to S3 criteria** mean (n=6): 41% min:37%; max:47%	Complies	**Non-compliant**
Gh/SP/2/1-06-08/82/S	Ally Pharma Options, India	SP-01	2010 May	3	Informal Market (Sodom and Gomorrah, Accra)	Southern	Passed	Passed	Passed	OK	Tablets powdery, yellow spot-minority affected	Complies	99.4	92.8	Complies at S1 mean (n=6): 92%	Does not comply at S1 to S1 criteria mean (n=6): 52% min:50%; max: 54%; not enough sample to continue	Complies	In-conclusive
Gh/SP/1/19-05-08/56	Atlantic Pharmaceutical Ltd, Ghana	7007	2011 Aug	1	Manufacturer-Private (Atlantic Pharmaceutical Ltd, Accra)	Southern	**Failed**	Passed	Passed	**Not OK**	OK	Complies	96.3	96.4	Complies at S2 mean (n=12): 61%	Does not comply at S2 to S2 criteria mean (n=12): 54% min:49%; max: 57%; not enough sample to continue	Complies	In-conclusive
Gh/SP/1/22-05-08/63	Danadams Pharmaceutical Industry Ltd, Ghana	0705022	2010 May	1	Manufacturer-Private (Danadams Pharm. Industry Ltd, Accra)	Southern	Passed	**Failed (45 min)**	Passed	**Not OK**	Some tablets affected by slight markings indicative of a second/faulty scoreline-minority affected	Complies	100.6	91.3	Complies at S1 mean (n=6): 92%	Complies at S1 mean (n=6): 74%	Complies	Compliant
Gh/SP/1/23-05-08/68	GR Industries Ltd, Ghana	5070701	2009 Jul	1	Manufacturer-Private (GR Industries, Accra)	Southern	Passed	Passed	Passed	OK	Powder on edges of tablets	Complies	96.5	96.7	Complies at S1 mean (n=6): 98%	Complies at S1 mean (n=6): 77%	Complies	Compliant
Gh/SP/1/23-05-08/67/S	Kinapharma Ltd, Ghana	007	2012 Apr	1	Manufacturer-Private (Kinapharma Ltd, Accra)	Southern	Passed	Passed	Passed	OK	1 tabl chipped	Complies	97.7	95.2	Does not comply at S1 to S2 criteria mean (n=6): 54% min:48%; max: 60%; not continued	**Does not comply at S1 to S3 criteria** mean (n=6): 23% min:20%; max:27%	Complies	**Non-compliant**
Gh/SP/2/14-05-08/25/S	Kinapharma Ltd, Ghana	005	2012 Mar	2	Retail Pharmacy (Hem Pharmacy, Ho)	Southern	**Failed**	Passed	Passed	**Not OK**	OK	Complies	92.3	**Does not comply 83.9**	Does not comply at S1 to S2 criteria mean (n=6): 55% min:37%; max: 65%; not continued	**Does not comply at S1 to S3 criteria** mean (n=6): 31% min:20%; max:40%	Complies	**Non-compliant**
Gh/SP/2/14-05-08/22/S	Kinapharma Ltd, Ghana	005	2012 Mar	2	Retail Pharmacy (Crown Chemist, Ho)	Southern	Passed	**Failed (>1 hour)**	Passed	**Not OK**	OK	Complies	92.2	91.9	Does not comply at S1 to S1 criteria mean (n=6): 67% min:61%; max: 70%; not continued	**Does not comply at S1 to S3 criteria** mean (n=6): 39% min:34%; max:42%	Complies	**Non-compliant**
Gh/SP/2/16-05-08/29/N/NR	Kinapharma Ltd, Ghana	007	2012 Apr	2	Wholesale Pharm (Kinapharma Ltd, Tamale)	Northern	Passed	Passed	Passed	OK	Chipped tablets at scoreline and edges	Complies	98.0	**Does not comply 86.4**	Does not comply at S1 to S1 criteria mean (n=6): 69%min:58%; max: 79%; not enough sample to continue	Does not comply at S1 to S2 criteria mean (n=6): 43%min:35%; max: 49%; not enough sample to continue	Complies	**Non-compliant**

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Sample code and country of collection*	Manufacturer	Batch number	Exp. Date	Sampling level	Sample collection site	Region	MINILAB SCREENING				LABORATORY TESTING							
							Phys/ Vis inspec-tion	Disintegra-tion	TLC	Conclusion (label and leaflet defects not taken into account)	Appearance	Identity	Assay 90.0 - 110.0 %		Dissolution Not less than 60% (Q) in 30 min		Uniformity of mass	Conclusion (appear-ance not taken into account)
													Sulfa-doxine %	Pyri-methamine %	Sulfadoxine	Pyrimethamine		
Gh/SP/1/22-05-08/60/S	Medreich Plc, India	470255	2010 Feb	1	Importer-Private (Ernest Chemist, Accra)	Southern	Passed	Passed	Passed	OK	OK	Complies	93.2	90.8	Complies at S1 mean (n=6): 85%	Complies at S2 mean (n=12): 92%	Complies	Compliant
Gh/SP/2/15-05-08/23/N/NR	Medreich Plc, India	470255	2010 Feb	2	Licensed Chemical Seller (Abukari Mohammed, Yendi)	Northern	Passed	Passed	Passed	OK	OK	Complies	98.1	95.0	Complies at S1 mean (n=6): 95%	Complies at S1 mean (n=6): 88%	Complies	Compliant
Gh/SP/1/13-05-08/07	Milan Laboratories Pvt Ltd, India	ME18-342	2011 Aug	1	Importer-Private (Daamass Company Ltd, Accra)	Southern	Passed	Passed	Passed	OK	Powder on tablets	Complies	95.4	91.7	Complies at S1 mean (n=6): 87%	Complies at S2 mean (n=12): 70%	Complies	Compliant
Gh/SP/2/14-05-08/19/M	Milan Laboratories Pvt Ltd, India	ME18-342	2011 Aug	2	Retail Pharmacy (Enapak Pharmacy, Berekum)	Middle	Passed	Passed	Passed	OK	Lot of powder in packaging	Complies	97.1	90.0	Does not comply at S1 to S1 criteria mean (n=6): 70% min:62%; max: 72%; not enough sample to continue	Complies at S1 mean (n=6): 89%	Complies	In-conclusive
Gh/SP/1/13-05-08/01	Mission Pharmaceuticals Ltd, India	SPP702	2010 Mar	1	Importer-Private (Osons Chemist, Accra)	Southern	Passed	Passed	Passed	OK	OK	Complies	91.6	91.6	Complies at S1 mean (n=6): 90%	Complies at S2 mean (n=12): 66%	**Does not comply:** mean: 581.0mg min: 92.8%; max: 106.0% **3 tabl outside ±5%** no tabl outside ±10%	**Non-compliant**
Gh/SP/1/19-05-08/55/S	Phyto-Riker Pharmaceuticals Ltd, Ghana	051 M02792	2012 Aug	1	Manufacturer-Private (Phyto-Ricker P'ceutical Ltd, Accra)	Southern	Passed	Passed	Passed	OK	OK	Complies	94.4	91.7	**Does not comply at S1 to S3 criteria** mean (n=6): 30% min:25%; max: 35**%**	**Does not comply at S1 to S3 criteria** mean (n=6): 30% min:24%; max:38%	Complies	**Non-compliant**
Gh/SP/2/14-05-08/19/M	Phyto-Riker Pharmaceuticals Ltd, Ghana	051-M01778	2011 Dec	2	Govt. Hospital (Juaben Govt. Hosp)	Middle	Passed	Passed	Passed	OK	OK	Complies	99.7	94.5	Complies at S1 mean (n=6): 98%	Complies at S1 mean (n=6): 76%	Complies	Compliant
Gh/SP/2/13-05-08/05/M	Phyto-Riker Pharmaceuticals Ltd, Ghana	051-M01778	2011 Dec	2	Regional Medical Store-public (Ashanti Region, Adum-Kumasi)	Middle	Passed	Passed	Passed	OK	OK	Complies	99.1	94.3	Complies at S1 mean (n=6): 97%	Complies at S1 mean (n=6): 97%	Complies	Compliant
Gh/SP/1/13-05-08/03/S	Uni-Med, India	MD/92027	2010 Jan	1	Importer-Private (Victory Pharmacy, Accra)	Southern	Passed	Passed	Passed	OK	OK	Complies	95.0	92.0	**Does not comply at S1 to S3 criteria** mean (n=6): 43% min:41%; max: 44%	**Does not comply at S1 to S3 criteria** mean (n=6): 19% min:17%; max:20%	Complies	**Non-compliant**
Gh/SP/2/1-06-08/84/S	Uni-Med, India	MD/92027	2010 Jan	3	Informal Market (Agbogloshie market, Accra)	Southern	Passed	Passed	Passed	OK	OK	Complies	94.8	88.9 5 tablets used for assay, limits adjusted according to BP guideline to 88.4-111.6%	Does not comply at S1 to S2 criteria mean (n=6): 49% min:44%; max: 53%; not continued	**Does not comply at S1 to S3 criteria** mean (n=6): 21% min:18%; max:24%	Complies	**Non-compliant**
Ke/SP/1/13.06.08/02	Cosmos Ltd, Kenya	080109	2012 Feb	1	MISSION FACILITY/ CMS - MEDS	Central	Passed	Passed	Passed	OK	OK	Complies	99.6	97.5	Complies at S1 mean (n=6): 97%	Complies at S1 mean (n=6): 93%	Complies	Compliant
Ke/SP/1/16.06.08/11	Cosmos Ltd, Kenya	080109	2012 Feb	1	PRIVATE/ MANUFACTURER - Cosmos	Central	Passed	Passed	Passed	OK	1 tabl with black spot	Complies	99.2	97.0	Complies at S1 mean (n=6): 98%	Complies at S1 mean (n=6): 93%	Complies	Compliant
Ke/SP/1/16.06.08/13	Cosmos Ltd, Kenya	80405	2012 Mar	1	PUBLIC/ CMS - KEMSA	Central	Passed	Passed	Passed	OK	OK	Complies	98.7	96.7	Complies at S1 mean (n=6): 97%	Complies at S1 mean (n=6): 93%	Complies	Compliant

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Sample code and country of collection*	Manufacturer	Batch number	Exp. Date	Sampling level	Sample collection site	Region	MINILAB SCREENING				LABORATORY TESTING							
							Phys/ Vis inspec-tion	Disintegra-tion	TLC	Conclusion (label and leaflet defects not taken into account)	Appearance	Identity	Assay 90.0 - 110.0 %		Dissolution Not less than 60% (Q) in 30 min		Uniformity of mass	Conclusion (appear-ance not taken into account)
													Sulfa-doxine %	Pyri-methamine %	Sulfadoxine	Pyrimethamine		
Ke/SP/11/19.06.08/45	Cosmos Ltd, Kenya	080153A	2012 Feb	2	PRIVATE/ WHOLESALER - Reeya Pharmaceuticals	Western	Passed	Passed	Passed	OK	Small spot on 1 tabl	Complies	98.5	96.4	Complies at S1 mean (n=6): 100%	Complies at S1 mean (n=6): 95%	Complies	Compliant
Ke/SP/11/24.06.08/96	Cosmos Ltd, Kenya	080153A	2012 Feb	3	PRIVATE/ INFORMAL - Nakumati Kisumu	Nyanza	Passed	Passed	Passed	OK	Scratches on 1 tabl	Complies	98.8	96.6	Complies at S1 mean (n=6): 98%	Complies at S1 mean (n=6): 92%	Complies	Compliant
Ke/SP/11/25.06.08/104	Cosmos Ltd, Kenya	080153A	2012 Feb	3	PRIVATE/ INFORMAL - Nakumati Kisii	Nyanza	Passed	Passed	Passed	OK	OK	Complies	98.3	96.0	Complies at S1 mean (n=6): 98%	Complies at S1 mean (n=6): 93%	Complies	Compliant
Ke/SP/11/01.07.08/127	Cosmos Ltd, Kenya	080153A	2012 Feb	2	PHARMACY-RETAIL OUTLET - Meliz Pharmacy	Coast	Passed	Passed	Passed	OK	OK	Complies	98.3	96.0	Complies at S1 mean (n=6): 96%	Complies at S1 mean (n=6): 91%	Complies	Compliant
Ke/SP/11/01.07.08/134	Ipca Laboratories Ltd, India	8010	2011 Jan	2	PRIVATE/ WHOLESALER - Oceanview Pharmaceuticals	Coast	Passed	Passed	Passed	OK	Tablets heavily mottled	Complies	98.2	96.3	Complies at S1 mean (n=6): 95%	Complies at S1 mean (n=6): 92%	Complies	Compliant
Ke/SP/11/02.07.08/151	Ipca Laboratories Ltd, India	8010	2011 Jan	2	PRIVATE/ WHOLESALER - Palmland Pharmaceuticals	Coast	Passed	Passed	Passed	OK	Tablets heavily mottled	Complies	98.1	96.1	Complies at S1 mean (n=6): 97%	Complies at S1 mean (n=6): 96%	Complies	Compliant
Ke/SP/11/24.06.08/86	Lupin Ltd, India	DM70066	2012 Sep	2	PRIVATE/ WHOLESALER - Harleys Pharmaceuticals	Nyanza	Passed	Passed	Passed	OK	1 tabl with spot	Complies	98.3	96.8	Complies at S1 mean (n=6): 94%	Complies at S1 mean (n=6): 95%	Complies	Compliant
Ke/SP/11/25.06.08/103	Lupin Ltd, India	DM70066	2012 Sep	2	PHARMACY-RETAIL OUTLET - Borabu Medicals	Nyanza	Passed	Passed	Passed	OK	Powder on tabl	Complies	98.3	94.6	Complies at S1 mean (n=6): 92%	Complies at S1 mean (n=6): 90%	Complies	Compliant
Ke/SP/1/17.06.08/20	Roche Products Pvt Ltd, South Africa	Z7707	2012 Nov	1	PRIVATE/ IMPORTER - Laborex	Central	Passed	Passed	Passed	OK	1 tabl with brown spot	Complies	100.7	95.5	Complies at S1 mean (n=6): 95%	Complies at S1 mean (n=6): 79%	Complies	Compliant
Ke/SP/11/19.06.08/47	Roche Products Pvt Ltd, South Africa	Z6844	2011 Sep	2	PRIVATE/ RETAILER - Interlake Pharmacy	Western	Passed	Passed	Passed	OK	OK	Complies	101.6	96.8	Complies at S1mean (n=6): 98%	Complies at S1 mean (n=6): 77%	Complies	Compliant
Ke/SP/11/19.06.08/53	Roche Products Pvt Ltd, South Africa	Z6844	2011 Sep	2	PHARMACY-RETAIL OUTLET - Interlake Pharmaceuticals	Western	Passed	Passed	Passed	OK	OK	Complies	101.0	96.9	Complies at S1 mean (n=6): 98%	Complies at S1 mean (n=6): 78%	Complies	Compliant
Ke/SP/11/24.06.08/92	Roche Products Pvt Ltd, South Africa	Z7601	2012 Sep	2	PRIVATE/ WHOLESALER - Kentons	Nyanza	Passed	Passed	Passed	OK	1 tabl with spot and chip	Complies	100.1	96.1	Complies at S1 mean (n=6): 89%	Complies at S1 mean (n=6): 79%	Complies	Compliant
Ke/SP/11/01.07.08/130	Roche Products Pvt Ltd, South Africa	Z7601	2012 Sep	2	PRIVATE/ WHOLESALER - Makadara Chemist	Coast	Passed	Passed	Passed	OK	1 tabl with chip	Complies	100.8	97.6	Complies at S1 mean (n=6): 87%	Complies at S1 mean (n=6): 80%	Complies	Compliant
Ke/SP/1/16.06.08/14	Universal Corporation Ltd, Kenya	721336	2010 Sep	1	PUBLIC/ CMS - KEMSA	Central	Passed	Passed	Passed	OK	1 tabl with black spot	Complies	95.4	104.0	Complies at S1 mean (n=6): 89%	Complies at S1 mean (n=6): 93%	Complies	Compliant
Ke/SP/1/17.06.08/19	Universal Corporation Ltd, Kenya	721334	2010 Sep	1	PRIVATE/ MANUFACTURER - Universal Corporation	Central	Passed	Passed	Passed	OK	Faulty printing on 1 box - double printing in different colours (erroneous printing)	Complies	100.8	97.3	Complies at S1 mean (n=6): 83%	Complies at S1 mean (n=6): 76%	Complies	Compliant
Ke/SP/11/19.06.08/26	Universal Corporation Ltd, Kenya	820017	2010 Dec	2	PUBLIC FACILITY/ HOSPITAL - Western Provincial General Hospital	Western	Passed	Passed	Passed	OK	1 tabl with brown spot	Complies	99.1	96.2	Complies at S1 mean (n=6): 67%	Complies at S2 mean (n=12): 62%; min:59%; max: 66%	Complies	Compliant

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Sample code and country of collection*	Manufacturer	Batch number	Exp. Date	Sampling level	Sample collection site	Region	MINILAB SCREENING				LABORATORY TESTING							
							Phys/ Vis inspec-tion	Disintegra-tion	TLC	Conclusion (label and leaflet defects not taken into account)	Appearance	Identity	Assay 90.0 - 110.0 %		Dissolution Not less than 60% (Q) in 30 min		Uniformity of mass	Conclusion (appear-ance not taken into account)
													Sulfa-doxine %	Pyri-methamine %	Sulfadoxine	Pyrimethamine		
Ng/SP/2/30—05-08/144	Baader Schulz Lab, India	MF 706	2010 Jul	2	Private wholesaler - Provida	South-East	Passed	Passed	Passed	OK	Tablets with big black spots, powder on surface, chipped engraving - majority affected	Complies	99.6	96.7	Complies at S1 mean (n=6): 91%	Complies at S1 mean (n=6): 79%	Complies	Compliant
Ng/SP/1/26 – 05 – 07/47	Bond Chemical Ind. Ltd, Nigeria	07003	2010 Mar	1	Manufacturer - Bond Chemical	South-West	Passed	Passed	Passed	OK	Tablets faintly mottled	Complies	90.2	**Does not comply 88.6**	Does not comply at S1 to S2 criteria mean (n=6): 52% min:47%; max: 55%; not continued	**Does not comply at S1 to S3 criteria** mean (n=6): 32% min:28%; max:34%	Complies	**Non-compliant**
Ng/SP/1/28 – 05 – 08/201	Emzor Pharm Ind. Ltd, Nigeria	1139M	2011 Mar	1	Private manufacturer/ wholesaler - Emzor Pharm	South-West	Passed	Passed	Passed	OK	Tablets faintly mottled, chipped	Complies	98.4	94.4	Does not comply at S1 to S1 criteria mean (n=6): 68% min:64%; max: 70%; not continued	**Does not comply at S1 to S3 criteria** mean (n=6): 32% min:30%; max:33**%**	Complies	**Non-compliant**
Ng/SP/1/26 – 05 – 08/40	Emzor Pharm Ind. Ltd, Nigeria	2149K	2010 Mar	1	Federal medical store	South-West	Passed	Passed	Passed	OK	Tablets chipped, with traces of powder and faint spots; upper part of blister has a rough appearance	Complies	102.2	100.6	Complies at S1 mean (n=6): 81%	**Does not comply at S1 to S3 criteria** mean (n=6): 27% min:25%; max:28%	**Does not comply:** mean: 640.9mg min: 96.2%; max: 111.0% **6 tabl outside ±5% 2 tabl outside ±10%**	**Non-compliant**
Ng/SP/2/28—05-08/162	Emzor Pharm Ind. Ltd, Nigeria	1139M	2011 Mar	2	Private retail outlet - Paxs	South-East	Passed	Passed	Passed	OK	Tablets heavily chipped, with traces of powder	Complies	97.0	92.9	Complies at S1 mean (n=6): 71%	**Does not comply at S1 to S3 criteria** mean (n=6): 35% min:33%; max:37%	**Does not comply:** mean: 623.4mg min: 92.8%; max: 107.6% **3 tabl outside ±5%** no tabl outside ±10%	**Non-compliant**
Ng/SP/2/28-05-08/133	Emzor Pharm Ind. Ltd, Nigeria	717M	2011 Feb	3	Informal - Namtex	South-West	Passed	**Failed (32 min)**	Passed	**Not OK**	Tablets with small chips	Complies	96.0	92.4	**Does not comply at S1 to S3 criteria** mean (n=6): 22% min:20; max: 24%	**Does not comply at S1 to S3 criteria** mean (n=6): 10% min:9%; max:11%	Complies	**Non-compliant**
Ng/SP/1/26 – 05 – 08/42	Evans Medical Plc, Nigeria	7001	2010 Feb	1	Federal medical store	South-West	Passed	Passed	Passed	OK	Tablets with misformed edges, chips in engraving	Complies	99.6	99.9	**Does not comply at S1 to S3 criteria** mean (n=6): 35% min:23%; max: 48%	**Does not comply at S1 to S3 criteria** mean (n=6): 12% min:8%; max:16%	**Does not comply:** mean: 619.5mg min: 87.9%; max: 112.5% **9 tabl outside ±5% 4 tabl outside ±10%**	**Non-compliant**
Ng/SP/1/28 – 05 – 08/202	Juhel Nigeria Ltd, Nigeria	0014	2011 May	1	Private manufacturer/ wholesaler - Juhel	South-West	Passed	Passed	Passed	OK	Tablets heavily mottled, 1 tabl with spot	Complies	96.6	96.7	Complies at S1 mean (n=6): 82%	Does not comply at S2 to S2 criteria mean (n=12): 47% min:46%; max: 49%; not enough sample to continue	Complies	In-conclusive
Ng/SP/1/28 – 05 – 08/192	May & Baker Nigeria Plc, Nigeria	IX 642	2010 May	1	Private manufacturer/ wholesaler - May & Baker	South-West	Passed	**Failed (40 min)**	Passed	**Not OK**	Tablets with black spots	Complies	98.1	95.7	**Does not comply at S1 to S3 criteria** mean (n=6): 5% min:5%; max: 5%	**Does not comply at S1 to S3 criteria** mean (n=6): 4% min:4%; max:4%	Complies	**Non-compliant**

*Cm=Cameroon, Et=Ethiopia, Gh=Ghana, Ke=Kenya, Ng=Nigeria, Tz=Tanzania

Sample code and country of collection*	Manufacturer	Batch number	Exp. Date	Sampling level	Sample collection site	Region	MINILAB SCREENING				LABORATORY TESTING							
							Phys/ Vis inspec-tion	Disintegra-tion	TLC	Conclusion (label and leaflet defects not taken into account)	Appearance	Identity	Assay 90.0 - 110.0 %		Dissolution Not less than 60% (Q) in 30 min		Uniformity of mass	Conclusion (appear-ance not taken into account)
													Sulfa-doxine %	Pyri-methamine %	Sulfadoxine	Pyrimethamine		
Ng/SP/1/26 – 05 – 08/49	Medrel Pharmaceuticals Ltd, India	SPG 0702	2011 Sep	1	Importer - Embassy Pharmaceuticals	South-West	Passed	Passed	Passed	OK	Tablets chipped, yellow layer colour is faded	Complies	93.7	100.4	Complies at S1 mean (n=6): 91%	Complies at S1 mean (n=6): 83%	**Does not comply:** mean: 571.6mg min: 87.6%; max: 107.4% **7 tabl outside ±5% 1 tabl outside ±10%**	**Non-compliant**
Ng/SP/1/27 – 05 – 08/48	Micro Labs Ltd, India	AMRK7003	2010 Dec	1	Importer - Elbe Pharma	South-West	Passed	Passed	Passed	OK	Tablets with dark spot- minor	Complies	100.5	105.4	Complies at S1 mean (n=6): 97%	Complies at S1 mean (n=6): 100%	Complies	Compliant
Ng/SP/2/27 – 05 – 08/127	Micro Labs Ltd, India	AMEC020	2010 Dec	2	Private retail/ dispensing outlet - Bolar	South-West	Passed	Passed	Passed	OK	Tablets with dark spot, small chips	Complies	102.5	105.8	Complies at S1 mean (n=6): 100%	Complies at S1 mean (n=6): 95%	Complies	Compliant
Ng/SP/2/30— 05-08/169	Micro Labs Ltd, India	AMEC020	2010 Dec	3	Informal - Man T. Group	South-East	Passed	Passed	Passed	OK	Tablets with small chips, faintly mottled	Complies	100.2	104.3	Complies at S1 mean (n=6): 97%	Complies at S1 mean (n=6): 91%	Complies	Compliant
Ng/SP/2/26- 05-08/43	Micro Labs Ltd, India	VITK6006	2010 Oct	2	Federal medical store	South-West	Passed	Passed	Passed	OK	Traces of powder in blister	Complies	98.2	104.8	Complies at S1 mean (n=6): 95%	Complies at S1 mean (n=6): 83%	Complies	Compliant
Ng/SP/1/28 – 05 – 08/199	Neimeth International Pharmaceuticals Plc, Nigeria	80161002A	2011 Apr	1	Private manufacturer/ wholesaler - Neimeth Int	South-West	Passed	Passed	Passed	OK	Some tablets with extra scoreline, chipped, misformed edge	Complies	97.5	97.6	Complies at S1 mean (n=6): 102%	Complies at S1 mean (n=6): 98%	**Does not comply:** mean: 628.6mg min: 91.4%; max: 106.7% **7 tabl outside ±5%** no tabl outside ±10%	**Non-compliant**
Ng/SP/2/29— 05-08/174	Neimeth International Pharmaceuticals Plc, Nigeria	70161003A	2010 Aug	2	Private retail/ dispensing outlet - Jeeitu	South-South	Passed	Passed	Passed	OK	Tablets heavily mottled, chipped engraving	Complies	98.1	97.3	Complies at S1 mean (n=6): 98%	Complies at S1 mean (n=6): 93%	Complies	Compliant
Ng/SP/2/28- 05-08/57	Neimeth International Pharmaceuticals Plc, Nigeria	70161003A	2010 Aug	3	Informal - Johnson	North-West	Passed	Passed	Passed	OK	Tablets mottled, chipped, misformed engraving, rough edges, traces of powder in blister	Complies	94.5	93.8	Not performed - not enough sample	Not performed - not enough sample	Not performed - not enough sample	Compliant
Ng/SP/2/23— 05-08/78	Shreechem Lab, India	EM-396	2009 Nov	2	Private pharmacy, retail/ dispensing outlet - Wellcare	North-West	Passed	**Failed (47 min)**	**Failed - No PYR spot**	**Not OK**	Tablets severely mottled, uneven surface, some with extra scoreline **Tablets appearance different from another sample of different batch (imprint, scoreline)!**	**Does not comply Pyrimethamine not detected**	**Does not comply 9.1**	**Does not comply Pyrimethamine not detected**	**Does not comply at S1 to S3 criteria** mean (n=6): 2% min:2%; max: 2%	**Does not comply at S1 to S3 criteria** Pyrimethamine not detected	Complies	**Non-compliant**
Ng/SP/2/28— 05-08/18	Shreechem Lab, India	EM-309	2010 Feb	2	Private retail/ dispensing outlet - Tinna Pharmaceuticals	North-Central	Passed	Passed	Passed	OK	Tablets with spots - minority affected	Complies	95.1	93.6	Complies at S1 mean (n=6): 90%	**Does not comply at S1 to S3 criteria** mean (n=6): 39% min:35%; max:43%	Complies	**Non-compliant**
Ng/SP/1/28 – 05 – 08/198	SKG - Pharma Ltd, Nigeria	8001	2013 Jan	1	Private manufacturer/ wholesaler - SKG-Pharma	South-West	Passed	Passed	Passed	OK	Tablets chipped, with black spots	Complies	98.3	94.4	Complies at S1 mean (n=6): 85%	Does not comply at S2 to S2 criteria mean (n=12): 51% min:48%; max: 53%; not enough sample to continue	Complies	In-conclusive

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Sample code and country of collection*	Manufacturer	Batch number	Exp. Date	Sampling level	Sample collection site	Region	MINILAB SCREENING				LABORATORY TESTING							
							Phys/ Vis inspec-tion	Disintegra-tion	TLC	Conclusion (label and leaflet defects not taken into account)	Appearance	Identity	Assay 90.0 - 110.0 %		Dissolution Not less than 60% (Q) in 30 min		Uniformity of mass	Conclusion (appear-ance not taken into account)
													Sulfa-doxine %	Pyri-methamine %	Sulfadoxine	Pyrimethamine		
Ng/SP/1/26 – 05 – 08/41	Swiss Pharma Nigeria Ltd, Nigeria	L27054	2012 Mar	1	Federal medical store	South-West	Passed	Passed	Passed	OK	Tablets with spots and chips	Complies	98.1	96.2	**Does not comply at S1 to S3 criteria** mean (n=6): 44% min:44%; max: 45%	**Does not comply at S1 to S3 criteria** mean (n=6): 32% min:30%; max:33%	Complies	**Non-compliant**
Ng/SP/1/28 – 05 – 08/196	Swiss Pharma Nigeria Ltd, Nigeria	L27123	2012 Aug	1	Private manufacturer/ wholesaler - Swiss Pharma	South-West	Passed	Passed	Passed	OK	Tablets mottled with small chips, traces of powder in blisters	Complies	97.6	97.2	Complies at S1 mean (n=6): 71%	Does not comply at S1 to S1 criteria mean (n=6): 51% min:47%; max: 55%; not enough sample to continue	Complies	In-conclusive
Ng/SP/2/29 – 05 – 08/120	Swiss Pharma Nigeria Ltd, Nigeria	L27123	2012 Aug	2	Private retail/ dispensing outlet - Alpha	South-West	Passed	Passed	Passed	OK	Tablets faintly mottled, chipped, traces of powder in blisters	Complies	96.4	96.3	Complies at S1 mean (n=6): 70%	Does not comply at S1 to S1 criteria mean (n=6): 49% min:49%; max: 50%; not enough sample to continue	Complies	In-conclusive
Ng/SP/1/26 – 05 – 08/46	VITAPHOS Laboratory Nigeria Ltd, Nigeria	V035	2011 Mar	1	Manufacturer - Vitaphos	South-West	Passed	Passed	Passed	OK	Tablets chipped, traces of powder in blister	Complies	96.4	**Does not comply 80.2**	**Does not comply at S1 to S3 criteria** mean (n=6): 34% min:4%; max: 51%	**Does not comply at S1 to S3 criteria** mean (n=6): 6% min:2%; max: 8%	Complies	**Non-compliant**
Tz/SP/1/13.05 .08/02	Elys Chemical Industries Ltd, Kenya	7E39	2011 Apr	1	Heko Pharmacy-Wholesale Pharmacy	Dar es Salaam	Passed	Passed	Passed	OK	OK	Complies	100.4	98.3	Complies at S1 mean (n=6): 92%	Complies at S1 mean (n=6): 88%	Complies	Compliant
Tz/SP/2/13.05 .08/07	Elys Chemical Industries Ltd, Kenya	8A126	2011 Dec	2	Safi Medics-Ilala	Dar es Salaam	Passed	Passed	Passed	OK	OK	Complies	98.8	97.4	Complies at S1 mean (n=6): 96%	Complies at S1 mean (n=6): 92%	Complies	Compliant
Tz/SP/2/19.05 .08/23	Elys Chemical Industries Ltd, Kenya	8A126	2011 Dec	2	Bakwata Dispensary (FBO)	Mtwara	**Failed**	Passed	Passed	**Not OK**	OK	Complies	99.8	96.8	Complies at S1 mean (n=6): 94%	Complies at S1 mean (n=6): 90%	Complies	Compliant
Tz/SP/2/19.05 .08/43	Elys Chemical Industries Ltd, Kenya	8A126	2011 Dec	2	Mamboleo Pharmacy ltd	Kigoma	**Failed**	Passed	Passed	**Not OK**	OK	Complies	98.4	96.7	Complies at S1 mean (n=6): 93%	Complies at S1 mean (n=6): 87%	Complies	Compliant
Tz/SP/2/18.05 .08/47	Elys Chemical Industries Ltd, Kenya	8A127	2011 Dec	2	Huruma Part II Poison Shop-Kasulu	Kigoma	**Failed**	Passed	Passed	**Not OK**	OK	Complies	99.1	96.9	Complies at S1 mean (n=6): 93%	Complies at S1 mean (n=6): 85%	Complies	Compliant
Tz/SP/2/15.05 .08/52	Elys Chemical Industries Ltd, Kenya	8A128	2011 Dec	2	Moshi Rashidi Duka la Dawa Baridi	Kigoma	**Failed**	Passed	Passed	**Not OK**	OK	Complies	99.3	97.7	Complies at S1 mean (n=6): 96%	Complies at S1 mean (n=6): 91%	Complies	Compliant
Tz/SP/2/21.05 .08/69	Elys Chemical Industries Ltd, Kenya	8A128	2011 Dec	2	Comm's Duka la Dawa Baridi	Mwanza	Passed	Passed	Passed	OK	OK	Complies	98.7	96.0	Complies at S1 mean (n=6): 99%	Complies at S1 mean (n=6): 95%	Complies	Compliant
Tz/SP/2/21.05 .08/71	Elys Chemical Industries Ltd, Kenya	8A127	2011 Dec	2	Tweyambe Duka la Dawa Baridi-Magu	Mwanza	Passed	Passed	Passed	OK	OK	Complies	99.3	96.5	Complies at S1 mean (n=6): 94%	Complies at S1 mean (n=6): 90%	Complies	Compliant
Tz/SP/2/29.05 .08/86	Elys Chemical Industries Ltd, Kenya	8A128	2011 Dec	2	Kavula Pharmacy	Tabora	Passed	Passed	Passed	OK	OK	Complies	99.3	96.6	Complies at S1 mean (n=6): 95%	Complies at S1 mean (n=6): 90%	Complies	Compliant
Tz/SP/2/29.05 .08/88	Elys Chemical Industries Ltd, Kenya	8A127	2011 Dec	2	Maningu Medical Stores-Urambo	Tabora	Passed	Passed	Passed	OK	Blister pocket had only 1/2 a tablet	Complies	97.8	93.0	Complies at S1 mean (n=6): 94%	Complies at S1 mean (n=6): 89%	Complies	Compliant
Tz/SP/2/28.05 .08/91	Elys Chemical Industries Ltd, Kenya	8A126	2011 Dec	2	Bue Med Store-Nzega	Tabora	Passed	Passed	Passed	OK	OK	Complies	99.3	96.4	Complies at S1 mean (n=6): 96%	Complies at S1 mean (n=6): 89%	Complies	Compliant

*Cm=Cameroon, Et=Ethiopia, Gh=Ghana, Ke=Kenya, Ng=Nigeria, Tz=Tanzania

Sample code and country of collection*	Manufacturer	Batch number	Exp. Date	Sampling level	Sample collection site	Region	MINILAB SCREENING				LABORATORY TESTING							
							Phys/ Vis inspec-tion	Disintegra-tion	TLC	Conclusion (label and leaflet defects not taken into account)	Appearance	Identity	Assay 90.0 - 110.0 %		Dissolution Not less than 60% (Q) in 30 min		Uniformity of mass	Conclusion (appear-ance not taken into account)
													Sulfa-doxine %	Pyri-methamine %	Sulfadoxine	Pyrimethamine		
Tz/SP/2/26.05.08/61	Intas Pharmaceutical Ltd, India	H002	2010 Jan	2	Agha Khan Medical Centre	Mwanza	Passed	Passed	Passed	OK	OK	Complies	97.8	93.6	Complies at S1 mean (n=6): 96%	Complies at S1 mean (n=6): 89%	Complies	Compliant
Tz/SP/1/19.05.08/01	Shelys Pharmaceuticals Ltd, Tanzania	7062	2011 Nov	1	Medical Stores Department (MSD)	Dar es Salaam	Passed	Passed	Passed	OK	OK	Complies	97.5	94.5	Complies at S1 mean (n=6): 77%	Complies at S1 mean (n=6): 72%	Complies	Compliant
Tz/SP/1/14.05.08/04	Shelys Pharmaceuticals Ltd, Tanzania	8004	2012 Feb	1	Shelys Pharmaceuticals ltd(Tanzania)	Dar es Salaam	Passed	Passed	Passed	OK	OK	Complies	98.3	91.4	Complies at S1 mean (n=6): 69%	**Does not comply at S1+S2+S3** mean (n=24): 48% min:46%; max:49%	Complies	**Non-compliant**
Tz/SP/1/19.05.08/15	Shelys Pharmaceuticals Ltd, Tanzania	7015	2011 Apr	1	Medical Stores Department (MSD)	Mtwara	**Failed**	Passed	Passed	**Not OK**	OK	Complies	98.3	95.3	Complies at S1 mean (n=6): 97%	Complies at S1 mean (n=6): 93%	**Does not comply:** mean: 662.6mg min: 94.0%; max: 114.7% **3 tabl outside ±5% 1 tabl outside ±10%**	**Non-compliant**
Tz/SP/2/20.05.08/16	Shelys Pharmaceuticals Ltd, Tanzania	7015	2011 Apr	2	Ligula Regional Hospital	Mtwara	**Failed**	Passed	Passed	**Not OK**	OK	Complies	100.6	97.3	Complies at S1 mean (n=6): 100%	Complies at S1 mean (n=6): 97%	**Does not comply:** mean: 668.6mg min: 96.1%; max: 121.1% 2 tabl outside ±5% **1 tabl outside ±10%**	**Non-compliant**
Tz/SP/2/20.05.08/17	Shelys Pharmaceuticals Ltd, Tanzania	7014	2011 Apr	2	Masasi District Hospital	Mtwara	**Failed**	Passed	Passed	**Not OK**	OK	Complies	99.2	95.4	Complies at S1 mean (n=6): 100%	Complies at S1 mean (n=6): 94%	Complies	Compliant
Tz/SP/2/21.05.08/18	Shelys Pharmaceuticals Ltd, Tanzania	7062	2011 Nov	2	Newala District Hospital	Mtwara	**Failed**	Passed	Passed	**Not OK**	OK	Complies	98.9	96.0	Complies at S1 mean (n=6): 77%	Complies at S1 mean (n=6): 75%	Complies	Compliant
Tz/SP/2/19.05.08/19	Shelys Pharmaceuticals Ltd, Tanzania	7015	2011 Apr	2	Huruma Dispensary	Mtwara	Passed	Passed	Passed	OK	OK	Complies	100.8	97.7	Complies at S1 mean (n=6): 97%	Complies at S1 mean (n=6): 92%	**Does not comply:** mean: 672.2mg min: 94.5%; max: 116.6% **3 tabl outside ±5% 1 tabl outside ±10%**	**Non-compliant**
Tz/SP/2/19.05.08/22	Shelys Pharmaceuticals Ltd, Tanzania	7015	2011 Apr	2	S.D.A Dispensary	Mtwara	**Failed**	Passed	Passed	**Not OK**	OK	Complies	99.8	96.9	Complies at S1 mean (n=6): 99%	Complies at S1 mean (n=6): 95%	Complies	Compliant
Tz/SP/2/19.05.08/26	Shelys Pharmaceuticals Ltd, Tanzania	7014	2011 Apr	2	Milanzi Medical Store-Mbuyuni Masasi	Mtwara	Passed	Passed	Passed	OK	OK	Complies	99.0	94.3	Complies at S1 mean (n=6): 98%	Complies at S1 mean (n=6): 92%	Complies	Compliant
Tz/SP/2/16.05.08/35	Shelys Pharmaceuticals Ltd, Tanzania	6039	2010 Aug	2	Matyazo Health Centre	Kigoma	Passed	Passed	Passed	OK	OK	Complies	98.7	93.7	Complies at S1 mean (n=6): 96%	Complies at S1 mean (n=6): 90%	Complies	Compliant
Tz/SP/2/21.05.08/56	Shelys Pharmaceuticals Ltd, Tanzania	6039	2010 Aug	2	Sokou Toure Hospital	Mwanza	Passed	Passed	Passed	OK	OK	Complies	98.8	94.3	Complies at S1 mean (n=6): 92%	Complies at S1 mean (n=6): 87%	Complies	Compliant

*Cm=Cameroon, Et=Ethiopia, Gh=Ghana, Ke=Kenya, Ng=Nigeria, Tz=Tanzania

Appendix 6: Sulfamethoxypyrazine/pyrimethamine samples – test results

Sample code and country of collection*	Manufacturer	Batch number	Exp. Date	Sampling level	Sample collection site	Region	MINILAB SCREENING				LABORATORY TESTING							
							Phys/ Vis inspection (excluding label and leaflet)	Dis-integra-tion	TLC	Conclusion (label and leaflet defects not taken into account)	App-ear-ance	Identity	Assay 90.0 - 110.0 %		Dissolution Not less than 80% (Q) in 30 min		Uniformity of mass	Conclusion of laboratory testing (appearance not taken into account)
													Sulfamethoxy-pyrazine %	Pyrimethamine %	Sulfamethoxy-pyrazine	Pyrimethamine		
Ke/SP/1/13.06.08/04	Dafra Pharma International Ltd, Belgium	07A2981	2010 Jan	1	PRIVATE/ IMPORTER - Dafra Pharma	Central	Passed	Passed	Passed	Not analysed	OK	Complies	98.9	100.1	Complies at S1 mean (n=6): 96%	Does not comply at S2 to S2 criteria mean (n=12):70% min:69%; max:71%; not continued	Complies	Inconclusive
Ng/SP/2/24-05-08/27	Drugfield Pharmaceuticals Ltd, Nigeria	06440701	2011 Jun	2	NGO wholesale/central store	North-Central	Passed	Passed	passed	OK	OK	Complies	95.7	96.8	Complies at S1 mean (n=6): 82%	**Does not comply at S2 to S3 criteria** mean (n=12): 23% min:22%; max:24%	Complies	**Non-compliant**
Tz/SP/2/20.05.08/62	Elys Chemical Industries Ltd, Kenya	8A129	2011 Dec	2	Sunpharm Pharmacy (Wholesale & Retail)	Mwanza	Passed	Passed	Passed	OK	OK	Complies	99.9	99.0	Complies at S1 mean (n=6): 97%	Complies at S1 mean (n=6): 83%	Complies	Compliant
Tz/SP/2/28.05.08/89	Elys Chemical Industries Ltd, Kenya	7E168	2011 Apr	2	Tiba Medical Store-Urambo	Tabora	Passed	Passed	Passed	OK	OK	Complies	99.3	99.8	Complies at S1 mean (n=6): 96%	Complies at S1 mean (n=6): 84%	Complies	Compliant
Tz/SP/2/20.05.08/72	Laboratory & Allied, Kenya	49798	2011 Mar	2	Kalala Duka la Dawa Baridi-Ngudu-Kwimba	Mwanza	**Failed**	Passed	Passed	**Not OK**	OK	Complies	107.9	103.9	Complies at S1 mean (n=6): 101%	Complies at S1 mean (n=6): 87%	Complies	Compliant
Tz/SP/2/29.05.08/92	Laboratory & Allied, Kenya	49496	2010 Nov	2	Gloria Medical Store-Sikonge	Tabora	Passed	Passed	Passed	OK	OK	Complies	101.0	100.1	Complies at S1 mean (n=6): 101%	Complies at S1 mean (n=6): 87%	Complies	Compliant
Tz/SP/1/13.05.08/03	Pharmacia & Upjohn, Italy	E089A	2010 Sep	1	Heko Pharmacy-Wholesale Pharmacy	Dar es salaam	Passed	Passed	Passed	OK	OK	Complies	99.1	98.7	Complies at S1 mean (n=6): 96%	Complies at S1 mean (n=6): 83%	Complies	Compliant
Tz/SP/2/19.05.08/40	Pharmacia & Upjohn, Italy	E039A	2010 Sep	2	Kigoma Pharmacy	Kigoma	Passed	Passed	Passed	OK	OK	Complies	98.8	99.2	Complies at S1 mean (n=6): 89%	Complies at S1 mean (n=6): 86%	Complies	Compliant
Tz/SP/2/19.05.08/42	Shelys Pharmaceuticals Ltd, Tanzania	8005	2010 Feb	2	Mamboleo Pharmacy ltd	Kigoma	**Failed**	Passed	Passed	**Not OK**	OK	Complies	100.1	98.9	Complies at S1 mean (n=6): 83%	**Does not comply at S2 to S3 criteria** mean (n=12):34% min:33%; max:35%	Complies	**Non-compliant**

*Cm=Cameroon, Et=Ethiopia, Gh=Ghana, Ke=Kenya, Ng=Nigeria, Tz=Tanzania

Malaria continues to be a major health threat to tropical countries, including in sub-Saharan Africa. Halting and reversing the incidence of malaria is one of the targets linked to the United Nations Millennium Development Goals and a priority for the World Health Organization (WHO). Efficacy and safety of antimalarial medicines, as measured by their quality, are essential in mitigating morbidity and reducing deaths. Assured quality also helps limit the development of drug resistance.

The survey reported here evaluated the quality of selected antimalarials in six sub-Saharan African countries (Cameroon, Ethiopia, Ghana, Kenya, Nigeria and the United Republic of Tanzania). These countries have been supported by WHO to strengthen their regulatory control of antimalarial products. The survey focused on the quality of artemisinin-based combination therapy products and sulfadoxine/pyrimethamine products, at different points of the regulated and informal distribution systems.

The survey was conducted by WHO in cooperation with the national drug regulatory authority of each participating country. In total, 935 samples were collected during April - June 2008 and were screened using GPHF-Minilab® kits. Based on predefined criteria, 306 samples (from 64 manufacturers and 218 sampling sites) were selected for full, quality control testing in a laboratory. Of these samples, 267 were fully tested, of which 28.5% failed to comply with specifications. Although non-compliance with pre-established criteria cannot be related directly to a risk for patients' health, such a high failure rate indicates a substantial problem in the quality of antimalarials present in distribution channels. For extreme deviations from specifications (as defined in this report), the failure rate was 11.6%. Extreme deviations are likely to be associated with health implications.

Data collected during the survey enabled comparison of the results of quality testing by country, distribution level, geographical region, domestic production or import, product types, registration status and prequalification status. The sensitivity of the screening methods of the GPHF-Minilab® in detecting non-compliance in dissolution and in assay/related substances tests was shown to be substantially lower than that of laboratory tests.

Survey results were discussed with regulators from participating countries and recommendations were agreed about the strategies necessary to strengthen medicines regulation, facilitate exchange of information and cooperation among countries, support the participation of local manufacturers in WHO prequalification and encourage the use of WHO-prequalified products. Three countries with high failure rates in the survey subsequently organized national stakeholders' consultations to review the survey findings and to address the gaps identified.

The information obtained through the survey has led to a better understanding of the quality profile of antimalarials in sub-Saharan Africa. It has contributed to evidence-based regulatory actions, the development of regulatory systems and enforcement capacity, the advancement of post-marketing surveillance, and increased cooperation between national drug regulatory authorities.

Quality Assurance and Safety: Medicines

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