Findings from the ACT Consortium Drug Quality Studies in 6 Countries

Harparkash Kaur

London School of Hygiene & Tropical Medicine
Falsified Antimalarials Abound

Health professionals and patients assume that the medicines that they are prescribing/prescribed are of good quality.
• Use 2 stage testing (MiniLab® and QC Lab) DO NOT differentiate drugs in terms of counterfeit, substandard or degraded

• WHO report of 6 countries in Africa highlights that 1/3 samples (ACTs and SP) are substandard possibly counterfeit. It also said that the MiniLab® underestimates the negative results by x3.

• Sampling method seems to be convenience, NOT random

ACTc DQ-project set out to determine the quality of drugs following representative sampling in various geographical regions.
Criteria for Site Selection

Utility and relevance

• How useful are the findings likely to be to policy makers and other stakeholders both within and outside the country?

• Is there an important initiative in the country that may impact on drug quality, in particular AMFm?

• Absence of other ongoing DQ surveillance

Feasibility

• Is there an existing ACTc project in that country?

• Is there potential for piggy backing on to ongoing surveys?

• Local co-operation – willing, capable and resources available

• Conducive political and regulatory environment
Countries where samples collected

- **Rwanda (2008)**
- **Tanzania (2010 & 2011)**
- **Cambodia (2010)**
- **Kintampo, Ghana (2011)**
- **Enugu, Nigeria (2013)**
- **Equatorial Guinea, Bioko Island (2014)**
- **Ilorin, Nigeria (2013)**
- **Thailand (2014)**
- **Burma (2014)**

*ACTc country

NON-ACTc country

*Affordable Medicines Facility for Malaria (AMFM)

†Tracking Resistance to Artemisinin Collaboration (TRAC)
Agreement Signed with MOH in a Country & LSHTM

Drug Quality and Authenticity Surveillance System and Counterfeit Drug Forensic Network

Agreement between:
London School of Hygiene & Tropical Medicine
Rwanda Ministry of Health Malaria Unit / TRAC Plus

Introduction

The London School of Hygiene & Tropical Medicine (LSHTM) is a principal investigator in the Artemisinin Combination Therapy (ACT) Consortium. Bill and Melinda Gates Foundation have awarded funds to support this coordinated research programme to identify how best to optimize the delivery and cost-effectiveness of ACTs for malaria in Africa and Asia across a range of epidemiological and healthcare settings.

The project entitled “A surveillance system and drug forensic network to monitor the quality and authenticity of artemisinin combination treatments in Africa” forms part of the group studying the deployment of ACTs to achieve maximum therapeutic and economic effectiveness and the desired public health goals by setting up a systematic surveillance system in areas that are most likely to trade in drugs of questionable quality. The proposal is designed to initially survey for the occurrence of substandard and counterfeit drugs in sentinel countries and subsequently undertake comprehensive surveys within selected settings found to be at risk. Suspected samples are to be characterised by standardised reference chemical and botanical tests within the Counterfeit Drug Forensic Network (CODFIN) to determine the exact composition of the tablets, helping to determine the origin of counterfeit ACTs. One of the countries proposed for this study is Rwanda and we now invite you enter into this agreement so that we may assess the quality of ACTs in selected sites in Rwanda.

The Agreement:

The Rwanda Ministry of Health Malaria Unit / TRAC Plus has agreed to collaborate with the LSHTM in the collection and shipment of ACT samples for analysis in London, England.

Rwanda’s Malaria Unit will provide the LSHTM:

1. Information on all artemisinin-derivatives available in country, containing detailed information on the appearance, packaging, batch numbers, date of manufacture, expiry, brand names and the quality of the drugs as well as the date and name of Institute from which the sample has been obtained.

LSHTM will provide Rwanda’s Malaria Unit:

1. Sample collection protocol and in-country orientation on collection methods;
2. Funds to cover the cost of ACTs and overseas shipment;
3. Results of the drug quality and authenticity analysis;

Duration:

This Agreement will commence on 01/01/2009 and will remain in effect until 12/31/2013 (5 years).

Date: 26th January 2009

Ms Penny Ireland
Research Co-ordinator Officer
London School of Hygiene & Tropical Medicine
Keppel Street, London

Director of the Malaria Unit
CIDC/TRAC Plus
Rwanda Ministry of Health
Rwanda
Ethics clearance LSHTM & Local plus Permission

LOCAL SCHOOL OF HYGIENE & TROPICAL MEDICINE
ETHICS COMMITTEE

APPROVAL FORM
Application number: 5804

Name of Principal Investigator: Harpreet Kaur, PhD
Department: Infectious and Tropical Diseases
Head of Department: Professor Simon Croy

Title: A surveillance system and drug forensic network to monitor the quality and authenticity of artemisinin combination treatments in Africa.

This application is approved by the Committee.

Chair of the Ethics Committee: ...

Date: 31 August 2010

Approval is dependent on local ethical approval having been received.

Any subsequent changes to the application must be submitted to the Committee via an E2 amendment form.

LSHTM ethics clearance

University of Nigeria Teaching Hospital
Ituku-Ozalla, P.M.B. 01129, Enugu.

Chairman, UTH Management Board
Barr. M.U. Okonkwo
Director of Administration/Secretary
UNTH Management Board

UNTH/CSA 329/VOL 5

Date: 4th Dec, 2012

UNIVERSITY OF NIGERIA TEACHING HOSPITAL

GOVERNMENT OF ENUGU STATE OF NIGERIA
Office of the Permanent Secretary
Ministry of Health Enugu
Telegram: PSMOH
Telephone: 042-490311

Date: 28th June, 2012

Sir,

PERMISSION TO COLLECT ARTEMISININ-BASED ANTIMALARIA DRUG SAMPLES FOR QUALITY TESTING

With reference to the above subject dated 21st June, 2012 on your request to collect ACT samples for quality testing. Permission is hereby given for you to purchase some of these antimalarials from drug retailers in Enugu State as requested.

I hope you will make available to us the findings from your study.

Regards,

Dr. Moses Onjigh
Permanent Secretary

Local clearance and permission to sample
Sample Collection

Questionnaire for the collection of drugs declared as containing artemisinin derivatives

- Country
- City
- Date of collection
- Name of drug outlet
  - hospital
  - dispensary
  - pharmacy
  - market
  - health center
  - Other (name is)
- Type of drug outlet
  - public
  - private
- Brand name of the collected medicine
- Name of declared active artemisinin ingredient
  - artemether
  - artesunate
  - DHA
  - Other (name is)
- Dose of active ingredient(s) mg
- Combined with mg
- mg
- mg
- Artemisinin ingredient formulated with
  - separate from
  - the other active ingredients
- Type of preparation (formulation)
  - tablet
  - suppository
  - injectable suspension
  - OTHER (name is)
- Batch number
- Date of manufacture
- Expiry date
- Description of primary container
- Description of secondary container
- Pack size
- Quantity collected
- Price per pack local currency
- Price per single dose local currency
- Special comments
- Name and signature of collector
Packaged Carefully Before Shipping to LSHTM
Processing

Logging onto Epi info
Flow of Sample & Corroborative Analyses

**Drug Samples**
- All collected samples

**LSHTM (UK)**
- Harparkash Kaur
- All samples logged
- Scanned & tablet dimensions noted
- HPLC analysis for % API content
- Results compiled into a report

**CDC (Atlanta)**
- Mike Green
- ~10 % of samples tested to confirm HPLC analysis from partner (LSHTM)

**GT (Atlanta)**
- Facundo Fernandez
- Mass spec analysis

All information is logged on to a database

Report compiled and sent

Information on quality of drugs disseminated to MoH

Manuscripts
% Active ingredients

HPLC

Degradation studies

Forced ageing at 60°C
0 - 21 days

LC/MS

Chemical Content Analysis of ACTs at LSHTM

Artemether – 3.8
Lumefantrine – 4.6
Stability Studies of AS/AQ and AM/LUM

Samples in a Chamber at LSHTM

Samples in dark

Samples in light

Conditions of the chamber set to mimic temperature and humidity in Ghana

Storage of Samples in the Clinic Kintampo, Ghana

Samples in light

Samples in the dark
**Results of stability Studies of AS/AQ and AM/LUM**

Laboratory analysis of ACTs aged in the stability chamber and clinic in Ghana over 4 years

- 3,000 tablets of AS/AQ
- 3,000 tablets of AM/LUM

**Results**

- After 18 months of ageing v low levels of degradation products detected.
- 0.7 % degradation of the artemisinin component of ACTs was found.
- Statically insignificant degradation in ACTs within expiry date.
- No difference in the samples aged in clinic and the chamber.
- None of the degradation products found exhibited antimalarial activity.
Degraded samples – Appearances are deceiving

- Blister torn & buckled
- Mottled brown
- Soft and sticky
- Residue
# Classification of ACTs

<table>
<thead>
<tr>
<th>Drug quality</th>
<th>% Stated API detected</th>
<th>Method used</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acceptable quality</td>
<td>85-115</td>
<td>HPLC &amp; MS &amp; LC/MS</td>
</tr>
<tr>
<td>Falsified</td>
<td>0</td>
<td>HPLC &amp; MS &amp; LC/MS</td>
</tr>
<tr>
<td>Substandard</td>
<td>&lt; 85 - &gt; 115</td>
<td>HPLC &amp; MS &amp; LC/MS</td>
</tr>
<tr>
<td>Degraded</td>
<td>&lt; 85 plus products of degraded API</td>
<td>MS &amp; LC/MS</td>
</tr>
</tbody>
</table>
Drug quality survey in Enugu Metropolis, Nigeria

Malaria Burden – Highest in SS Africa; 48 Million clinical episodes; 180,000 deaths per year
ACTs adopted in 2005

Types of providers – pharmacy, patent medicine vendors and public health facilities

Sampling methods – convenience, mystery client and overt sampling approaches

Total no of samples analysed – 3024 artemisinin containing antimalarials
### Results of Chemical Analyses ACAs purchased in Enugu, Nigeria; n = 3024

<table>
<thead>
<tr>
<th>Outlets</th>
<th>Acceptable Quality</th>
<th>Substandard</th>
<th>Degraded</th>
<th>Falsified</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Convenience (n = 200; total brands = 49; brands per outlet = 2.1)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pharmacies (4)</td>
<td>62 (88.6%)</td>
<td>4 (5.7%)</td>
<td>2 (2.9%)</td>
<td>2 (2.9%)</td>
<td>70</td>
</tr>
<tr>
<td>PMVs (16)</td>
<td>97 (81.5%)</td>
<td>16 (13.4%)</td>
<td>2 (1.7%)</td>
<td>4 (3.4%)</td>
<td>119</td>
</tr>
<tr>
<td>Public health facilities (2)</td>
<td>4 (80.0%)</td>
<td>1 (20.0%)</td>
<td>0</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Market stalls (1)</td>
<td>6 (100.0%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td><strong>All outlets (23)</strong></td>
<td>169 (84.5%)</td>
<td>21 (10.5%)</td>
<td>4 (2.0%)</td>
<td>6 (3.0%)</td>
<td>200</td>
</tr>
<tr>
<td><strong>Mystery clients (n = 1919; total brands = 102; brands per outlet = 0.4)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pharmacies (92)</td>
<td>803 (90.0%)</td>
<td>68 (7.6%)</td>
<td>16 (1.8%)</td>
<td>5 (0.6%)</td>
<td>892</td>
</tr>
<tr>
<td>PMVs (174)</td>
<td>94 (91.9%)</td>
<td>51 (5.2%)</td>
<td>9 (0.9%)</td>
<td>19 (2.0%)</td>
<td>973</td>
</tr>
<tr>
<td>Public health facilities (13)</td>
<td>51 (94.4%)</td>
<td>3 (5.6%)</td>
<td>0</td>
<td>0</td>
<td>54</td>
</tr>
<tr>
<td><strong>All outlets (279)</strong></td>
<td>1748 (91.1%)</td>
<td>122 (6.4%)</td>
<td>25 (1.3%)</td>
<td>24 (1.2%)</td>
<td>1919</td>
</tr>
<tr>
<td><strong>Overt (n = 905; total brands = 79; brands per outlet = 0.7)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pharmacies (54)</td>
<td>488 (89.4%)</td>
<td>50 (9.2%)</td>
<td>8 (1.5%)</td>
<td>0</td>
<td>546</td>
</tr>
<tr>
<td>PMVs (65)</td>
<td>340 (94.7%)</td>
<td>13 (3.6%)</td>
<td>1 (0.3%)</td>
<td>5 (1.4%)</td>
<td>359</td>
</tr>
<tr>
<td>Public health facilities (0)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>All outlets (119)</strong></td>
<td>828 (91.5%)</td>
<td>63 (6.9%)</td>
<td>9 (1.0%)</td>
<td>5 (0.6%)</td>
<td>905</td>
</tr>
</tbody>
</table>
Quality of ACAs at 98 Outlets visited during both Mystery Clients and Overt Sampling in Enugu, Nigeria

<table>
<thead>
<tr>
<th>Variable</th>
<th>Sampling method</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mystery clients</td>
<td>Overt</td>
<td>p-value</td>
<td></td>
</tr>
<tr>
<td>Outlets</td>
<td>98 of 277 (35.4%)</td>
<td>98 of 119 (82.4%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Samples</td>
<td>720</td>
<td>721</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brands</td>
<td>78 (72.9%)</td>
<td>72 (67.3%)</td>
<td>0.37</td>
<td></td>
</tr>
<tr>
<td>Authentic</td>
<td>669 (92.9%)</td>
<td>665 (92.2%)</td>
<td>0.62</td>
<td></td>
</tr>
<tr>
<td>Substandard</td>
<td>35 (4.9%)</td>
<td>46 (6.4%)</td>
<td>0.21</td>
<td></td>
</tr>
<tr>
<td>Degraded</td>
<td>7 (1.0%)</td>
<td>5 (0.7%)</td>
<td>0.56</td>
<td></td>
</tr>
<tr>
<td>Falsified</td>
<td>9 (1.3%)</td>
<td>5 (0.7%)</td>
<td>0.28</td>
<td></td>
</tr>
</tbody>
</table>

Note: No of brands purchased = 107
## Risk Factors Associated with Poor Quality ACAs (substandard, degraded and falsified); n=2824.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total samples</th>
<th>Poor quality samples</th>
<th>Adjusted odds ratios (95% CI)</th>
<th>LR test p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Risk factors for poor quality (substandard, degraded and falsified) ACAs</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Generic type</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AM</td>
<td>1701</td>
<td>4.7%</td>
<td>1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DHA</td>
<td>501</td>
<td>14.4%</td>
<td>2.4 (1.6,3.4)</td>
<td></td>
</tr>
<tr>
<td>AS</td>
<td>622</td>
<td>6.9%</td>
<td>1.4 (0.9,2.2)</td>
<td></td>
</tr>
<tr>
<td>WHO prequalified/QAACT</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not prequalified</td>
<td>2047</td>
<td>9.3%</td>
<td>1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>prequalified</td>
<td>777</td>
<td>0.6%</td>
<td>0.08 (0.02,0.3)</td>
<td></td>
</tr>
<tr>
<td><strong>AMFm</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>non AMFm drugs</td>
<td>2072</td>
<td>9.3%</td>
<td>1</td>
<td>0.012</td>
</tr>
<tr>
<td>AMFm drugs</td>
<td>752</td>
<td>0.5%</td>
<td>0.24 (0.1,0.8)</td>
<td></td>
</tr>
<tr>
<td><strong>Region of stated country of manufacture</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asia</td>
<td>1940</td>
<td>8.2%</td>
<td>1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Africa</td>
<td>546</td>
<td>5.5%</td>
<td>2.1 (1.3,3.2)</td>
<td></td>
</tr>
<tr>
<td>Europe</td>
<td>141</td>
<td>0.7%</td>
<td>0.04 (0.06,0.4)</td>
<td></td>
</tr>
<tr>
<td>North America</td>
<td>197</td>
<td>2.6%</td>
<td>12.5 (2.7,56.9)</td>
<td></td>
</tr>
<tr>
<td><strong>Expired at time of analysis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>not expired</td>
<td>2537</td>
<td>5.2%</td>
<td>1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>expired*</td>
<td>275</td>
<td>21.5%</td>
<td>6.4 (4.4,9.3)</td>
<td></td>
</tr>
</tbody>
</table>
## Risk Factors Associated with Falsified ACAs

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total samples</th>
<th>Poor quality samples</th>
<th>Adjusted odds ratios (95% CI)</th>
<th>LR test p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Risk factors specifically for falsified ACAs</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Outlet type</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>pharmacies</td>
<td>1438</td>
<td>5 (0.4%)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>PMVs</td>
<td>1332</td>
<td>24 (1.8%)</td>
<td>3.9 (1.5, 10.1)</td>
<td>0.002</td>
</tr>
<tr>
<td>public health facilities</td>
<td>54</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td><strong>Generic type</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AM</td>
<td>1701</td>
<td>8 (0.5%)</td>
<td>1</td>
<td>0.001</td>
</tr>
<tr>
<td>DHA</td>
<td>501</td>
<td>18 (3.6%)</td>
<td>5.9 (1.9, 18.1)</td>
<td></td>
</tr>
<tr>
<td>AS</td>
<td>622</td>
<td>3 (0.5%)</td>
<td>0.9 (0.2, 3.5)</td>
<td></td>
</tr>
<tr>
<td><strong>Region of stated country of manufacture</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asia</td>
<td>1940</td>
<td>7 (0.4%)</td>
<td>1</td>
<td>0.002</td>
</tr>
<tr>
<td>Africa</td>
<td>546</td>
<td>17 (3.1%)</td>
<td>5.0 (1.9, 13.2)</td>
<td></td>
</tr>
<tr>
<td>Europe</td>
<td>141</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>North America</td>
<td>197</td>
<td>5 (2.5%)</td>
<td>27.9 (5.2, 149.4)</td>
<td></td>
</tr>
</tbody>
</table>
Nigeria Falsified samples; LSHTM - HPLC

Artsunate - 4.8
Artemisinin - 5.5
Dihydroartemisinin - 5.2
Impurity DHA - 4.3
Artemether - 8.1

Lumefantrine – 4.6
Artemether – 3.8

Fake
Acceptable quality

DHA - 3.097

PIP - 1.98

Nigeria ACT Results: Samples of Acceptable Quality

DART-MS

[Artemether + NH$_4$]$^+$

[Artesunate + NH$_4$]$^+$

[Dihydroartemisinin + NH$_4$]$^+$

[Piperaquine + H]$^+$

[Amodiaquine + H]$^+$

Lumefantrine + H]$^+$

+MS, 4.6-5.5min #(276-328), Background Subtracted

+MS, 0.8-1.8min #(49-107), Background Subtracted

+MS, 0.5-0.7min #(29-44), Background Subtracted
Nigeria Falsified samples; DART-MS at GT

[DART-MS]
[Ciprofloxacin + H]^+ instead of artemether

[DART-MS/MS]
Fragmentation pattern indicates ciprofloxacin

[Ciprofloxacin NIST MS/MS]
### Falsified samples from Nigeria – Details

<table>
<thead>
<tr>
<th>Stated brand</th>
<th>Stated country of manufacture</th>
<th>Stated manufacturer</th>
<th>Stated API</th>
<th>Compound found</th>
</tr>
</thead>
<tbody>
<tr>
<td>Artesunat®</td>
<td>Vietnam</td>
<td>Mekophar</td>
<td>AS†</td>
<td>DEHA or DOA</td>
</tr>
<tr>
<td>Artesunat®</td>
<td>Vietnam</td>
<td>Mekophar</td>
<td>AS†</td>
<td>DEHA or DOA</td>
</tr>
<tr>
<td>Artesunat®</td>
<td>Vietnam</td>
<td>Mekophar</td>
<td>AS†</td>
<td>Acetaminophen</td>
</tr>
<tr>
<td>Artesmequine®</td>
<td>China</td>
<td>Greenfield</td>
<td>AS-MEF</td>
<td>Unidentified</td>
</tr>
<tr>
<td>Coartem® (USA)</td>
<td>USA</td>
<td>Novartis</td>
<td>AM-LUM</td>
<td>Chlorzoxazone (Muscle relaxant)</td>
</tr>
<tr>
<td>Coartem® (USA)</td>
<td>USA</td>
<td>Novartis</td>
<td>AM-LUM</td>
<td>Chlorzoxazone</td>
</tr>
<tr>
<td>Coartem® (USA)</td>
<td>USA</td>
<td>Novartis</td>
<td>AM-LUM</td>
<td>Chlorzoxazone</td>
</tr>
<tr>
<td>Lonart-DS®</td>
<td>India</td>
<td>Bliss GVS</td>
<td>AM-LUM</td>
<td>Ciprofloxacin (antibiotic)</td>
</tr>
<tr>
<td>Lonart-DS®</td>
<td>India</td>
<td>Bliss GVS</td>
<td>AM-LUM</td>
<td>Ciprofloxacin</td>
</tr>
<tr>
<td>Duo-Cotecxin®</td>
<td>China</td>
<td>Zheijang Holley</td>
<td>DHA-PIP</td>
<td>DEHA or DOA</td>
</tr>
<tr>
<td>Waipa Act</td>
<td>Nigeria</td>
<td>Kunimed</td>
<td>DHA-PIP</td>
<td>Acetaminophen</td>
</tr>
</tbody>
</table>

**Note:** † = mono therapy;  
DEHA or DOA = petroleum products [Bis(2-ethylhexyl) adipate or Dioctyl adipate]
Examples of Falsified Samples from Enugu

AM/LUM

AS monotherapy

DHA/PIP formulation locally manufactured

AS/MF
Visual inspection of Falsified samples from Nigeria

DHA/PIP formulation locally manufactured

AM/LUM formulations

No S-APIs detected

Yes S-APIs detected

Pkt has 1 extra marking
No falsified Co-formulation of ASAQ found

WHY?
Countries where samples collected

RWANDA (2008)
TANZANIA (2010 & 2011)*
CAMBODIA (2010)*
KINTAMPO, GHANA (2011)*
ENUGU, NIGERIA (2013)
EQUATORIAL GUINEA, BIOKO ISLAND (2014)
ILORIN, NIGERIA (2013)†
THAILAND (2014)†
BURMA (2014)†

ACTc COUNTRY
NON-ACTc COUNTRY

*AFFORDABLE MEDICINES FACILITY FOR MALARIA (AMFM)
†TRACKING RESISTANCE TO ARTEMISININ COLLABORATION (TRAC)
### ACTc DQ: Sampling methods used

<table>
<thead>
<tr>
<th>COUNTRY</th>
<th>Method of sampling OUTLETS</th>
<th>Method of sampling DRUGS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bioko Island, Equatorial Guinea</td>
<td>Random / National survey</td>
<td>• Mystery client</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Overt</td>
</tr>
<tr>
<td>Cambodia</td>
<td>Random / National survey*</td>
<td>• Mystery client</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Overt</td>
</tr>
<tr>
<td>Ghana</td>
<td>Random / 1 locality</td>
<td>• Mystery client</td>
</tr>
<tr>
<td>Nigeria</td>
<td>Random / 1 region</td>
<td>• Mystery client</td>
</tr>
<tr>
<td>Rwanda</td>
<td>Random / National survey</td>
<td>• Mystery client</td>
</tr>
<tr>
<td>Tanzania</td>
<td>Random / National survey</td>
<td>• Overt</td>
</tr>
</tbody>
</table>

* from malaria endemic areas only
### Quality of ACTs found per country

Of all 10,079 samples analysed we found:

<table>
<thead>
<tr>
<th>Country (date of collection)</th>
<th>Samples</th>
<th>Brands</th>
<th>Quality assured</th>
<th>Substandard</th>
<th>Falsified</th>
<th>Artemisinin Monotherapy Tablets</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rwanda (2008)</td>
<td>97</td>
<td>1</td>
<td>93.8%</td>
<td>6.2%</td>
<td>0 found</td>
<td>Not Found</td>
</tr>
<tr>
<td>Cambodia (2010)</td>
<td>291</td>
<td>21</td>
<td>68.7%</td>
<td>31.3%</td>
<td>0 found</td>
<td>Found</td>
</tr>
<tr>
<td>Ghana - Kintampo (2011)</td>
<td>257</td>
<td>31</td>
<td>63.0%</td>
<td>37.0%</td>
<td>0 found</td>
<td>Not Found</td>
</tr>
<tr>
<td>Tanzania (2010)</td>
<td>1737</td>
<td>37</td>
<td>88.0%</td>
<td>12.0%</td>
<td>0 found</td>
<td>Found</td>
</tr>
<tr>
<td>Tanzania (2011)</td>
<td>2546</td>
<td>46</td>
<td>97.8%</td>
<td>2.2%</td>
<td>0 found</td>
<td>Found</td>
</tr>
<tr>
<td>Nigeria - Enugu Metropolis (2013)</td>
<td>3024</td>
<td>131</td>
<td>92.2%</td>
<td>6.6%</td>
<td>1.2%</td>
<td>Found</td>
</tr>
<tr>
<td>Bioko Island- Equatorial Guinea (2014)</td>
<td>677</td>
<td>142</td>
<td>91.0%</td>
<td>1.6%</td>
<td>7.4%</td>
<td>Found</td>
</tr>
<tr>
<td>Nigeria - Ilorin city (2013)</td>
<td>1450</td>
<td>77</td>
<td>91.5%</td>
<td>7.7%</td>
<td>0.8%</td>
<td>Found</td>
</tr>
</tbody>
</table>
Quality of ACTs in the Countries where we sampled

- NO falsified ACTs found in 4 of 6 countries
- Substandard drugs were found in all countries
Summary of Findings

Large sample sizes in a wide range of geographic settings.
- Corroborated between 3 laboratory findings and 2 different detection methods.
- Results inform understanding of the reliability of stated APIs, unexpected (toxic) compounds and risk factors

Overall reassuring results, but “no room for complacency”
- Results from Nigeria and Bioko Island show falsified
- Substandard drugs are prevalent in all countries (up to 1 in 3 samples)
- Monotherapy tablets still available

Data highlights the need for continuous drug quality monitoring by NRAs
- ACTcDQ provides insights into the performance of different sampling approaches and sample analysis methods.

We are happy to share our experience and methods to ensure better monitoring to stop this scourge of poor quality drugs.
ACKNOWLEDGEMENTS

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ACTc – IMPACT-2 teams at LSHTM, CDC and Tanzania, Ghana team

GUARD team – Cambodia

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Masters students - M El Sherbiny, I Fadeyi & I Mamadu

Teams on the ground purchasing and packaging the samples

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More information

www.actconsortium.org/drugquality

http://malaria.lshtm.ac.uk/facilities/analytical-service-measuring-antimalarials-drugs-and-insecticides