



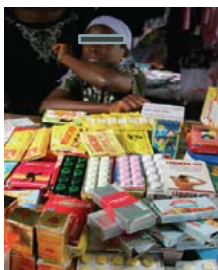
**A SURVEILLANCE SYSTEM AND DRUG FORENSIC NETWORK TO MONITOR THE QUALITY AND AUTHENTICITY OF ARTEMISININ TREATMENTS IN AFRICA**

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Paul Newton – Oxford  
MD Green - CDC

***DRUG OUTLETS - AFRICA***



**PHARMACY**



**MARKET STALL**



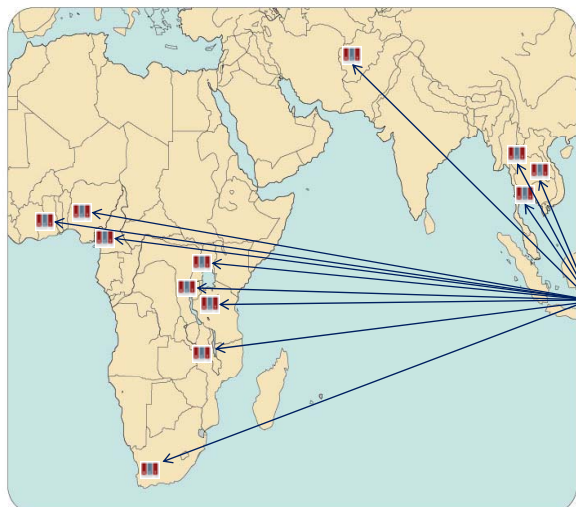
**MOBILE DRUG SELLER**

**VARIETIES OF ARTEMISININ MONOTHERAPIES AND ACTs**



**51 VARIETIES IN 1 PART OF A TOWN IN A COUNTRY IN AFRICA**

**SYSTEMATIC SURVEILLANCE WILL BE CARRIED OUT IN THE FOLLOWING NAMED COUNTRIES**



- RWANDA; TANZANIA;
- UGANDA; MALAWI;
- SOUTH AFRICA;
- NIGERIA, CAMEROON;
- GHANA;
- AFGHANISTAN; LAOS;
- CAMBODIA; VIETNAM

Sampling in other countries will be considered but have not been budgeted in the project ie Mali

## THE DETAIL OF THIS PROJECT



- **Surveillance** – Collecting samples of artemisinin monotherapies and ACTs to assess their quality from a range of settings
- **Stability** - Lab and field based studies to access the possible degradation under different storage conditions
- **Forensic and Quality Network** - Establish “Counterfeit Drug Forensic Network –CODFIN” to investigate the origin of fakes and compile a comprehensive record of drugs analysed

### STEP 1: AGREEMENTS WITH MOH IN EACH COUNTRY AND LSHTM

#### Drug Quality and Authenticity Surveillance System and Counterfeit Drug Forensic Network

Agreement between:  
London School of Hygiene & Tropical Medicine

#### 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 optimise 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 with maximum risk. Suspect samples are to be characterised by sophisticated 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 \_\_\_\_\_ 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 \_\_\_\_\_ has agreed to collaborate with the LSHTM in the collection and shipment of ACT samples for analysis in London, England. \_\_\_\_\_ 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 \_\_\_\_\_:

- (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.

\_\_\_\_\_ has been identified to coordinate the study in \_\_\_\_\_. All \_\_\_\_\_ involved in this study will be cited appropriately in any publications resulting from the study of quality of drugs from \_\_\_\_\_ either as authors (whenever they meet standard criteria for authorship as laid down by the International Committee of Medical Journal Editors (ICMJE) 2008), or in acknowledgement.

#### Duration:

This Agreement will commence on \_\_\_\_\_ and will remain in effect until 31/31/2013 (\_\_\_\_\_ years).

Date:

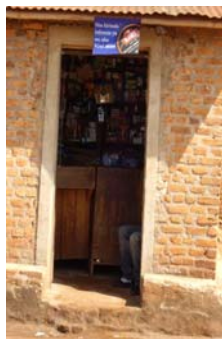
Date:

M. Peadar Ireland  
Research Contracts Office  
London School of Hygiene & Tropical Medicine  
Keppel Street, London

**STUDY STARTED IN RWANDA**



Pharmacy in Kigali



Shop in a remote town  
No drugs



Market in that remote town – No drugs



Actual pharmacy in that remote town

**CENTRAL DRUG DEPOT**



195 pharmacies / Comptoirs – List has named proprietor, location, province

**STEP 2: COLLECTION & FILLING IN THE QUESTIONNAIRE**



Submit by e-mail    Print Form

**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 it) \_\_\_\_\_

Type of drug outlet    public     private

Brand name of the collected medicine \_\_\_\_\_

Name of declared active artemisinin ingredient    artesunate     artemether     DHA     Other (name it) \_\_\_\_\_

Dose of active ingredient/s \_\_\_\_\_ mg    combined with \_\_\_\_\_ mg    \_\_\_\_\_ mg

Artemisinin ingredient formulated with     separate from     the other active ingredients

Type of preparation (formulation)    tablet     suppository     paediatric suspension     Other (name it) \_\_\_\_\_

Batch/lot number \_\_\_\_\_    Date of manufacture \_\_\_\_\_    Expiry date \_\_\_\_\_

Description of primary container \_\_\_\_\_    Description of secondary container \_\_\_\_\_

Pack size \_\_\_\_\_ x \_\_\_\_\_ x \_\_\_\_\_ cm    Quantity collected \_\_\_\_\_

Price per pack    local currency \_\_\_\_\_    £ \_\_\_\_\_    Price per single dose    local currency \_\_\_\_\_    £ \_\_\_\_\_

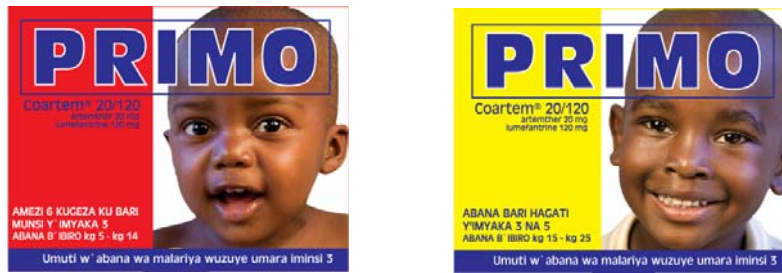
Special comments \_\_\_\_\_

Name and signature of collector \_\_\_\_\_

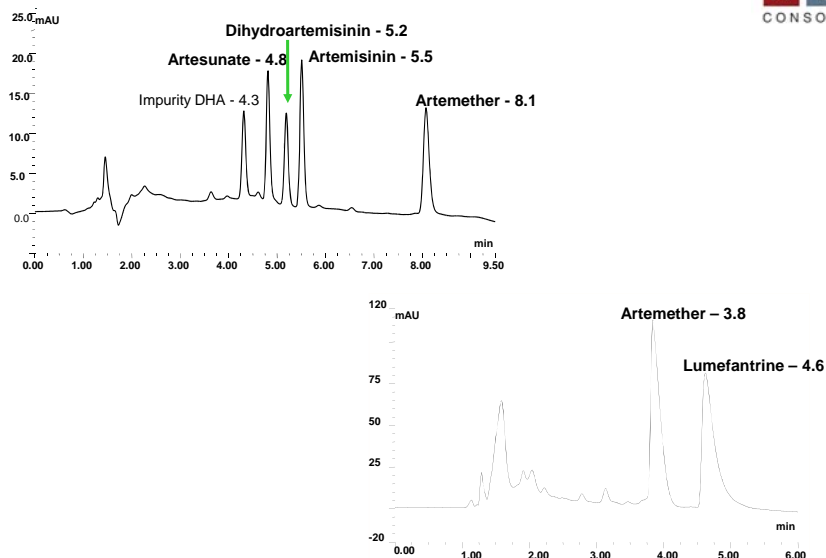
**STEP 3: ADD ALL THE INFORMATION FROM THE QUESTIONNAIRE TO AN EXCEL SHEET**

1	2	Q.num	City	Date	Description of primary container	Description of secondary container	Pack size (cm)	Quantity collected	Price per pack	Price per single dose	Special comments	Name of collector		
									Local currency / Sterling	Local currency / Sterling				
4	1	Nyamashoke	18/07/2008	Blister			12 tablets	free				Noella Umulisa		
5	2	Kigese	Jul-08	Blister			06 tablets	free				Rolande Uwase		
6	2	Kigese	Jul-08	Blister			06 tablets	free						
7	2	Kigese	Jul-08	Blister			06 tablets	free						
8	3	Kinisi	Jul-08	Blister			06 tablets	free				Rolande Uwase		
9	4	Nyamure	Jul-08	Blister			12 tablets	not available				Noella Umulisa		
10	4	Nyamure	Jul-08	Blister			06 tablets	not available				Noella Umulisa		
11														
12														
1	2	Q.num	City	Date	Active artemisinin ingredient	Dose of Active ingredient(s) mg	Combined with	mg	Formulated with	Separate from	The other active ingredient	Tablet	Suppository	Paediatric suspension
4	1	Nyamashoke	18/07/2008		20	Lumefantrine	120	X	X			X		
5	2	Kigese	Jul-08		20	Lumefantrine	120	X	X			X		
6	2	Kigese	Jul-08		20	Lumefantrine	120	X	X			X		
7	2	Kigese	Jul-08		20	Lumefantrine	120	X	X			X		
8	3	Kinisi	Jul-08		20	Lumefantrine	120	X	X			X		
9	4	Nyamure	Jul-08		20	Lumefantrine	120	X	X			X		
10	4	Nyamure	Jul-08		20	Lumefantrine	120	X	X			X		
11														
12														
1	2	Q.num	City	Date	Batch lot number	Date of manufacture	Expiry date	Description of primary container	Description of secondary container	Pack size (cm)	Quantity collected	Price per pack	Price per single dose	
												Local currency / Sterling	Local currency / Sterling	
4	1	Nyamashoke	18/07/2008	F0378		Aug-08	Blister				12 tablets	free		
5	2	Kigese	Jul-08	F0602		May-07	Apr-09	Blister			12 tablets	free		
6	2	Kigese	Jul-08	F0510			Apr-09	Blister			06 tablets	free		
7	2	Kigese	Jul-08	F0510			Apr-09	Blister			06 tablets	free		
8	3	Kinisi	Jul-08	F0510		May-07	Apr-09	Blister			06 tablets	free		
9	4	Nyamure	Jul-08	F0602		May-07	Apr-09	Blister			12 tablets	not available		
10	4	Nyamure	Jul-08	F0510			Apr-09	Blister			06 tablets	not available		
11											12 tablets	not available		
12														
1	2	Q.num	City	Date	Description of primary container	Description of secondary container	Pack size (cm)	Quantity collected	Price per pack	Price per single dose	Special comments	Name of collector		
									Local currency / Sterling	Local currency / Sterling				
4	1	Nyamashoke	18/07/2008	Blister				12 tablets	free			Noella Umulisa		
5	2	Kigese	Jul-08	Blister				12 tablets	free			Rolande Uwase		
6	2	Kigese	Jul-08	Blister				06 tablets	free					
7	2	Kigese	Jul-08	Blister				06 tablets	free					
8	3	Kinisi	Jul-08	Blister				06 tablets	free			Rolande Uwase		
9	4	Nyamure	Jul-08	Blister				12 tablets	not available			Noella Umulisa		
10	4	Nyamure	Jul-08	Blister				06 tablets	not available			Noella Umulisa		
11	5	Kamonyi	14/07/2009	Blister				12 tablets	not available			Rolande Uwase		
12	5	Kamonyi	14/07/2009	Blister				06 tablets	free			Rolande Uwase		
13	6	Kiambi	Jul-08	Blister				12 tablets	free			Noella Umulisa		
14	6	Kiambi	Jul-08	Blister				06 tablets	free			Noella Umulisa		

**STEP 4: SCAN THE PACKET**



**STEP 5 - ANALYSIS USING HPLC**



### STABILITY STUDIES



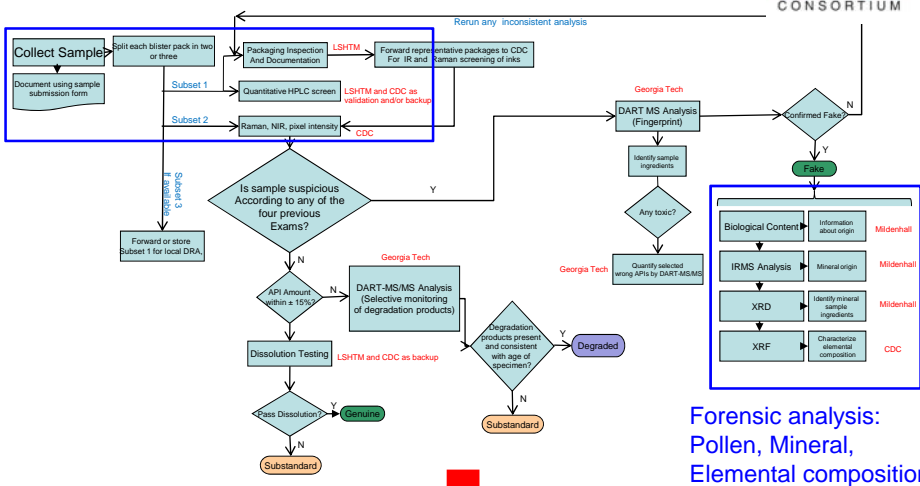
#### Africa

- Coartem® and AS/AQ tablets will be placed in field locations and in the chamber to mimic the field conditions

#### SE Asia

- Drugs purchased with WT funds have been placed at sites and samples will also be placed in chambers in USA

### DRUG QUALITY AND FORENSIC ANALYSIS WORKFLOW



Forensic analysis:  
Pollen, Mineral,  
Elemental composition

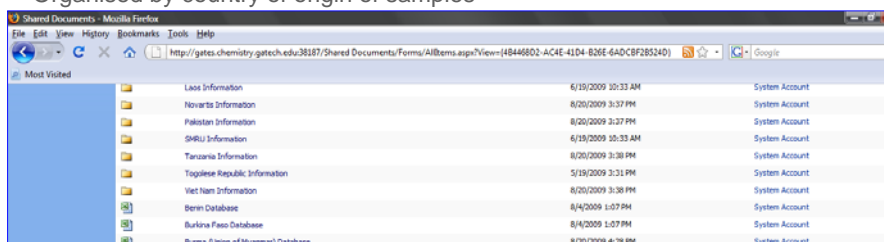
ALL INFORMATION FED INTO CODFIN

### CODFIN DATABASE – GEORGIA TECH

Database is built in Microsoft SharePoint but can be accessed by any browser



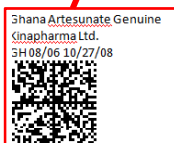
- Organised by country of origin of samples



Detail of a database with information with samples from Ghana:



A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S									
1	Sample C	Barcode	Barcode In Picture	Received	Sender	Country of	Commerci	Claimed	MBatch/Lot	Expiration	Class of M	Physical	P	A	I	Indicate	AI by	DAR	DART	Date	Test	AI by	DES	DESI	Data	Du	
2	GH 08/01	<a href="#">http://gat</a>	<a href="#">http://gat</a>	10/27/08	Mike Gree	Ghana	Malasate	F	Ernest Ch	0810G	Oct-10	Monothera	White	tour	Artesunate	Artesunate	<a href="#">http://gat</a>	<a href="#">http://gat</a>	11/14/08								
3	GH 08/02	<a href="#">http://gat</a>	<a href="#">http://gat</a>	10/27/08	Mike Gree	Ghana	Artesunate	XL	Laborat	7002	May-10	Monothera	White	tour	Artesunate	Artesunate	<a href="#">http://gat</a>	<a href="#">http://gat</a>	11/14/08								
4	GH 08/03	<a href="#">http://gat</a>	<a href="#">http://gat</a>	10/27/08	Mike Gree	Ghana	N/A	N/A	N/A	N/A	ACT	Yellow	dou	Artesunate	Artesunate	<a href="#">http://gat</a>	<a href="#">http://gat</a>	11/14/08									
5	GH 08/03E	<a href="#">http://gat</a>	<a href="#">http://gat</a>	10/27/08	Mike Gree	Ghana	N/A	N/A	N/A	N/A	ACT	White	dou	Artesunate	Artesunate	<a href="#">http://gat</a>	<a href="#">http://gat</a>	11/14/08									
6	GH 08/04	<a href="#">http://gat</a>	<a href="#">http://gat</a>	10/27/08	Mike Gree	Ghana	Gesante	1	GVVS	Labs	G0-01	Jan-09	ACT	Small	white	Artesunate	Artesunate	<a href="#">http://gat</a>	<a href="#">http://gat</a>	11/14/08							
7	GH 08/04E	<a href="#">http://gat</a>	<a href="#">http://gat</a>	10/27/08	Mike Gree	Ghana	Gesante	1	GVVS	Labs	G0-01	Jan-09	ACT	Large	yellow	Artesunate	Artesunate	<a href="#">http://gat</a>	<a href="#">http://gat</a>	11/14/08							
8	GH 08/05	<a href="#">http://gat</a>	<a href="#">http://gat</a>	10/27/08	Mike Gree	Ghana	Camosuna	Darpono	F	702005	Feb-10	ACT	Off	white	g	Artesunate	Artesunate	<a href="#">http://gat</a>	<a href="#">http://gat</a>	11/14/08							
9	GH 08/05E	<a href="#">http://gat</a>	<a href="#">http://gat</a>	10/27/08	Mike Gree	Ghana	Camosuna	Darpono	F	702005	Feb-10	ACT	Yellow	pow	Artesunate	Artesunate	<a href="#">http://gat</a>	<a href="#">http://gat</a>	11/14/08								
10	GH 08/06	<a href="#">http://gat</a>	<a href="#">http://gat</a>	10/27/08	Mike Gree	Ghana	Artesun	Z	Kinapham	7	Sep-09	Monothera	Oblong	wh	Artesunate	Artesunate	<a href="#">http://gat</a>	<a href="#">http://gat</a>	11/14/08								
11	GH 08/07	<a href="#">http://gat</a>	<a href="#">http://gat</a>	10/27/08	Mike Gree	Ghana	Cotecin	Belino	Hol	10106	Jan-09	Monothera	White	tour	Dihydroate	Dihydroate	<a href="#">http://gat</a>	<a href="#">http://gat</a>	11/14/08								



LINK 1: BAR CODE



LINK 2: PICTURE & PACKAGING

m/z	Relative Intensity
102.0303	492.4359
102.1312	655.9682
114.0997	20276.4873
114.2545	8600.2790
114.6520	176.6310
114.7946	110.2546
115.0483	35.7711
115.1050	1469.6599
119.0420	3999.1055
119.2213	1331.3444
125.1044	314.3786
129.0000	100.0000
129.1237	624.8434
155.1195	156.2357
155.1487	213.8320
163.1285	1351.9096
171.1239	496.2790
173.1102	613.3455
176.1188	455.9637
181.1302	4276.3233
182.1346	304.3218
183.1496	232.1370
189.1380	240.7055
190.1323	445.4896
191.1203	478.1743
193.1700	447.4143
195.1469	396.2282
199.1529	1606.5555

LINK 3: RAW MASS SPECTRAL DATA



## CONCLUSION

- Samples will be classified as counterfeit, substandard, degraded or genuine based on packaging and chemical analysis
- Frequency of poor drug quality in relation to type of drug, formulation, type of drug outlet and study site in each country
- CODFIN will provide a comprehensive listing of name, packaging, composition declared / found and other revealing ingredients (e.g. pollen grains) to help locate the origin of the drugs