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# **Costing Artemisinin- based Combination Therapy and Rapid Diagnostic Tests for Malaria in Democratic Republic of Congo**

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*June 2005*

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Prepared by:

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- ▲ *Availability and appropriate use of health commodities.*

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# Abstract

Malaria is one of the largest causes of morbidity and mortality in the Democratic Republic of Congo (DRC), leading to a dramatic loss of life and productivity. As a result of increasing resistance to traditional antimalarials in various parts of the country, the government of DRC (GoDRC) is in the process of changing its malaria treatment policy to focus on artemisinin-based combination therapy (ACT).

Working in collaboration with the Roll Back Malaria partnership, the Partners for Health Reform*plus* project undertook a costing study to estimate the five-year financing needs for ACT drug procurement under two possible ACT combinations: Coartem® and artesunate amodiaquine (ART AQ). In order to estimate financing needs for ACT procurement, the variables population, age-specific malaria incidence, health center utilization, health center coverage, and drug pricing were estimated for the years 2005-2009.

It is anticipated that given the current epidemiological situation, utilization of health services, and costs of the various ACTs, ACT financing needs for DRC will reach US\$84.8 million per year for Coartem® and US\$44.4 million per year for the ART AQ combination.

Following the preliminary results of the costing, the GoDRC has made a policy change to name ART AQ as the national first-line treatment for malaria. Once current Global Fund to Fight AIDS Tuberculosis and Malaria ACT procurement resources are exhausted in Year 2 of implementation, ACT funding must be secured for the medium- to long-term future. ACT funding is likely to come from the Global Fund, the World Bank, and the various other partner agencies.

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# Acronyms

<b>ACT</b>	Artemisinin-based Combination Therapy
<b>ART AQ</b>	Artesunate Amodiaquine
<b>DRC</b>	Democratic Republic of Congo
<b>CRS</b>	Catholic Relief Services
<b>GoDRC</b>	Government of Democratic Republic of Congo
<b>IPT</b>	Intermittent Preventative Therapy
<b>ITN</b>	Insecticide-treated Bednet
<b>MICS</b>	Multiple Indicator Cluster Survey
<b>MSF</b>	<i>Médecins Sans Frontières</i> (Doctors without Borders)
<b>NGO</b>	Non-governmental organization
<b>PHR<sub>plus</sub></b>	Partners for Health Reform <sub>plus</sub>
<b>PNLP</b>	<i>Programme National de Lutte contre le Paludisme</i> (National Malaria Control Program)
<b>RBM</b>	Roll Back Malaria Partnership
<b>RDT</b>	Rapid Diagnostic Test
<b>SP</b>	Sulfadoxine-Pyrimedthamine
<b>USAID</b>	United States Agency for International Development
<b>WHO</b>	World Health Organization



# Acknowledgments

This study of artemisinin-based combination therapy costing needs in DRC was informed by discussions with the U.S. Agency for International Development (USAID) and the World Bank in Washington DC, the U.S. Centers for Disease Control and Prevention in Atlanta, and the World Health Organization in Geneva.

At the country level, several government and non-governmental organizations provided input on both the costing assumptions and methodology, including the National Malaria Control Program, SANRU, Médecins sans Frontières France and Belgium, Catholic Relief Services, and the European Commission for Humanitarian Aid.

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# Executive Summary

Malaria is one of the largest causes of morbidity and mortality in the Democratic Republic of Congo (DRC), leading to a dramatic loss of life and productivity. The government of DRC (GoDRC) has adopted the Abuja Targets to Roll Back Malaria in Africa, which specify that at least 60 percent of those suffering from malaria have prompt access to, and are able to correctly use, affordable and appropriate treatment within 24 hours of the onset of symptoms.

As a result of increasing resistance to traditional antimalarials in various parts of the country, the GoDRC underwent the revision process for its anti-malarial treatment policy to switch from sulphadoxine-pyrimethamine to an artemisinin-based combination therapy (ACT).

The Partners for Health Reform *plus* (PHR *plus*) project undertook a costing study to estimate the five-year financing needs for ACT drug procurement under two possible ACT combinations, Coartem® and artesunate amodiaquine (ART AQ). PHR *plus*' ACT costing study was undertaken on behalf of the Roll Back Malaria Partnership in conjunction with the World Bank to establish the financing needs for implementation of ACT drugs. The results of this study were designed to help inform the policy dialogue on the national guidelines for treating malaria and to provide the World Bank, a potential funder, with information on the magnitude of the ACT financing gap. The estimate uses a population-based malaria incidence approach incorporating the variables: population, age-specific malaria incidence, health center utilization, health center coverage, and drug pricing, estimated for the years 2005-2009.

Rapid diagnostic tests (RDTs) were also costed for cost-effectiveness when used in conjunction with ACT drugs. However given current RDT costs combined with implementation concerns, RDTs are not currently considered to be a practical cost reduction intervention at this time.

It is anticipated that, given the current epidemiological situation, utilization of health services and costs of the various ACTs, ACT financing needs for DRC will reach US\$84.8 million per year for Coartem® or US\$44.4 million per year for the ART AQ combination. Following the preliminary results of the costing, the GoDRC has made a policy change to name ART AQ as the national first-line treatment for malaria.

The Global Fund to Fight AIDS Tuberculosis and Malaria award for malaria during the third round of proposals will cover the first year and part of the second year of ACT implementation. ACT funding must be secured for the medium- to long-term future. Financing for the purchase of ACTs is likely to come from the Global Fund, the World Bank, and the various other partner agencies.



# 1. Introduction

Malaria is one of the largest causes of morbidity and mortality in the Democratic Republic of Congo (DRC), where 53.8 percent of the population is infected with malarial parasites (MARALite 2002). The majority of the population lives in malaria-endemic regions where transmission occurs year-round at varying intensities (Roll Back Malaria [RBM] 2005). Approximately 95 percent of the population is at risk of malaria (Adeya 2004), with malaria responsible for 68 percent of outpatient visits and 30 percent of hospital admissions (RBM 2005) in DRC. The burden of malarial disease causes excessive morbidity and mortality, leading to a dramatic loss of life and productivity.

Malaria control efforts can be divided into preventative and curative. Prevention typically focuses on the distribution of insecticide-treated bednets (ITNs) and intermittent preventative therapy (IPT) or chemoprophylaxis to protect women during pregnancy. Curative care for malaria typically involves outpatient treatment with first-line antimalarials and hospitalization for complicated cases. The government of DRC (GoDRC) has adopted the Abuja Targets to Roll Back Malaria in Africa, which state that at least 60 percent of those suffering from malaria have prompt access to, and are able to correctly use, affordable and appropriate treatment within 24 hours of the onset of symptoms (RBM 2000).

The national malaria drug policy identified sulphadoxine-pyrimethamine (SP) as the first-line drug to be used in treating malaria until March of 2005. However, as growing resistance to SP ranges from a low of 1-2 percent in the Kasai to a high of 60 percent in eastern regions of the country,<sup>1</sup> the GoDRC, led by the National Malaria Control Program (*Programme National de Lutte contre le Paludisme*, PNLP), has taken significant steps to introduce more effective antimalarial drugs.

The DRC is divided into approximately 500 health zones, the basic operational unit of the health system. Around two-thirds of health zones provide primary health care (Adeya 2004); the remaining third do not have ready access to health services. Most of the health zones are administered by partner agencies that work in conjunction with the GoDRC to provide primary health services. Because of the decentralized nature of the health system and the autonomy that implementing agencies have in all of their health zones, some of the partner organizations, such as *Médecins sans Frontières* France and Belgium (MSF-F, MSF-B), already provide ACT drugs as primary antimalarials, while others, such as SANRU III and Catholic Relief Services (CRS) provide SP.

The Partners for Health Reform<sup>plus</sup> project implemented a costing study in December 2004 to estimate the five-year financing needs for artemisinin-based combination therapies (ACTs) to treat malaria. This study was undertaken on behalf of the Roll Back Malaria Partnership in conjunction with the World Bank to estimate the financing need for ACT drugs in DRC. The costing study was implemented with the intention of 1) informing the policy dialogue on the national guidelines for treating malaria, and 2) identifying for the World Bank and other donors the financing gap between what was available through the Global Fund to Fight AIDS, Tuberculosis and Malaria award for malaria and the financing needs for ACT drugs. The estimate uses a population-based malaria

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<sup>1</sup> Efficacy trials, see Annex A.

incidence approach incorporating the variables: population, age-specific malaria incidence, health center utilization, health center coverage, and drug pricing, estimated for the years 2005-2009.

In March of 2005, following the dissemination of costing study results, the PNLP issued the Implementation Plan for the New Policy on the Antimalarial Treatment in DRC (PNLP 2005). This policy outlines the change to artesunate amodiaquine (ART AQ), which will be distributed by health centers at the health zone level.

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## 1.1 Artemisinin-based Combination Therapy

Artemisinin-based combination therapy is a new type of antimalarial drug combination, based on a derivative of the *Artemisia* plant combined with another antimalarial drug, such as SP or amodiaquine. Trials of ACTs have proved these combinations to be effective at treating malaria and reducing malaria transmission (Arrow et al. 2004). The use of combination therapies as first-line treatment aims to reduce the growth of resistance to new malaria medications, making treatment regimens effective for a longer period of time. There is currently only one Artemisinin-based combination therapy that is coformulated, Coartem<sup>®</sup>, which is produced by Novartis. The World Health Organization (WHO) has negotiated a public sector price with Novartis, provided that the procuring government purchases Coartem<sup>®</sup> through the WHO. Several other coformulated combinations are due on the market shortly, including Artecon<sup>®</sup> and a coformulation of artesunate and amodiaquine that is being produced by Sanofi-Aventis. Generic combinations, such as artesunate amodiaquine and artesunate-SP can be purchased separately or co-packaged.

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## 1.2 Rapid Diagnostic Tests

In rural areas, malaria is often detected through a syndromic diagnosis. However, approximately half of all cases of syndromically diagnosed malaria are actually malaria (communication with MSF-France in DRC). Rapid diagnostic tests (RDTs) have the potential to provide an accurate diagnosis of malaria in areas where microscopy is not an option (WHO 2004). RDTs diagnose malaria by detecting antigens produced by malaria parasites. RDTs can detect the antigens of up to three species of malaria through the detection of antigens. These tests come in the form of dipsticks, cassettes, or cards and typically cost US\$0.65-1.00 (WHO 2004). Cost savings on antimalarial drugs through the use of RDTs will depend on the level of parasitemia in the population, as well as on correct storage and usage of tests. A 'cool chain' is recommended for the transport and storage of RDTs, as their sensitivity decreases significantly in temperatures over 30°C. RDTs are not recommended for use in young children living in highly endemic areas.

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## 1.3 Global Fund to Fight AIDS, Tuberculosis and Malaria

The Global Fund to Fight AIDS, Tuberculosis and Malaria has been an important financing mechanism for enabling national governments to procure ACT drugs, which cost several times more than previously used antimalarials. The Global Fund's move toward ACTs occurred in June of 2004, when a group of experts recommended to the Global Fund Secretariat that, due to growing non-ACT antimalarial drug resistance, certain countries, including DRC, should reprogram part of their Global Fund awards for malaria to include procurement funds for ACT drugs (Feachem 2004).

The Global Fund awarded US\$53.9 million in malaria funds to the GoDRC during the third round of proposals, US\$25.0 million of which has been reprogrammed for the procurement of ACT

drugs. The GoDRC also plans to submit an application to the Global Fund's 5<sup>th</sup> Round of proposals to supplement contributions for ACT drug procurement by the World Bank, European Union, and U.S. Agency for International Development.

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## 1.4 Financing Gap

In order to estimate the financing needs for the implementation of ACT drugs in DRC, two potential drug choices were costed. Coartem<sup>®</sup> and ART AQ were analyzed to establish the costs incurred over the first five years of implementation. The Global Fund monies will cover the bulk of the first two years of funding. The five-year projections allow the GoDRC to plan for the medium-term financing of ACT drugs in DRC. The GoDRC then has the option to seek the balance of funds through future Global Fund round or other sources.

As ACT drugs are significantly more expensive than traditional antimalarials, an analysis of rapid diagnostic tests for malaria was included in this exercise to determine whether screening potential malaria cases with RDTs would ease the financial burden of ACTs.



## 2. Methodology

The financing needs for ACT drugs in DRC were calculated using a population-based fever incidence model. The following formula was used to determine the total cost of ACTs.

### 2.1 Formula

Total drug cost per year for using ACT treatment option = population by age \* yearly episodes of malaria by age group \* % health facility utilization \* health zone coverage \* (1-public health impact) \* drug cost (including estimated handling fees)

In order to arrive at the total drug cost per year, certain data were collected (Table 1) and assumptions were made (see below). The assumptions and data were validated with the PNLP and other experts in-country.

**Table 1. Data Collected in ACT Costing**

Variable	Data source
Population figures by province	<i>Institut National de Statistiques</i> 2004
Population distribution by age	Multiple Indicator Cluster Survey 2001
Population growth rate	World Bank 2002
Episodes per person within age group	<i>Programme National de Lutte Contre le Paludisme</i> and non-governmental organization (NGO) implementing partners
% clinical failure for antimalarials by sentinel site	University of Kinshasa, U.S. Centers for Disease Control and Prevention, <i>Médecins Sans Frontières</i>
Utilization of health services	Malaria Strategic Plan 2002-2006, implementing agencies
Health zone coverage*	Local experts' consensus
Cost of drug combinations in DRC	International costs**, obtained from Novartis, PNLP

\* Health zone coverage refers to the percentage of the population covered by health zones offering ACTs at the health center level.

\*\* WHO (2004)

ACT needs were assessed at the national level and recommendations for implementation made. Province-level recommendations are outlined in Annex A. The model estimates treatment cost for all febrile patients received at the health center in health zones implementing ACTs.

### 2.2 Assumptions

- ▲ The model projects ACT need based on episodes per person within each age group.

- ▲ The model assumes that everyone presenting with fever<sup>2</sup> in ACT-implementing health zones received at the health center will be treated for malaria with ACTs.
- ▲ The model has not integrated data on the operational costs associated with switching anti-malarial therapies (policy change, training of health workers, distribution of new drugs, etc.) in DRC.
- ▲ A public health impact was included to account for reductions in febrile illness as a result of ITN and ACT use. Because ITN use is not currently widespread, the public health impact increases from 0 percent in the first year to 5 percent by 2009 but does not exceed it.<sup>3</sup>
- ▲ In anticipation of reaching the WHO-recommended threshold of 15 percent SP resistance (RBM n.d.), ACTs will be used in provinces where sentinel surveillance data indicates that SP resistance has already reached 10 percent (Annex A).<sup>4</sup>
- ▲ The drug combinations to be considered are:
  - △ **Coartem®** (Artemether-Lumefantrine): Coartem® is currently the only WHO-approved coformulated ACT and is available through WHO at a negotiated public sector price. A curative dose of Coartem® consists of four tablets four times over three days.
  - △ **Amodiaquine artesunate:** ART AQ is a WHO-approved co-packaged ACT. Because its elements are available as generics, the price is considerably lower than that of Coartem®. A curative dose of ART AQ for an adult is one tablet of ART with four tablets of AQ taken as one dose for three consecutive days. Sanofi-Aventis' coformulation of ART AQ, which will be available in 2006, will consist of two tablets per day for three days.
- ▲ Due to increasing levels of SP resistance throughout DRC, amodiaquine-SP and artemether-SP were not considered as viable combination therapies.
- ▲ The model does not account for wastage or leakage, as there are no data to support these variables.
- ▲ The costs of drug procurement for IPT were not included in this estimate, as ACTs are not currently approved for use in pregnant women.

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## 2.3 Estimation of Needed ACT Doses and Costs

The national population is divided into age groups and assigned appropriate drug doses. The number of malarial episodes per year per age group is used to estimate the number of malarial episodes nationally each year. At this time, there are no national-level estimates of number of fever episodes per year per person. Therefore the number of episodes used in this model is based on a

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<sup>2</sup> While Coartem® is currently not recommended for use in pregnant women, it is anticipated that the drug will soon be approved. Because of this, pregnant women were included in all cost calculations.

<sup>3</sup> SANRU has reported a reduction of 20-25 percent among children with febrile illness in areas with high ITN coverage, however this level of coverage is not widespread throughout health zones.

<sup>4</sup> There are no sentinel site data for Equateur, Kasai-Oriental, and Maniema. All are assumed to have less than 10 percent SP resistance.

consensus of experts on malaria in DRC, including the PNL, SANRU III, CRS, and MSF-France and MSF-Belgium. Estimates for episodes in children under five were corroborated by Snow et al's 2003 paper estimating ACTs needs in Africa. The health center utilization rate is derived from the national average health center utilization rate and the utilization rates of implementing partners in health zones that are likely to implement ACTs in the near future. Health center utilization is used to determine the number of age-specific ACT doses for malaria cases likely to be distributed at the health center. Once the number of treatments at each dosage has been established, the total drug cost per each treatment scenario, including estimated shipping charges, is calculated.

**Table 2. Variables Used in ACT Costing**

Population growth rate	3.0%	
Fever episodes per year, for age group	Under 5:	6.9 – 8
	5-14:	3.5 – 4
	15 and over:	1.7 - 2
Utilization (% of episodes treated with antimalarials at health center)	2005-6	30%*
	2007-9	40%**
Public/nonprofit sector coverage (% of population living in ACT-implementing health zones, with 1 health zone = ~100,000 people)	2005	20%
	2006	30%
	2007	40%
	2008	50%
	2009	60%***
Public health impact (reduction of episodes) due to ITN use and more effective antimalarials, per year	2005	0%
	2006	2%
	2007	2%
	2008	5%
	2009	5%
WHO handling fee (Coartem®)	3%§	
Private sector handling fee (ART AQ)	5%	
Internal handling charges (Coartem® and ART AQ)	N/A§§	
ACT costs (adult treatment dose in first year, including above fees)§§§	2005-9	US\$2.47
Coartem®	2005-6	US\$1.79 •
ART AQ	2007-9	US\$1.05 • •

\* The Malaria Implementation Strategy cites health center utilization as 17.9 percent nationally, while NGO implementing partners list health zone-specific rates around 30 percent. The initial health zones selected for implementation have a strong NGO presence and are likely to have utilization rates closer to 30 percent than to the national average.

\*\* The Malaria Implementation Strategy cites health center utilization as 17.9 percent nationally, while NGO implementing partners list health zone-specific rates around 30 percent. The initial health zones selected for implementation have a strong NGO presence and are likely to have utilization rates closer to 30 percent than to the national average.

\*\*\* Approximately two-thirds of the health zones in DRC are currently covered by implementing partners. It is assumed that ACTs will only be implemented in health zones with partners. It is also assumed that it is not feasible to implement ACTs in a small number of partnering health zones, due to problems with transport and storage of drugs.

§WHO (May 2004)

§§Domestic handling fees for ACT drugs and RDTs are presumed to be covered by current partner-organization distribution methods and funds.

§§§ No discount rate for future costs of money has been used in this exercise; all figures are constant.

• The price used in estimating costs for ART AQ was obtained through the PNL. While this figure is higher than the international price, it is the price that the PNL anticipates paying for this combination in DRC.

• • This change in price is intended to reflect the upcoming availability of a coformulation of ART AQ, manufactured by Sanofi-Aventis and due in 2006.



### 3. Financing Needs for ACT Scenarios

The cost of ACT drugs was estimated for Coartem® and ART AQ over a period of five years, from 2005 to 2009. The cost of ACT implementation increases with higher utilization and greater coverage throughout the country.

Financing needs for Coartem® range from US\$21.7 million in 2005 to US\$84.8 million in 2009, while ART AQ financing needs range from US\$12.7 million to US\$44.4 million for the same period (Table 3).

**Table 3. ACT Financing Needs, 2005–2009**

	<b>Coartem®</b>	<b>AQ ART</b>
<b>2005</b>	US\$21,734,561	US\$12,723,550
<b>2006</b>	US\$32,908,299	US\$19,264,728
<b>2007</b>	US\$59,053,576	US\$30,912,625
<b>2008</b>	US\$72,229,905	US\$37,810,004
<b>2009</b>	US\$84,812,355	US\$44,396,507

The reallocation of US\$25 million from DRC’s Global Fund Round 3 award can be applied to cover ACT financing for 2005 and part of 2006. The financing gaps and consequent adult dosage shortages (if gaps are not filled) for Coartem® and ART AQ begin in 2006 and remain substantial, reaching US\$84.8 million and US\$44.4 million (Table 4), or 34.3 million and 42.3 million adult doses respectively (Table 5).

**Table 4. Balance Needed to Fund Annual ACT Needs, 2005–2009**

	<b>Coartem®</b>	<b>AQ ART</b>
<b>2005</b>	US\$ (3,265,439)	US\$ (12,276,450)
<b>2006</b>	US\$ 29,642,860	US\$ 6,988,278
<b>2007</b>	US\$ 59,053,576	US\$ 30,912,625
<b>2008</b>	US\$ 72,229,905	US\$ 37,810,004
<b>2009</b>	US\$ 84,812,355	US\$ 44,396,507

**Table 5. Adult Dosage Deficit, 2005–2009**

	<b>Adult dose deficit for Coartem®</b>	<b>Adult dose deficit for ART AQ</b>
<b>2005</b>	0	0
<b>2006</b>	11,991,448	3,915,002
<b>2007</b>	23,888,987	29,440,595
<b>2008</b>	29,219,217	36,009,528
<b>2009</b>	34,309,205	42,282,387

Note: The dosage deficit is calculated in adult doses, since it is assumed that in an ACT shortage, children would be given priority access to ACT drugs. Because the dosage weighting for age groups differs between Coartem® and ART AQ, the number of adult doses is not equal.

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### **3.1 Key ACT Implementation Concerns in DRC**

- ▲ There is currently a global shortage of ACT drugs. Timely drug procurement has the potential to avoid disruptions in ACT supply once implementation has begun. Because the GoDRC has opted to procure ART AQ, an effective antimalarial at an attainable cost, it is likely that global drug shortages will not affect procurement as significantly as with Coartem®.
- ▲ Dispensing ART AQ through health facilities will present a risk of ACT leakage to other health zones where ACTs are not being dispensed as well as across international borders.
- ▲ ACTs are more sensitive and have a shelf-life of two years, substantially shorter than that of traditional antimalarials such as SP and chloroquine. Because of this, appropriate transport and storage of ACTs are necessary to minimize drug wastage. This will be a challenge in many areas of DRC where transport from storage facilities to health centers can take up to two days, with little temperature control measures available (Adeya 2004).
- ▲ Health staff training and supervision are necessary to ensure regime compliance, particularly with ART AQ, which is not coformulated. It is expected that a coformulated version of ART AQ will be available by 2007. While the introduction of a coformulated version of ART AQ has the potential to improve regime compliance, its introduction would necessitate another round of health worker training on the new ART AQ regimen.

## 4. Rapid Diagnostic Test Cost Analysis for Sample Year

An analysis of the costs of rapid diagnostic tests was conducted to determine the cost effectiveness of RDT use once ACTs have been implemented. In order to conduct this analysis, the international price of RDTs was compared to the international landed price of Coartem® and artesunate amodiaquine. Because RDTs are not recommended by WHO for children under 5 in highly endemic areas (Shapira 2004), RDTs were only costed for individuals age five and older.

**Table 6. Variables used in Rapid Diagnostic Test Analysis**

Percentage of fever cases testing positive for parasitemia	50%
Cost of RDT	US\$0.65-US\$1.00*
RDT Sensitivity	90%**
RDT Specificity	95%***
Compliance	75-100%

\* RDTs pricing begins at US\$.65 for *P.falciparum* tests and US\$1 for *P.f./P.v.* tests and ranges upward. We were not able to obtain an actual quote for RDTs, including shipping and handling charges for DRC.

\*\* Approximate value, depending on transport and storage conditions. Personal communications from D Bell at WHO.

\*\*\* Personal communications from D Bell at WHO.

### 4.1 Assumptions

- ▲ Half of fevers presenting at the health center are parasitemic (MSF-France in DRC)
- ▲ Sensitivity and specificity are maintained through a ‘cool chain,’ including appropriate transport and storage.
- ▲ Adequate training in use of RDT and interpretation of results.
- ▲ Reasonable compliance with test results on the part of clinicians or RDT administrators. The term ‘compliance’ is used to represent the likelihood that the RDT administrator will act in accordance with a negative RDT result and not treat the patient for malaria. It is assumed that all patients with a positive RDT result will be treated with ACTs.

### 4.2 Formula

Total cost per year of RDTs in combination with ACT treatment = (yearly episodes of malaria (among those 5 years and older) \* cost of RDTs + (yearly episodes of malaria for those over 5 \* % fever cases testing positive for malaria \* RDT test result compliance \* cost of ACT)

Four scenarios were costed for RDT implementation:

- ▲ Coartem® at 100 percent compliance with RDT results
- ▲ Coartem® at 75 percent compliance with RDT results
- ▲ ART AQ at 100 percent compliance with RDT results
- ▲ ART AQ at 75 percent compliance with RDT results

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### 4.3 RDT Cost Analysis

The cost analysis for RDTs uses the number of fever episodes for 2005 only as a representative example. The analysis was performed at an RDT cost of US\$1 and US\$0.65, as these are the respective base prices for *P.falciparum*/*P.vivax*-detecting tests and *P.falciparum*-detecting tests.<sup>5</sup>

**Table 7. Comparison of ACT Costs with and without the Use of RDTs at US\$1/test**

	100% Compliance	75% Compliance
Coartem® alone	US\$16,603,690	US\$16,603,690
Coartem® with RDTs	US\$15,954,850	US\$18,134,085
Savings/cost of RDTs	US\$648,840	(US\$1,530,395)
ART AQ alone	US\$10,553,862	US\$10,553,862
ART AQ with RDTs	US\$13,081,182	US\$14,466,376
Savings/cost of RDTs	(US\$2,527,320)	(US\$3,912,514)

Initially, it appears that Coartem® implementation with RDTs at US\$1/test costs approximately the same as implementation without an RDT. However this is at 100% compliance (only those with a positive test result receive ACTs), which is not realistic in a practical setting. Full compliance means that those who are parasitemic but whose test resulted in a negative result would not receive antimalarial treatment, but would be diagnosed for other causes of illness. When compliance falls to 75 percent, drug costs increase, making RDTs less cost-effective but increasing the chances that all of those who are parasitemic will receive antimalarials. The cost effectiveness of RDT usage declines when used in combination with ART AQ, making a scenario with RDTs about US\$2.5-4 million more costly than implementing ART AQ alone.

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<sup>5</sup> According to Wobin (2004), *P.falciparum* causes the majority of malaria cases in DRC.

**Table 8. Comparison of ACT Costs with and without the Use of RDTs at US\$0.65/Test**

	<b>100% Compliance</b>	<b>75% Compliance</b>
Coartem® alone	US\$16,603,690	US\$16,603,690
Coartem® with RDTs	US\$13,131,016	US\$15,310,250
Savings/Cost of RDTs	US\$3,472,674	US\$1,293,440
ART AQ alone	US\$10,553,862	US\$10,553,862
ART AQ with RDTs	US\$10,257,348	US\$11,642,542
Savings/Cost of RDTs	US\$296,514	(US\$1,088,680)

At US\$0.65 per RDT, the tests become more cost-effective for use with Coartem®, even at a lower compliance. With ART AQ, the cost of RDTs at 100 percent compliance is not substantially lower from that of ART AQ alone. The cost for RDTs with ART AQ does not increase prohibitively at 75 percent compliance when compared to the cost of ART AQ alone, however the RDTs do not yield any savings.

In addition to the four scenarios costed, the break-even price for RDTs was calculated. At the break-even price, there is neither benefit nor cost in using RDTs.<sup>6</sup>

**Table 9. Break-even Point for RDTs**

	<b>100% Compliance</b>	<b>75% Compliance</b>
Coartem® with RDTs	US\$1.05	US\$0.80
ART AQ with RDTs	US\$0.65	US\$0.50

#### 4.4 Key RDT Implementation Concerns in DRC

- ▲ RDTs are not currently stable over time and can lose sensitivity when stored at temperatures above 30°C. The WHO recommends that RDTs be implemented in conjunction with a ‘cool’ chain. RDTs – especially the WHO-recommended cassette RDTs – can be fairly bulky. Developing a functional cool chain in a country such as DRC would prove to be a significant and costly challenge without yielding great savings in ACT costs.
- ▲ Significant training and supervision are recommended by WHO to ensure correct reading and response to RDT results. The quality of training and supervision will affect both RDT cost-effectiveness and the febrile patient’s likelihood of receiving appropriate treatment. The financial and public health effectiveness of RDTs is dependent on the administrator’s compliance with the test results. If the administrator views results too liberally, a large number of ACT doses will be wasted in those who are not parasitemic. Conversely, if the administrator is too strict, those who test negative but are parasitemic will not be treated, reducing the public health benefit of more efficacious drugs.

<sup>6</sup> The breakeven point accounts for commodity cost alone and does not include additional costs incurred, such as the implementation of a cool chain or staff training costs.

- ▲ The choice of available RDTs also presents several issues to be addressed:
  - △ Some types of RDTs are not effective in areas with a high density of parasitemia.
  - △ Tests can detect either *P.falciparum* (approximately US\$.65) or both *P.falciparum* and *P.vivax* (approximately US\$1).
- ▲ As mentioned earlier, RDTs are not recommended for children under five in areas of high malaria transmission.

## 5. Recommendations

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### 5.1 Artemisinin-based Combination Therapy Drug Choice

The GoDRC has selected artesunate amodiaquine as the first-line ACT in the malaria treatment implementation plan (PNLP 2005). While ART AQ is currently not coformulated, Sanofi-Aventis has plans to release a coformulated combination in 2006. By procuring ART AQ, DRC potentially will have better leverage in reaching the funding targets necessary to achieve ACT drug coverage, as overall drug cost will be significantly lower than the cost of Coartem®. GoDRC may also have an easier time procuring an adequate supply of ART AQ than Coartem®, as there are multiple suppliers.

Despite the procurement and financial advantages that ART AQ offers, the implementation challenges will be greater. The daily regimen for an adult ART AQ is currently five tablets taken as one dose daily for three days. Until a coformulated ART AQ combination is available, achieving drug compliance on such a regimen will be a challenge in both the training of health care workers and the counseling of patients.

In order to effectively roll out ART AQ with a reasonable degree of compliance at the primary health care level, the PNLP will need to develop a detailed implementation plan that includes a communication plan, primary health worker training, and job aids to promote knowledgeable counseling and regime compliance. Training materials should be developed and distributed in appropriate languages.

Another important aspect of the implementation plan will be to designate secure measures for the transport and storage of ACT drugs. As outlined in the Rational Pharmaceutical Management *plus* report on antimalarial drug management in DRC (Adeya 2004), many areas of the country face serious challenges in the transport and storage of temperature-sensitive commodities. While some storage facilities have cool stockrooms or refrigeration available, local distribution from depot to health center can often take several days, exposing the drugs to temperatures regularly above 30°C, which can negatively impact the integrity of the drugs. The PNLP should work together with partner organizations to share experiences and scale up models currently being used by ACT-dispensing partners.

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### 5.2 Rapid Diagnostic Tests

A preliminary analysis of the costs of RDT implementation in conjunction with ACTs does not look promising. The prices used in the estimates for RDTs, US\$0.65 and US\$1, reflect the base prices of RDTs before handling fees are included. In order to break even on RDT use in the adult population with the implementation of ART AQ, the price would have to fall to a maximum of US\$0.65, including all handling fees.

In addition to pricing concerns, the implementation concerns for RDTs in DRC do not make for a worthwhile investment. The reported condition of storage facilities and transport from depot to health zone in rural areas is not conducive to maintaining the sensitivity of RDTs.

Aside from the logistical limitations of RDT implementation in DRC, WHO recommends that RDTs not be used in children under five, who bear the burden of malarial disease.

If RDTs are to be implemented in DRC, pilot trials should begin in urban areas such as Kinshasa, Kisangani, or Lubumbashi where transport and storage facilities can be relatively assured up to time of use. In addition to practical constraints, RDTs have the potential to be more cost-effective in areas where the burden of malarial disease is lower and fevers are therefore less likely to be malarious in nature.

## 6. Conclusions

The implementation of ACT drugs in DRC has the potential to significantly reduce the burden of disease caused by malaria in this highly endemic country. The results of this costing exercise contributed to the national debate on updated malaria treatment policy guidelines, including the selection of an ACT drug for implementation. By selecting artesunate amodiaquine, GoDRC will be able to more readily meet the finance and procurement needs of population. However, by selecting a drug that is not currently coformulated, the PNLP must take on the responsibility of developing effective protocols to promote regime compliance. Given the cost-effectiveness analysis of RDTs, and the added implementation complications for using RDTs, RDTs are not recommend at current prices. ACT drugs have the potential to reduce the level of parasitemia in the population when taken appropriately, thereby reducing the level of transmission through maximizing the curative benefits of ACTs and preventing future drug resistance. However this can only be achieved through the proper training of health care workers.

In addition to implementation considerations, the GoDRC now has the cost information necessary to solicit the international donor community for the funding necessary to initiate and maintain ACT implementation nationally. Following the release of the ACT financing requirement for DRC, the World Bank pledged an additional malaria component as part of the essential health package in the Bank's Health Rehabilitation program to be implemented in underserved areas of DRC.

Through the continued funding of ACT antimalarial drugs in DRC, combined with adequate attention to implementation concerns, the government of Democratic Republic of Congo will have the ability to reduce the overwhelming burden of malaria on its population.



# Annex A. Antimalarial Resistance at Selected Sentinel Sites

It is recommended that ACTs be implemented first in health zones where the provincial SP failure rate exceeds 10 percent. A threshold of 10 percent assumes that by the time a resistance level of 10 percent is detected and ACT implementation begun, the level of SP resistance will have reached 15 percent, the WHO threshold for SP resistance. In provinces where no sentinel site resistance data is available, assumptions should be based on expert opinion and data from neighboring provinces.

**Table A-1. Results from CQ and SP Efficacy Trials, May 2000–November 2001**

Sites	Drug	Total clinical failure rate (%)
Bukavu, Kivu Sud	CQ	80
	SP	9.3
Kapolowe, Katanga	CQ	34
	SP	4
Kimpese, Bas Congo	CQ	50
	SP	10.2
Kinshasa, Kinshasa	CQ	35.2
	SP	5.5
Kisingani, Orientale	CQ	48
	SP	19.2
Mikalayi, Kasai Occidental	CQ	29.4
	SP	0
Vanga, Bandundu	CQ	48.8
	SP	4.8
Pweto, Katanga	SP	51%*

Source: Wobin (2004)

\* MSF (2004)

**Table A-2. Results from SP, SP+AQ, SP+ART Efficacy Trials, June 2002–February 2003**

Sites	Drug	Total clinical failure rate (%)
Kisingani, Orientale	SP	22
	SP+AQ	3
	SP+ART	0
Rutshuru, Kivu Nord	SP	60.6
	SP+AQ	32
	SP+ART	21
Kimpese, Bas Congo	SP	39.6
	SP+AQ	1.8
	SP+ART	1.6

**Table A-3. Results from SP, SP+AQ, SP+ART Efficacy Trials, December 2003–June 2004**

Sites	Drug	Total clinical failure rate (%)
Kapolowe, Katanga	SP	13.8
	SP+AQ	2.8
	SP+ART	0
	AQ+ART	1.4
Mikalayi, Kasai Occidental	SP	1.6
	SP+AQ	1.4
	SP+ART	0
	AQ+ART	0
Shabunda, Kivu Sud	SP+ART	1
	AQ+ART	0

The U.S. Centers for Disease Control and Prevention is currently conducting Coartem® trials at several sites throughout DRC; however, the results of these trials are not yet available.

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