Impact of Artemisinin-Based Combined Therapy for Malaria in Various Countries and Implications for the Countries of the Amazon Basin: Final Report

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About SPS

The Strengthening Pharmaceutical Systems (SPS) Program strives to build capacity within developing countries to effectively manage all aspects of pharmaceutical systems and services. SPS focuses on improving governance in the pharmaceutical sector, strengthening pharmaceutical management systems and financing mechanisms, containing antimicrobial resistance, and enhancing access to and appropriate use of medicines.

Recommended Citation

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ACRONYMS AND ABBREVIATIONS

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<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>AMI</td>
<td>Amazon Malaria Initiative</td>
</tr>
<tr>
<td>ACT</td>
<td>artemisinin-based combination therapy</td>
</tr>
<tr>
<td>AQ</td>
<td>amodiaquine</td>
</tr>
<tr>
<td>AS</td>
<td>artesunate</td>
</tr>
<tr>
<td>AT</td>
<td>artemether</td>
</tr>
<tr>
<td>CQ</td>
<td>chloroquine</td>
</tr>
<tr>
<td>DOX</td>
<td>doxycycline</td>
</tr>
<tr>
<td>ITN</td>
<td>insecticide-treated bednet</td>
</tr>
<tr>
<td>LM</td>
<td>lumefantrine</td>
</tr>
<tr>
<td>MQ</td>
<td>mefloquine</td>
</tr>
<tr>
<td>PAHO</td>
<td>Pan American Health Organization</td>
</tr>
<tr>
<td>PQ</td>
<td>primaquine</td>
</tr>
<tr>
<td>RAVREDA</td>
<td>Red Amazónica de Vigilancia de la Resistencia a los Antimaláricos (Amazon Network for the Surveillance of Antimalarial Drug Resistance)</td>
</tr>
<tr>
<td>RDT</td>
<td>rapid diagnostic test</td>
</tr>
<tr>
<td>Q</td>
<td>quinine</td>
</tr>
<tr>
<td>SP</td>
<td>sulfadoxine-pyrimethamine</td>
</tr>
<tr>
<td>USAID</td>
<td>U.S. Agency for International Development</td>
</tr>
<tr>
<td>USD</td>
<td>U.S. dollar</td>
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<tr>
<td>WHO</td>
<td>World Health Organization</td>
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This study implemented a systematic process aimed at analyzing the factors that contributed to the reduction of *Plasmodium falciparum* cases in the countries of the Amazon region, emphasizing an analysis of the contribution of artemisinin-based combination therapy (ACT). First, a comprehensive literature review was undertaken. Based on the findings of this review, a research protocol was designed and applied in five of the region’s countries. The objectives of this research included—

1. Systematizing the ACT introduction process in the countries of the Amazon Basin

2. Documenting the results and impact of ACT introduction in the countries of the Amazon Basin and the contribution of other malaria control strategies

3. Proposing recommendations to improve medicine selection, procurement, distribution, and use and the actions to systematize this type of process in the future

The findings corresponding to objective 1 indicate that in connection with the introduction of ACT, the Amazon Network for the Surveillance of Antimalarial Drug Resistance (RAVREDA, for its Spanish acronym) and the Amazon Malaria Initiative (AMI) have been successful experiences based on sound scientific practices. Additionally, new strategies were implemented to promote collaboration and learning initiatives among the network’s members.

With respect to objective 2, a rapid performance evaluation was applied to the main control strategies implemented by the counties: household spraying, insecticide-treated bednets (ITNs), timely diagnosis, and ACT. The evaluation used an adequacy design (adhering to technical standards, including the necessary resources and expected service coverage). Of the four control strategies that were analyzed, only ACT is adequately implemented. The adequacy and implementation level of the remaining three strategies generally ranges between intermediate and deficient, and only one country achieved an adequate score in timely diagnosis. Even though the ACT strategy has attained an adequate implementation level, some criteria still must be strengthened, such as medicine supply and implementation of systematic processes to monitor the adequate application of regulations and protocols.

Estimating the specific contribution of ACT was approached by analyzing the *P. falciparum* trend between 1995 and 2008 and the ACT coverage for reported *P. falciparum* cases since the introduction of ACT in each country. This analysis identified that four countries had begun to experience a rapid decrease in the number of cases before the introduction of ACT (Bolivia, Colombia, Ecuador, Peru). In Guyana, a recent decreasing trend of *P. falciparum* appears in line with the introduction of ACT to the treatment regimen. This analysis also revealed discrepancies in several years between the number of reported cases and the number of cases that were treated, which evidences the existing deficiencies in the countries’ routine information systems or possible problems in the application of national treatment protocols. These deficiencies are consistent with the findings of objective 2, where weaknesses were identified in terms of the implementation of systematic processes to monitor regulations and protocols.
Within objective 3, it was noted that the countries had been implementing reforms in their health systems that affected their national control programs. The vertical control program model no longer exists in the region, and multiple actors currently play specific roles within the technical, regulatory, and supervisory processes, including pharmaceutical supply management. This situation has affected the possibility of advancing ACT consolidation in the region’s countries. The study concludes that this new context requires AMI-RAVREDA to redefine its intervention strategies and recommends the application of a health systems strengthening approach.
INTRODUCTION

Designed and financed by the U.S. Agency for International Development (USAID), AMI has been supporting malaria control initiatives in seven South American countries since 2001: Bolivia, Brazil, Colombia, Ecuador, Guyana, Peru, and Suriname, grouped under RAVREDA.

In Mexico and Central America, the main parasite is *P. vivax*, and chloroquine (CQ) is the first-line medication. *P. falciparum* is endemic in the Amazon subregion and on the island of Hispaniola (Haiti and the Dominican Republic).

The first years of AMI-RAVREDA’s activities focused mainly on the implementation of antimalarial drug resistance and sensitivity tests using standardized protocols. In light of scientific evidence of resistance problems to first-line treatments, the South American countries that had yet not done so changed their traditional *P. falciparum* treatment regimens to ACT.

By 2008, a 67 percent drop in *P. falciparum* cases was reported in the Amazon region in comparison to the cases reported in 2001.\(^1\) The mortality rate associated with malaria was also significantly reduced.

Even though the reduction in the number of *P. falciparum* cases in the Amazon countries is very clear, the factors that contributed to this change are not. Likely it cannot be attributed to a single factor, but rather to many, which include ACT, other control strategies, and favorable environmental and epidemiological conditions.

Until now, a detailed analysis of the situation has not been undertaken. This study intends to fill this gap, emphasizing ACT, whose introduction was one of the main elements of AMI-RAVREDA’s support to the countries of the Amazon region. To conduct this analysis, this study implements a systematic process that begins with a comprehensive review of available literature, based on which a research protocol is designed and applied, whose results are presented here, discussed, and used as the basis to offer some recommendations.

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LITERATURE REVIEW

Artemisinin-Based Combination Therapy

The past decades witnessed the development and expansion of *P. falciparum* resistance to conventional antimalarial medicines (CQ, sulfadoxine-pyrimethamine [SP], and amodiaquine [AQ]). Among the factors that contributed to the development of such resistance were the inadequate use of antimalarial medicines, mainly when they were used on a large scale as monotherapies, as well as weak management under which medicines continued to be used despite the fact that available data had already shown high resistance levels.2

The development of new antimalarial medicines based on artemisinin components (artesunate [AS], artemether [AT], and dihydroartemisinin) began in 2000. These medicines have shown a rapid therapeutic response (reducing the parasite’s biomass and eliminating the symptoms), and they are effective against multidrug-resistant *P. falciparum*, are well tolerated by patients, and reduce the number of gametocyte carriers. The last makes the introduction of artemisinin an intervention with the potential of reducing malaria transmission.3

To prevent the development of resistance to artemisinin, it is used in combination with other medicines—hence the name “artemisinin-based combination therapy.” The logic behind this strategy is that the development of parasite resistance would require two simultaneous events, which is less likely to occur.4 Evidence also indicates that ACT reduces symptoms much faster than the monotherapies that had been used previously.5

One of the main limitations to the expansion of artemisinin use is its cost. In a 2006 publication, the estimated cost of one ACT treatment ranged between 2 and 9.12 U.S. dollars (USD).6 A recent study undertaken in several countries of Sub-Saharan Africa estimated an average of USD 4.96 per treatment with ACT.7 The previously mentioned costs per treatment are beyond reach for many developing countries. Therefore, a pilot initiative is currently being implemented: “Affordable Medicine Facility-malaria (AMFm),” which, through public-private collaboration managed by the Global Fund to Fight AIDS, Tuberculosis and Malaria, allows sale of ACT to public institutions at cost. This initiative is estimated to reduce by USD 0.20 to USD 0.50 the cost of each course of treatment with ACT.8

3 Ibid.
5 WHO. 2006. Facts on ACTS.
6 Ibid.
Introduction and Expansion of ACT in Malaria Control Programs at the Global Level and Specifically in the Amazon Region

During the past eight years, an exponential increase has occurred in the number of countries that have adopted ACT as first-line treatment. As a result, a medicine shortage occurred that lasted approximately 12 months. Since then, changes have been introduced to the manufacturing processes with the aim of ensuring that these problems will not recur in the near future and that the capacity will be there to meet the ongoing growth demand.

In the Amazon subregion, ACT is used as the first-line treatment for *P. falciparum* in the eight countries of the Amazon Basin. By the end of 2008, the countries in that subregion had attained an ACT treatment rate of approximately 100 percent for *P. falciparum*.

Peru introduced ACT in November 2001 as the first-line treatment for *P. falciparum* uncomplicated malaria. Two types of ACT for oral use were introduced: (a) SP plus AS and (b) mefloquine (MQ) plus oral AS. Given that Peru was the first country to implement ACT in the region, safety and efficacy studies were carried out as well as adverse reaction studies. The largest study monitored a sample of patients during two years and found infrequent adverse symptoms that were also mild.

The remaining countries in the Amazon Basin gradually adopted an ACT modality, until 2006, when all of them had introduced changes in their treatment regimens. Currently, all the countries in the region have adopted ACT as their first-line treatment. Table 1 shows the changes in treatment regimens between 1998 and 2010 for the region’s countries.

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9 WHO. 2006. Facts on ACTS.
10 PAHO. Malaria Day in the Americas 2009.
Table 1. Changes in \textit{P. falciparum} Treatment Regimens in the Countries of the Amazon Basin

<table>
<thead>
<tr>
<th>Country</th>
<th>1998</th>
<th>2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bolivia</td>
<td>Q 7 days</td>
<td>AS + MQ</td>
</tr>
<tr>
<td>Brazil</td>
<td>Q 3 days + DOX 5 days</td>
<td>AS-LM AS-MQ</td>
</tr>
<tr>
<td>Colombia</td>
<td>CQ + SP</td>
<td>AT-LM</td>
</tr>
<tr>
<td>Ecuador</td>
<td>CQ</td>
<td>AS + SP</td>
</tr>
<tr>
<td>Guyana</td>
<td>Q 5 days + SP</td>
<td>AT-LM</td>
</tr>
<tr>
<td>Peru-Amazon coast</td>
<td>Q 7 days + tetracycline 7 days</td>
<td>AS + MQ</td>
</tr>
<tr>
<td>Peru-rest of the country</td>
<td>CQ/SP</td>
<td>AS + SP</td>
</tr>
<tr>
<td>Suriname</td>
<td>Q 5 days</td>
<td>AT + LM</td>
</tr>
</tbody>
</table>


\textit{Note:} AS = artesunate; AT = artemether; CQ = chloroquine; DOX = doxycycline; LM = lumefantrine; MQ = mefloquine; Q = quinine; SP = sulfadoxine-pyrimethamine.

\textbf{ACT Achievements Documented in the Countries Applying ACT}

It has been documented that the implementation of traditional measures to control vectors (ITNs, residual household spraying, and search for active malaria cases, among others) in conjunction with ACT, generates dramatic achievements. During 2001, an epidemic outbreak in a South African region was rapidly controlled using the mentioned interventions.\textsuperscript{13} In Zanzibar, Tanzania, delivery of ACT to all malaria patients in public facilities achieved a rapid reduction in morbidity and mortality rates associated with malaria within a two-year period. The delivery of ITNs in addition to ACT produced a dramatic drop in parasitemia prevalence within only one year.\textsuperscript{14} In Zambia, the introduction of ACT in 2002 in conjunction with residual household spraying and ITNs led to a 66 percent reduction in the malaria mortality rate by 2008.\textsuperscript{15} In Ethiopia, during the 2005 epidemic, the districts that had a network of promoters responsible for the distribution of ACT registered a mortality rate that was equivalent to half the rate registered in the districts where ACT was delivered only at health facilities. During a two-year follow-up, the districts that had a network of promoters in charge of delivering ACT reduced the risk of malaria deaths by 37 percent.\textsuperscript{16}


\textsuperscript{16} Ibid.
Challenges and Limitations Associated with the Evaluation of ACT Impact

The surprising achievements of several countries in terms of controlling and decreasing the number of cases during the past decade, especially after the introduction of ACT, have generated interest in evaluating the impact of its use. The World Health Organization (WHO) reported that this task has two important limitations—

- Specific routine information is necessary for each intervention (ITNs, residual spraying, ACT, etc.) that will allow conducting a separate analysis of their possible effects. To date, the information produced by countries does not allow this separation.

- The most successful experiences result from a combination of interventions. Therefore, the effect attained is actually the sum of the different strategies and interventions.\(^{17}\)

The preceding is clearly revealed in several of the most successful cases that were documented. For example, in Vietnam’s southern region, the population percentage with parasitemia was registered at approximately 50 percent, and within a five-year period it was reduced to levels below 5 percent. This was the result of implementing universal distribution of ITNs, providing early diagnosis (microscopic), annually studying parasitemia prevalence among the population, and treating all individuals with parasitemia (\(P. falciparum\) with AS and \(P. vivax\) with \(CQ +\) primaquine [PQ]).\(^{18}\)

To address the preceding situation, an alternative is to carry out studies in which an impact analysis of the trends in malaria behavior can be attributed to the malaria control activities that were implemented. WHO suggests that a study of this nature should compare control strategies (coverage, resources, quality, etc.) with trend changes. For example, if one country has implemented malaria control activities in a technically adequate way, with the necessary resources and adequate controls as well as increased coverage, and simultaneously observes a drop in the number of cases, a reduction of the annual parasite index, a decrease of positive smears, and after ruling out other possible explanations that are foreign to such control activities, then it is plausible that the interventions achieved said effects.\(^{19}\)

Applying the foregoing logic, it is also possible to conduct a plausibility analysis of the relative contribution of the interventions if those that were not applied under optimal conditions are ruled out. For example, if the ITNs are used by only a very low percentage of the population, then it is possible to infer that their contribution to malaria control is relatively low, if compared to the interventions that comprise a larger proportion of the population (for example, ACT is used in 100 percent of confirmed \(P. falciparum\) cases).

In the Amazon region, an impact analysis of ACT presents more challenges because the trends in the prevalence of malaria cases differ in different countries. For example, several countries (Bolivia, Peru, and Ecuador) showed a decreasing trend in the number of cases before ACT


introduction. There are also countries where even after the introduction of ACT, the number of malaria cases increased (Venezuela and Bolivia).\textsuperscript{20}

The foregoing indicates that in the analysis, whether the interventions have been adequately implemented must be reviewed, because the efficacy of a technically effective intervention (in this case ACT) is reduced if it is not adequately implemented. Therefore, it is recommended that prior to associating changes in disease indicators (in this case malaria) as a plausible result of public health interventions, a previous step should be evaluated, which is the adequate implementation of the interventions.\textsuperscript{21}

The preceding logic is clear and simple; if one lacks the knowledge or evidence that a program has been adequately implemented, in adherence to technical standards and with the necessary resources, then a probabilistic evaluation is not warranted because the effects and impacts identified by the evaluation cannot be attributed to the intervention. Likewise, if the program has not been adequately implemented, it is possible to anticipate that it will not have an impact. In this case, it is convenient to first conduct an evaluation of the programs’ adequacy. Table 2 summarizes a design of this type.

\textbf{Table 2. Evaluation Design for Malaria Control Programs Following an Adequacy Approach}

<table>
<thead>
<tr>
<th>Evaluation level</th>
<th>Indicators to be analyzed</th>
<th>Indicators for comparison</th>
<th>Inferences to be achieved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention performance</td>
<td>Longitudinal analysis of the interventions’ process indicators (activities, coverage, use, monitoring, etc.)</td>
<td>• National protocols to implement, monitor, and evaluate interventions</td>
<td>• The interventions were adequately implemented, with the necessary resources, and the expected goals were attained (coverage, use, and others)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Pan American Health Organization (PAHO) and WHO Protocols</td>
<td>• The interventions were not adequately implemented</td>
</tr>
<tr>
<td>Impact</td>
<td>Longitudinal analysis of malaria indices</td>
<td>Indicator trends for the 1995–2009 period</td>
<td>The observed trend is consistent with the performance of the interventions that were implemented</td>
</tr>
</tbody>
</table>


Other Interventions That Have Shown Malaria Control Efficacy

To carry out a plausibility exercise such as in the examples explained in the preceding section, one must know the interventions implemented by the countries, their efficacy, and their control goals, which are discussed below.

**ITNs**

ITNs are one of the vector control interventions most used at the global level. It is considered a preventive intervention, which seeks to protect the population against the vector’s infectious bite. At the community or local level, extended use of ITNs results in reduction of transmission intensity. To attain optimum protection levels and vector control efficacy, ITNs should be universally (or almost universally) implemented. Therefore, they should be delivered free or at a highly subsidized cost to the population living in high-risk areas.\(^22\)

This intervention has shown significant efficacy. In the island of Vanuatu in the Pacific Ocean, a reduction of more than 50 percent for both species (*P. falciparum* and *P. vivax*) was documented following the introduction of bednets on a large scale (with coverage of approximately 80 percent of the population).\(^23\)

In Kenya, an evaluation of the efficacy of ITNs (using permethrin) to reduce child mortality in intense transmission areas found that they prevented one-fourth of all children’s deaths from malaria.\(^24\)

However, the efficacy of ITNs is reduced if the bednet is not systematically retreated with insecticide. A study found a drop in efficacy when retreatment is carried out after a six-month period.\(^25\) Another current problem with ITNs is growing resistance to pyrethroids, which are the only insecticide approved to treat bednets.\(^26\)

**Residual Indoor Spraying**

The same as use of ITNs, indoor residual spraying forms part of the interventions aimed at controlling vectors. This intervention is considered preventive, given that it seeks to reduce or eliminate the vector inside the home, thereby reducing transmission intensity at the local level. The same as for ITNs, broad intervention coverage is required to attain the intervention’s desired effect. The recommendation is to implement it universally or almost universally in risk areas.\(^27\)

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\(^{25}\) Ibid.

\(^{27}\) Ibid.
Residual indoor spraying has shown its efficacy in controlling malaria transmission when approximately 80 percent of the households and stables are sprayed. However, this efficacy only occurs when spraying is carried out in a technically adequate fashion, which presupposes the existence of infrastructure at all levels (national, provincial, and district) and the program’s capacity to conduct implementation, monitoring, and evaluation tasks.  

**Intermittent Preventive Treatment**

This intervention involves preventive treatment delivered to the population at risk during several periods throughout the year. The studies that evaluated the efficacy of intermittent preventive treatments found that they are quite effective, particularly when combined with home treatment of suspected malaria fever. For example, in a recent study in Ghana, intermittent preventive treatment was delivered to all children under the age of five (AQ + AS) every four months. This, in combination with the care of children with malaria-related fever, attained a reduction of parasite prevalence from 25 percent to 3 percent.

**Timely Diagnosis and Treatment**

Timely diagnosis and treatment are considered critical interventions to reduce malaria-related morbidity and mortality rates. A timely and prompt diagnosis reduces the likelihood of transmission and also reduces the disease’s negative effect.

The microscopic thick blood smear is the standard procedure to diagnose malaria. However, in remote rural areas that are distant from the health facilities that have microscopes and trained staff, timely diagnosis and treatment are compromised. One of the goals of timely diagnosis is the initiation of patient treatment within the first 24 hours. However, in rural areas, the time required to obtain the sample, send it to a facility that has microscopic capacity, and receive the diagnosis is easily many days. A study conducted in the Peruvian Amazon region determined that an average of three days was needed to carry out a diagnostic procedure with the thick blood smear. During this waiting period, presumptive treatment is commonly begun, which can mean that patients with negative test results will also receive treatment, as well as those cases for which the treatment that is administered is ineffective for the identified parasite (either *P. falciparum* or *P. vivax*).

The use of rapid diagnostic tests (RDTs) considerably increases the likelihood of timely diagnosis and appropriate treatment (for the type of Plasmodium). A longitudinal study with pre-

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and postintervention evaluation in Peru showed that the use of RDTs by health promoters reduces the time elapsed between the onset of symptoms and the initiation of treatment from almost five days to less than two days. The greatest contribution to this reduction occurred when the waiting time for diagnosis was shortened: from almost three days to 20 minutes. The result of having a timely diagnosis has also led to an increased percentage of patients receiving timely treatment for malaria (from 16 percent to 55 percent) and appropriate for the parasite species (from 27 percent to 84 percent). The percentage of patients that received adequate treatment for *P. falciparum* also increased considerably (from 5 percent to 73 percent).  

RDTs have shown high efficacy (high sensitivity and specificity). Therefore, in specific situations where quality is assured (training on the application and interpretation and adequate maintenance of the cold chain), their use is a good technical option compared to microscopic diagnosis. Additionally, it has been shown that RDTs are cost-effective. They are used in remote areas in 11 countries of the Americas. Approximately 28,000 RDTs were used in 2008.  

The improvement of diagnostic methods, either microscopic or rapid diagnosis, enhances the benefits of effective medicines and reduces the misuse of resources. However, the clinical response to the results of diagnostic tests is vital. A recent study in Tanzania estimated that the cost of diagnosis, especially in the case of rapid tests, increases considerably if clinicians (even in low percentages) ignore test results (especially when they are negative) and prescribe antimalarial treatments even if the results do not warrant it. Consequently, prescription habits could reduce the cost-effectiveness of diagnostic methods.  

The implementation of RDTs has undoubtedly had an important effect on timely diagnosis. In Peru’s case, a study was conducted that disclosed this has been one of the most relevant contributions. However, enormous challenges must be addressed to be able to implement use of RDTs on a routine and sustainable basis. These challenges range from financing and logistics to official guidelines for the procurement, transportation, and quality control of various supplies.  

**Ecosystem Interventions That Affect Malaria**  
The intensity and transmission trends of the parasites that cause malaria, including the epidemiology of the infection and disease, occur mainly as a result of seasonal abundance and  

37 PAHO. Malaria Day in the Americas 2009.  
the feeding habits of Anopheles mosquitoes (as the vector). Therefore, ecosystem changes also influence disease trends. Evidence exists from some countries (for example, Thailand) showing that malaria transmission has been experiencing a sustained reduction associated with economic development, the expansion of the health facilities network, and the continuous implementation of vector control measures. Therefore, urbanization processes as well as network and access improvement have had significant impacts.

Evidence also indicates that the increased development of livestock breeding activities has been directing mosquitoes toward livestock and thus away from human beings. Human malaria parasites are not transmitted to livestock; therefore, this change in agricultural practices has influenced the vector’s feeding habits. It is maintained that this is one of the factors that had an influence on the reduction of malaria in warm climates. Ecosystem studies in Kenya have shown that malaria prevalence is lower among the populations that carry out livestock breeding activities. Cattle act as a decoy, attracting the vector and keeping it away from human beings.

From the above-mentioned evidence, one can infer that the advance of the livestock-breeding frontier in the Amazon Basin could be having an effect that is modifying the vector’s feeding habits. But at the same time, the deforestation of the Amazon region, including the ensuing ecological alterations, is associated with an increase in larvae, thus enhancing the risk of malaria.

Conclusions of Literature Review

After many decades during which malaria control was an uphill climb, coupled with the disease’s resurgence and the expansion of resistance-related problems, several regions around the globe have recently begun to experience favorable trends in terms of controlling and eliminating the disease. The appearance of ACT is one of the main factors that have generated these advances. Until now, ACT’s clinical efficacy has been such that it led to the forecast that if all or most countries used it, a considerable reduction of the morbidity and mortality rates attributable to malaria would be attained at the global level.

None of these countries has implemented ACT as a single intervention, but rather in combination with other interventions. Current evidence shows that the most effective control methods are

42 Reiter, P. 2008. Global warming and malaria: Knowing the horse before hitching the cart. Malaria Journal 7(suppl1):S3.
those that implement a series of interventions and tools that attack both the vector and parasite transmission.\(^{46}\)

This fact hinders the possibility of carrying out impact studies of specific interventions, given that the effects and results constitute the sum of the different interventions that form part of the malaria control effort.\(^{47}\) However, it is feasible to carry out studies to evaluate the adequacy of the interventions as well as the plausibility that the observed changes in disease trends are associated to the interventions implemented by the countries.

\(^{46}\) Ibid.

\(^{47}\) Annex C discusses the information required to carry out an impact study and the availability of such information in the countries of the Amazon region.
METHODOLOGY

Study Objectives

Objective 1: Systematize the ACT introduction process in the countries of the Amazon Basin.

Objective 2: Document the results and impact of ACT introduction in the countries of the Amazon Basin and the contribution of other control strategies.

Objective 3: Propose recommendations to improve medicine selection, procurement, distribution, and use as well as actions to systematize this type of process in the future.

Approaches Used to Attain the Study’s Objectives

Objective 1

With respect to this objective, data collection and analysis were conducted following chronological order and underscoring the different implementation steps during ACT introduction process in these countries. The specific sources of information are shown in table 3. The analysis emphasizes the identification of key factors for introducing and sustaining changes to public health policies.

Objective 2

During the literature review, it was identified that the impact on malaria indices is the result of the series of interventions that are implemented (for example, ITNs, indoor residual spraying, ACT). Therefore, to identify and make inferences concerning the relative contribution of each intervention, the performance of each intervention should be analyzed individually in the countries that have been implementing these interventions between 1995 and 2009. To do this, in addition to the information related to ACT, information corresponding to three interventions was rapidly gathered: ITNs, indoor residual spraying, and timely diagnosis. An analysis of level of adequacy in adherence to the protocols and guidelines developed by PAHO and WHO was applied in all countries.

Objective 3

Toward the end of 2008, Management Sciences for Health (MSH)/USAID carried out a detailed study on the situation of pharmaceutical supply management in the different countries of the Amazon Basin. The study identifies the main strengths and weaknesses of pharmaceutical supply management and proposes specific recommendations for improvement. Because that

study is fairly recent and it contains detailed information, this objective focuses on analyzing progress, problems, barriers, and other factors related to consolidation of medicine management. Based on this analysis, recommendations will be proposed.

Variables and Indicators

Table 3 summarizes the variables, indicators, and information sources used for each of the study’s three objectives.

Table 3. Summary of Methodological Design Applied

<table>
<thead>
<tr>
<th>Objectives</th>
<th>Variables and factors</th>
<th>Main indicators</th>
<th>Information sources</th>
</tr>
</thead>
</table>
| Objective 1: Systematize ACT introduction process | - Implementation of evidence-based decision-making processes (resistance and sensitivity studies)  
- Development of innovative surveillance processes (RAVREDA)  
- Commitment of national authorities in terms of resource allocation  
- Role of international technical assistance | - Influence of resistance and sensitivity studies carried out by the network’s researchers within the decision-making processes  
- Use of information generated by the RAVREDA network  
- Allocation of financial and human resources to implement and expand ACT  
- Modalities and strategies to deliver international technical assistance | - RAVREDA reports  
- Reports on specific resistance and sensitivity studies  
- National guidelines and technical documents  
- Interviews with key officers: national malaria program, PAHO focal points, USAID-AMI, and PAHO’s central level |
| Objective 2: Document the results and impact of ACT introduction in the countries of the Amazon Basin and the contribution of other control strategies | Rapid performance evaluation—  
- Indoor residual spraying  
- ITNs  
- Timely diagnosis  
- ACT | - Percent of vulnerable population that uses ITNs  
- Percent of population at risk that received ITNs  
- Percent of population at risk whose homes have been treated with residual spraying  
- Percent of febrile patients that underwent a microscopic evaluation or RDT  
- Percent of *P. falciparum* cases treated with ACT  
- Percent of *P. falciparum* patients who received treatment within 24 hours after the onset of febrile symptoms | - Program’s annual reports  
- Surveillance reports  
- Household survey and other specific studies  
- Interviews with key officers |
| Adequacy analysis of the implementation of control strategies | Adequacy of implementation in accordance with national, PAHO, and WHO protocols and guidelines |
**Methodology**

<table>
<thead>
<tr>
<th>Objectives</th>
<th>Variables and factors</th>
<th>Main indicators</th>
<th>Information sources</th>
</tr>
</thead>
</table>
| Objective 3: Propose recommendations to improve medicine selection, procurement, distribution, and use, as well as actions to systematize this type of process in the future | Updating and monitoring the recommendations of the pharmaceutical supply management study carried out by MSH/USAID, August 2008 | Progress and barriers to implementation of standardized procedures for malaria medicine management, diagnosis, and treatment | - Program’s annual reports  
- Interviews with key officers |

**List of Criteria to Analyze the Adequacy of Control Strategies**

As explained in the “Literature Review” section, the rapid evaluation of performance of the control strategies implemented by the countries was carried out through an exercise that analyzed whether control strategies are adequately implemented (in accordance with technical standards, with the necessary resources and the expected service coverage). To that effect, lists of criteria were prepared for each strategy included in the study: household spraying, ITNs, timely diagnosis, and ACT. Each of the following tables contains criteria associated with three areas: (a) prior research, (b) coverage, and (c) quality. The criteria were obtained from the technical guidelines prepared by WHO and PAHO.

Each criterion was assessed in terms of the existence of evidence of compliance (1 point), noncompliance (0 points), or partial compliance (0.5 points) with the criterion. The scores obtained were summed and reported using a scale divided into three categories: adequate implementation, intermediate implementation, and deficient implementation. The number of criteria that were met corresponds to each of the three categories on the scale, and it differs for each strategy, given that the number of criteria also varies in each list. Each of these four lists is presented below with the respective rating scale.
### Table 4. Implementation Criteria for Household Residual Spraying Strategy

<table>
<thead>
<tr>
<th>No.</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Research phase prior to the program's start-up</strong></td>
</tr>
<tr>
<td>1</td>
<td>A stratification of the population at risk was performed based on disease burden and transmission epidemiology*</td>
</tr>
<tr>
<td>2</td>
<td>Vector habits were studied and verified*</td>
</tr>
<tr>
<td>3</td>
<td>The susceptibility of prospective insecticides was verified before selecting the insecticide(s) that yielded the best results*</td>
</tr>
<tr>
<td></td>
<td><strong>Coverage</strong></td>
</tr>
<tr>
<td>4</td>
<td>100 percent of target households (according to national regulations) were sprayed at least once a year*</td>
</tr>
<tr>
<td>5</td>
<td>Stock-outs of spray insecticides did not exceed six months in any case*</td>
</tr>
<tr>
<td></td>
<td><strong>Quality</strong></td>
</tr>
<tr>
<td>6</td>
<td>Current regulations and programs are in place to implement residual spraying*</td>
</tr>
<tr>
<td>7</td>
<td>A system is in place to monitor the resistance and sensitivity of insecticides used for household spraying*</td>
</tr>
<tr>
<td>8</td>
<td>Systematic procedures are in place to monitor the vectors' habits*</td>
</tr>
<tr>
<td>9</td>
<td>Systematic procedures are in place to monitor the residual effect of the insecticide used to spray the household*</td>
</tr>
</tbody>
</table>

Table 5. Adequacy Criteria for ITN Strategy

<table>
<thead>
<tr>
<th>No.</th>
<th>Criteria</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Research phase prior to the program's start-up</td>
<td>A stratification of the population at risk was performed based on disease burden and transmission epidemiology*</td>
</tr>
<tr>
<td>2</td>
<td>Vector habits were studied and verified</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>The susceptibility of prospective insecticides was verified prior to selecting the insecticide(s) that yielded the best results*</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Coverage</td>
<td>80 percent of the population at risk received ITNs*</td>
</tr>
<tr>
<td>5</td>
<td>80 percent of pregnant women in the risk area received ITNs*</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>80 percent of the children under five in the risk area received ITNs*</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>80 percent of the people surveyed stated that they had slept under a bednet the previous night*</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Stock-outs of the insecticide used to impregnate bednets did not exceed three months during the past five years*</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Stock-outs of new bednets for delivery to the population did not exceed six months in any case*</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Quality</td>
<td>Regulations and programs for retreatment of ITNs are in place at the household or community level*</td>
</tr>
<tr>
<td>11</td>
<td>A systematic procedure is in place to monitor whether the families that have bednets use them adequately (including retreatment and washing)*</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>A resistance and sensitivity monitoring system is in place for insecticides used in bednets*</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>A systematic procedure is in place to monitor the vectors’ habits*</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>A systematic procedure is in place to monitor residual insecticide in bednets*</td>
<td></td>
</tr>
</tbody>
</table>

### Table 6. Adequacy Criteria for Timely Diagnosis Strategy

<table>
<thead>
<tr>
<th>No.</th>
<th>Criteria</th>
<th>Coverage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>At least 80 percent of all cases are diagnosed during the first 24 hours (time elapsed between the blood sample taken for the thick blood smear or rapid test and the delivery of results in endemic areas)</td>
<td>SCORE: Total number of criteria: 7 &lt;br&gt; 6 to 7 criteria met = The program is adequately implemented &lt;br&gt; 4 to 5 criteria met = The program is implemented with an intermediate level of adequacy &lt;br&gt; 1 to 3 criteria met = The program is deficiently implemented</td>
</tr>
<tr>
<td>2</td>
<td>No stock-outs of rapid tests occurred in any facilities of the public network in endemic areas</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>A system is in place to monitor the quality of microscopic diagnosis in the public network</td>
<td>Quality</td>
</tr>
<tr>
<td>4</td>
<td>A system is in place to monitor the quality of rapid tests</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>National regulations are in place for the application, distribution, transportation, and storage of rapid tests</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>A systematic process is in place to monitor compliance with distribution, transportation, and storage regulations</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Staff training and supervision programs are in place for personnel who apply rapid tests</td>
<td></td>
</tr>
</tbody>
</table>

Table 7. Adequacy Criteria for ACT Strategy

<table>
<thead>
<tr>
<th>No.</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Prior studies</strong></td>
</tr>
<tr>
<td>1</td>
<td>In vivo or in vitro studies were carried out to determine drug resistance of <em>P. falciparum</em> in previous treatment regimens*</td>
</tr>
<tr>
<td>2</td>
<td>In vivo or in vitro studies were carried out to determine the sensitivity of <em>P. falciparum</em> to ACT*</td>
</tr>
<tr>
<td></td>
<td><strong>Coverage</strong></td>
</tr>
<tr>
<td>3</td>
<td>At least 80 percent of <em>P. falciparum</em> cases receive ACT*</td>
</tr>
<tr>
<td>4</td>
<td>No ACT stock-outs have occurred in the public network during the past three years*</td>
</tr>
<tr>
<td></td>
<td><strong>Quality</strong></td>
</tr>
<tr>
<td>5</td>
<td>The country’s treatment regimens have up-to-date regulations and protocols for ACT*</td>
</tr>
<tr>
<td>6</td>
<td>A system in place to monitor therapeutic failures of ACT*</td>
</tr>
<tr>
<td>7</td>
<td>According to current regulations, ACT is delivered only when test results are positive (either microscopic or rapid test) for <em>P. falciparum</em></td>
</tr>
<tr>
<td>8</td>
<td>A systematic procedure is in place to monitor the adequate application of ACT regulations and protocols*</td>
</tr>
</tbody>
</table>


Information Sources for Rapid Evaluation of Control Strategies' Adequacy

A questionnaire was prepared for each strategy, which was jointly filled out by the national authorities and consultants in each country. The questionnaires were completed with official information. In those cases where answers were left blank, the lack of information was corroborated with the national authorities. In several cases, the information in the questionnaires was completed from reports prepared by PAHO or databases available online. These data are considered equally valid given that they were obtained from the countries’ official data.

Sampling and Statistical Approach

The study gathered information from five countries in the Amazon Basin (Bolivia, Colombia, Ecuador, Guyana, and Peru). Secondary information was collected in each country based on routine information and official data corresponding to coverage, guidelines, and protocols. Primary data were also collected through interviews with key officers: malaria national authorities, PAHO focal points for AMI-RAVREDA in each country, and USAID and PAHO officers in charge of managing the AMI-RAVREDA program.
Data Processing

Quantitative data were entered into an Excel database. Based on these data, the reported trends were graphed for each country. The responses to each of the four questionnaires were entered into an Excel database.

Most of the interviews with key officers were recorded and transcribed. Summaries were drafted for the few interviews that were not recorded. The information stemming from the interviews was analyzed and extracted directly from the transcriptions and summaries.
FINDINGS

Systematization of ACT Introduction Process in the Countries of the Amazon Basin

Background

Antimalarial drug resistance evaluation studies were carried out in some countries of the Amazon Basin between 1990 and 1998. These studies were not part of a systematic process that would allow establishing the geographical distribution of drug resistance. In 1998, PAHO convened a group of experts in Brazil to discuss and agree on a protocol for the surveillance of antimalarial medicine efficacy. Consequently, a standardized protocol was obtained to evaluate the therapeutic efficacy of antimalarial medicines used to handle uncomplicated P. falciparum cases in the Americas.49

Always using the standardized protocol, during the following years resistance studies were carried out in Bolivia,50 Colombia,51 Ecuador, Peru,52 and Venezuela53 between 1999 and 2002. The results showed therapeutic failures of official first-line treatments in these countries. Additional studies were carried out in Peru,54 Bolivia, Ecuador, and Suriname with the standardized protocol.

In light of increasing evidence of resistance problems in the region, in 2001 the countries of the Amazon Basin decided to establish a surveillance network. The initiative’s coordinator at PAHO remembers it as follows—

Falciparum resistance to the antimalarial medicines used at the time had been detected. With this information, the countries at a meeting held in 2001 requested PAHO to establish a network among the eight countries of the Amazon region to carry out efficacy studies.  

Based on the conclusions of that meeting, the Amazon Network for the Surveillance of Antimalarial Drug Resistance was established (Red Amazónica de Vigilancia de la Resistencia a los Antimaláricos; RAVEDRA), which, since early 2001, has been receiving support from USAID-funded AMI.

**Implementation of Evidence-Based Decision-Making Processes**

The actions of the AMI-RAVREDA network officially began in 2002. From the beginning, AMI-RAVREDA’s main purpose was the development and implementation of a surveillance system that would allow evaluation of malaria treatment efficacy on a systematic basis.

Between 2002 and 2005, the countries of the Amazon region that had not yet done so started to conduct antimalarial drug resistance studies. These studies followed the standardized protocol based on the recommendations issued by WHO, which encompass a sample of patients who seek care at certain malaria diagnostic facilities of the health system identified as sentinel sites.  

Table 8 identifies the studies implemented with AMI-RAVREDA’s support.

The surveillance system that was developed provided reliable and standardized information with respect to medicine efficacy. Such information was vital for decision making, particularly for the countries that introduced ACT after 2002 (Ecuador, Guyana, Colombia, Brazil, Suriname, Venezuela); Peru and Bolivia had already introduced changes to their ACT regimens in 2001.

Efficacy studies showed that “all the countries had resistance to the first-line treatment” they had been using. From then, actions were adopted to change treatment regimens and incorporate ACT.

---

57 Interview with Keith Carter, PAHO’s general coordinator for AMI-RAVREDA.
59 Interview with Keith Carter, PAHO’s general coordinator for AMI-RAVREDA.
### Table 8. Evaluations of Medicine Efficacy for the Treatment of Uncomplicated *P. falciparum* Malaria Promoted by AMI-RAVREDA between 2002 and 2005

<table>
<thead>
<tr>
<th>Country</th>
<th>Medicine</th>
<th>Year</th>
<th>Number of studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brazil</td>
<td>AT+LM</td>
<td>2005</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>MQ</td>
<td>2005</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Q+DOX</td>
<td>2005</td>
<td>2</td>
</tr>
<tr>
<td>Colombia</td>
<td>AQ</td>
<td>2002–04</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>AQ+SP</td>
<td>2002–03</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>AS+SP</td>
<td>2003–04</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>MQ</td>
<td>2002–03</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>MQ+SP</td>
<td>2003–04</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>SP</td>
<td>2002–03</td>
<td>1</td>
</tr>
<tr>
<td>Ecuador</td>
<td>AQ</td>
<td>2004</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>AQ+SP</td>
<td>2004</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>AS+SP</td>
<td>2003</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>AT+LM</td>
<td>2005</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>CQ</td>
<td>2002–03</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>CQ+SP</td>
<td>2003</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>SP</td>
<td>2002–03</td>
<td>1</td>
</tr>
<tr>
<td>Guyana</td>
<td>AS+MQ</td>
<td>2005</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>AT+LM</td>
<td>2004</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>MQ</td>
<td>2005</td>
<td>1</td>
</tr>
<tr>
<td>Peru</td>
<td>CQ</td>
<td>1998-2002</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>SP</td>
<td>1999-2002</td>
<td>4</td>
</tr>
<tr>
<td>Suriname</td>
<td>AS+DOX</td>
<td>2002–03</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>AS+MQ</td>
<td>2002</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>AT+LM</td>
<td>2003</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>MQ</td>
<td>2002</td>
<td>1</td>
</tr>
<tr>
<td>Venezuela</td>
<td>AS+MQ</td>
<td>2004</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>AT+LM</td>
<td>2004</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>CQ</td>
<td>2002</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Q+PQ</td>
<td>2003</td>
<td>2</td>
</tr>
</tbody>
</table>


*Note:* AS = artesunate; AT = artemether; CQ = chloroquine; DOX = doxycycline; LM = lumefantrine; MQ = mefloquine; PQ = primaquine; Q = quinine; SP = sulfadoxine-pyrimethamine.

Changes in national policies, regulations, and guidelines are processes that can be quite slow. In the case of the switch to ACT, this process was relatively rapid from the adoption of a new treatment regimen to the development of regulations and training sessions for national teams. Clearly, the scientific evidence generated by the resistance studies was vital. However, these were not the only factors. National authorities and regional advisers identified that the concurrence of a combination of factors was significant. These factors are presented below.
AMI-RAVREDA’s Impact on Countries’ Malaria Policies

Sound evidence was generated through the surveillance network, which, coupled with the countries’ political pressure to address the increasing number of *P. falciparum* cases, generated consensus with respect to policy changes in the countries. The person in charge of the network at the regional level analyzes this as follows—

I think there were other factors. Parallel to the evidence on resistance, orientation was provided by WHO with the aim of changing therapeutic regimens toward artemisinin derivatives. There was also the epidemiological situation characterized by the high transmission of falciparum malaria, which constituted a concern for these countries, especially Brazil, Colombia, Guyana, and Suriname.60

PAHO’s general coordinator for AMI-RAVREDA also identifies the fortuitous combination of factors—

I think we were lucky to combine scientific evidence with WHO’s new regulations for ACT as well as the fact that Coartem facilitated treatment because it came in blisters.61

The technicians that provided advice during this period also identify as a relevant factor that Peru and Bolivia had already made the transition to ACT—

Two countries were already using it—Peru and Bolivia—and they had made a relatively rapid transition. This meant that there was already experience in the region about what the treatment regimen means and how to change it.62

The relative ease with which Coartem was prescribed and used were a contributing factor, as mentioned above. The regional adviser describes this in greater detail—

The fact that WHO had the entire package ready also had an influence, given that the regimens had been developed and the guidelines were already in place. For us at PAHO, it was simply a matter of gathering the information and translating it into Spanish, and then assisting every country to put it in an adequate format. Dosage tables had already been prepared together with the prescription strategy and formulation of fixed dosages, which simplified matters. Coartem facilitated this process, because the medicine was very easy to prescribe and use, which made it attractive to the people who decided to become involved in this change process.63

In Bolivia, one of the countries that introduced the switch to ACT before the existence of AMI-RAVREDA, a different process is identified in which resistance studies had a significant influence—

The switch occurred fundamentally through the head of the malaria program. He was involved in the resistance study as coauthor of that particular research. After completing the study, he was

60 Interview with Roberto Montoya, PAHO’s former regional coordinator for AMI-RAVREDA.
61 Interview with Keith Carter, PAHO’s general coordinator for AMI-RAVREDA.
62 Interview with Roberto Montoya, PAHO’s former regional coordinator for AMI-RAVREDA.
63 Ibid.
fully convinced, and even before the article was published, he had already introduced changes to the country’s treatment regimen.\footnote{64 Interview with Arleta Añez, PAHO’s local coordinator for AMI-RAVREDA-Bolivia.}

**Development of Innovative Network Collaboration Processes**

Undoubtedly, the countries’ joint work through AMI-RAVREDA has been successful, and it has also generated learning and collaboration experiences among the countries. This outcome has been to a large extent the result of the work strategies that were used—

Many of the issues we work on at AMI-RAVREDA did not imply an additional investment for the malaria program within any context and in any country; our work at AMI consisted of doing things better with what we had at hand. Except for insecticide-treated bednets, which had to be purchased, the rest was related to the activities that the countries carried out anyway, for example, diagnosis, supervision of malaria posts, etc.\footnote{65 Ibid.}

Another important strategy was the implementation of demonstration pilot projects—

I think that the fact of working with pilot data in some countries—showing that this actually works and yields significant findings—was also important. For example, the initial studies conducted by MSH focused our attention on critical problems of medicine quality, access, availability, and use. Both medicine efficacy studies and medicine use studies affected the fostering of other processes and changes.\footnote{66 Ibid.}

Since its inception, AMI-RAVREDA has worked through technical meetings to foster exchanges and reach consensus among the countries. Country authorities and advisers who were interviewed agreed on the relevance of such meetings. One of them describes what happened in connection with some specific meetings—

The technical meetings were important to discuss and review strategies. Entomology and vector control issues were the key topics. We held three very good meetings where we saw that the product was completely novel; the first one held in Lima in 2005 was difficult, but in the end we managed to straighten it out. Then came Panama in 2006 and thereafter Guayaquil in 2008. The three meetings were very productive in terms of generating an innovative proposal to improve entomology and vector control practices. It is clear that at these meetings the results were not limited to the meetings themselves. There was also prior work to be done, which implied finalizing the preliminary documents so the meetings would be more productive, and it was quite an enriching experience.\footnote{67 Ibid.}

Another country adviser also identified the importance of the meetings and refresher workshops—

It was important to have forums for national authorities and technicians to participate in regional events, both in the refresher workshops as well as the review of technical issues.\footnote{68 Interview with José Pablo Escobar, PAHO’s local coordinator for AMI-RAVREDA-Colombia.}
Another innovative element in AMI-RAVREDA was the modality used to deliver technical assistance, which is a consortium of specialized organizations that includes the following entities in addition to PAHO: the U.S. Centers for Disease Control and Prevention, MSH’s Rational Pharmaceutical Management Plus Program, and the United States Pharmacopoeia Drug Information and Quality Program (USP/DQI). More recently, the following entities were integrated: Links Media to support the communication strategy and the Research Triangle Institute to share its experience in the area of vector control. In addition to the previously mentioned entities, USAID has played an active role in technical discussions and provision of strategic supplies that have guided the program’s implementation.

The consortium provides technical assistance at the regional and country levels. In the words of PAHO’s general coordinator for AMI-RAVREDA, the relevance of the strategy is the following—

Through AMI-RAVREDA, the countries secured the support of human resources in technical issues as well as support for their daily activities through PAHO’s focal points. I think this was a key element, because we must remember that malaria programs had become weakened in previous years because of the health reform processes implemented in the different countries.69

Even though AMI-RAVREDA’s initial efforts focused on resistance studies, the actions were expanded to improvement of diagnosis as well as medicine quality control, supply, and use strategies, among others. This was a gradual process that arose from the need to address the key components of malaria control in their entirety—

Following the implementation of changes in treatment regimens, we began to expand our work to analyze medicine quality as well as the fact that it was not only a question of quality. We cannot afford to have medicines available only in the capital cities and not in the countries’ most remote rural areas. Therefore, what is important at this point is the supply, as well as satisfactory storage and estimation of required medicine quantities. The partners of AMI-RAVREDA became gradually involved in this process.70

All the work strategies that were described above generated important collaboration processes. In the words of AMI-RAVREDA’s global coordinator—

A catalyzing effect was created where countries work together, sharing information and experiences. This is a very important aspect of AMI-RAVREDA.71

**Current Challenges to Consolidate the ACT Strategy**

Even though the process of changing the treatment regimen and developing national guidelines and training activities for the workers was relatively rapid and successful, the same was not true in terms of the consolidation of processes and regulations for ACT procurement, distribution, use, and adherence. National authorities recognize that such processes currently constitute the greatest challenge to consolidate the ACT strategy in the region.

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69 Interview with Keith Carter, PAHO’s general coordinator for AMI-RAVREDA.
70 Ibid.
71 Ibid.
Findings

The reasons behind the difficulties encountered in terms of consolidating the processes related to pharmaceutical supply management mainly have to do with the fact that these processes exceed the scope of malaria control programs and they fall under other departments, processes, and purchase and procurement mechanisms of the ministry of health (or its equivalent) in the different countries. The authorities and advisers in the countries explain this as follows—

Changing therapeutic regimens was relatively easy because there was scientific and technical support. It was not even an economic issue, because the region’s countries did not experience financial difficulties when purchasing the new medicines. On the other hand, the issue of pharmaceutical management and supply is complicated because it involves correcting many structural and process-related deficiencies in the ministries, and those deficiencies have multiple arms stretching in all directions, including legal issues. There are also other factors such as the incapacity or incompetence of human resources coupled with bad work habits or scarcity of adequate human resources.72

Additionally, national authorities identify specific difficulties within the country contexts. For example, in Colombia’s case the following was identified—

A serious problem is the scarcity of human resources both at the national level as well as within territorial entities, because they start implementing many initiatives but fail to follow them through. For example, when the pilot test on malaria information systems was carried out, only the individuals who were part of the pilot test submitted information, and not so the remaining 36 territorial entities. There are not enough human resources to monitor directly those territorial entities so they can collect and analyze the information.73

In Bolivia, some challenges were identified that are related to reorganization of the department and national authority in charge of pharmaceutical management—

We have a medicine supply unit; this unit has a certain weight throughout the entire supply management environment, and additionally software was made available to collect incoming and outgoing medicine-related information. Simultaneously, malaria medicines have taken a different course. The time has come to ask ourselves, what are we doing? Do we stand alone with the malaria program within the pharmaceutical supply management processes? Or do we adhere to the global pharmaceutical supply management system that is in charge of managing the country’s social security system? After analyzing all these elements we were able to see that the management process that is being implemented at the national level, although slow, is also the most sustainable. This has generated delays; we have to move at the same pace as the social security pharmaceutical supply management system.74

The problem related to the scarcity of human resources is also present in Guyana—

The problem we have in Guyana is the scarcity of human resources. Sometimes, the same individual who is implementing one activity must also work in another area. Therefore it will depend on the number of human resources we have available, as well as the ministry’s disposition

72 Interview with Roberto Montoya, PAHO’s former regional coordinator for AMI-RAVREDA.
73 Idelfonso Cepeda and Yolanda Mosquera, Colombia.
74 Interview with Arleta Añez, PAHO’s local coordinator for AMI-RAVREDA-Bolivia.
and interest in implementing the new regimen. There is also a high staff turnover; therefore constant training sessions are necessary.\textsuperscript{75}

Since the countries in the region introduced ACT, several of them have experienced medicine stock-outs, and all of them also experienced problems in terms of guaranteeing an adequate medicine supply. Contrary to what occurred in other countries that introduced ACT and experienced stock-outs because of the high cost of the medicine (some countries in Africa), in the countries of the Amazon region, the stock-outs were attributable to other factors, which include the timing of public bidding processes and the insufficient number of suppliers, among others. National authorities describe it as follows—

In Colombia it is viable and possible to purchase the necessary medicines. Stock-outs occur as a result of the difficulty of identifying and selecting prospective bidders for the bidding processes, which could be a quite lengthy and burdensome procedure due to bureaucratic issues. As a result, there are not many bidders, which in turn leads institutions to declare that the contracts are illegal because of failure to comply with the established legal-administrative requirements, or to declare the annulment of a bidding process, or sometimes no local medicine suppliers are available.\textsuperscript{76}

The difficulties and challenges generated by medicine supply management have direct effects on the possibility of adequately implementing the ACT strategy. This situation is addressed in the following section.

**Rapid Evaluation of the Performance of the Four Strategies Using the “Intervention Adequacy” Approach**

**Residual Indoor Spraying**

Residual indoor spraying is one of the oldest strategies implemented in the countries throughout the region. The countries included in this study reported incomplete information with respect to the program’s research, coverage, and quality aspects. However, through a series of interviews with key officers in each country, it was possible to determine that generally the countries failed to follow a systematic implementation approach adhering to the technical criteria established by WHO. Table 9 shows compliance with the criteria for each country included in the study. Note that Guyana reported that the residual indoor spraying program simply does not exist in the country.

\textsuperscript{75} Interview with Dr. Cerón, PAHO’s local coordinator for AMI-RAVREDA-Guyana.

\textsuperscript{76} Interview with Idelfonso Cepeda and Yolanda Mosquera, Colombia.
### Findings

#### Table 9. Evaluation Results of Adequacy Criteria in the Implementation of the Residual Spraying Strategy in Five Countries

<table>
<thead>
<tr>
<th>No.</th>
<th>Criterion</th>
<th>Ecuador</th>
<th>Peru</th>
<th>Bolivia</th>
<th>Colombia</th>
<th>Guyana</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>A stratification of the population at risk was conducted based on disease burden and transmission epidemiology</td>
<td>0</td>
<td>0</td>
<td>0.5</td>
<td>1</td>
<td>N/A</td>
</tr>
<tr>
<td>2</td>
<td>The vector’s habits were studied and verified</td>
<td>0</td>
<td>0</td>
<td>0.5</td>
<td>1</td>
<td>N/A</td>
</tr>
<tr>
<td>3</td>
<td>The susceptibility of prospective insecticides was verified before selecting the insecticide(s) that yielded the best results</td>
<td>0</td>
<td>0</td>
<td>0.5</td>
<td>1</td>
<td>N/A</td>
</tr>
<tr>
<td>4</td>
<td>100 percent of the target households (according to national regulations) had been sprayed at least once a year</td>
<td>0.5</td>
<td>0</td>
<td>0.5</td>
<td>0.5</td>
<td>N/A</td>
</tr>
<tr>
<td>5</td>
<td>Stock-outs of the insecticide used for spraying did not exceed six months in any case</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>N/A</td>
</tr>
<tr>
<td>6</td>
<td>Up-to-date regulations and programs exist to implement residual spraying</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>N/A</td>
</tr>
<tr>
<td>7</td>
<td>A system is in place to monitor the resistance and sensitivity of insecticides used for household spraying</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>0.5</td>
<td>N/A</td>
</tr>
<tr>
<td>8</td>
<td>Systematic procedures are in place to monitor the vector’s habits</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>N/A</td>
</tr>
<tr>
<td>9</td>
<td>Systematic procedures are in place to monitor the residual effect of insecticides in the households that were sprayed</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0.5</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>2.5</td>
<td>3.0</td>
<td>6.0</td>
<td>7.5</td>
<td></td>
</tr>
</tbody>
</table>

*Note: 1 = Yes; 0 = No; 0.5 = Partial; N/A = not applicable.*

Table 10 presents the results in the adequacy scale. Two countries present an intermediate implementation and two countries a deficient implementation.

#### Table 10. Results of the Implementation of the Residual Household Spraying Strategy in Four Countries in the Adequacy Scale

<table>
<thead>
<tr>
<th>Country</th>
<th>Score</th>
<th>Adequacy scale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bolivia</td>
<td>6.0</td>
<td>Intermediate</td>
</tr>
<tr>
<td>Colombia</td>
<td>7.5</td>
<td>Intermediate</td>
</tr>
<tr>
<td>Ecuador</td>
<td>2.5</td>
<td>Deficient</td>
</tr>
<tr>
<td>Peru</td>
<td>3.0</td>
<td>Deficient</td>
</tr>
</tbody>
</table>
The scores in the adequacy scale are congruent with what was perceived by regional technicians and authorities. For example, a technical adviser who worked in most of the countries in the region stated the following—

Vector control is not systematically carried out in any country, and it is actually done based on scarce evidence. In general, the households that have minimum building conditions for spraying to work properly are also accessible to facilities with diagnosis and treatment options; therefore, the population that most needs this intervention is actually left out.\footnote{77 Interview with Gustavo Bretas, PAHO’s local coordinator for AMI-RAVREDA-Ecuador.}

PAHO’s general coordinator expressed it as follows—

There is a problem in this region because of the absence of entomologists in many countries. Therefore we must try to strengthen entomology to enable decisions to be made to control vectors based on evidence instead of to continue spraying and not really know whether the insecticides are actually working.\footnote{78 Interview with Keith Carter, PAHO’s general coordinator for AMI-RAVREDA.}

The national authority in one of the countries recognized the difficulties of implementing the indoor spraying strategy as follows—

Spraying is not carried out following the guidelines or directed at the target populations. In many cases, this decision depends on whether a request is submitted to the authorities by some municipalities asking them to spray the area prior to a fair; therefore, spraying is done mostly as a political decision and without following the program’s technical criteria.\footnote{79 Interview with the malaria national authority, Ecuador.}

**ITNs**

This strategy is currently being implemented in five countries. However, it is relatively recent if compared to residual spraying. The implementation of this strategy had some particularities in the different countries. For example, Bolivia and Colombia carried out studies on population stratification, vector habits, and susceptibility of insecticides before introducing bednets, whereas in other countries, ITNs were introduced without carrying out these studies. In spite of the fact that bednets were distributed in these countries, none of them complied with the criterion of 80 percent coverage among the country’s target population. Table 11 presents the scores obtained for each criterion in each country, and table 12 presents the scores in the adequacy scale.
### Table 11. Evaluation Results of Adequacy Criteria in the Implementation of the ITN Strategy in Five Countries

<table>
<thead>
<tr>
<th>No.</th>
<th>Criterion</th>
<th>Ecuador</th>
<th>Peru</th>
<th>Bolivia</th>
<th>Colombia</th>
<th>Guyana</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>A stratification of the population at risk was conducted based on disease burden and transmission epidemiology</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>The vector’s habits were studied and verified</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>The susceptibility of prospective insecticides was verified before selecting the insecticide(s) that yielded the best results</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>80 percent of the population at risk received ITNs</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>5</td>
<td>ITNs were distributed to 80 percent of pregnant women within the risk area</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>6</td>
<td>ITNs were distributed to 80 percent of children under five within the risk area</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>7</td>
<td>80 percent of the respondents stated that they had slept under a bednet the previous night</td>
<td>0</td>
<td>0.5</td>
<td>0.5</td>
<td>0</td>
<td>0.5</td>
</tr>
<tr>
<td>8</td>
<td>Stock-outs of insecticides used for treatment did not exceed three months during the past five years</td>
<td>0</td>
<td>0</td>
<td>N/A</td>
<td>1</td>
<td>0.5</td>
</tr>
<tr>
<td>9</td>
<td>Stock-outs of new bednets for delivery to the population did not exceed six months in any case</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>10</td>
<td>Retreatment regulations and programs are in place at the household or community levels</td>
<td>0</td>
<td>0</td>
<td>N/A</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>11</td>
<td>A systematic procedure is in place to monitor whether the families that have bednets use them adequately (including retreatment and washing)</td>
<td>0</td>
<td>0.5</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>12</td>
<td>A system is in place to monitor the resistance and sensitivity of the insecticide used in bednets</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0.5</td>
</tr>
<tr>
<td>13</td>
<td>Systematic procedures are in place to monitor the vector’s habits</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>0.5</td>
</tr>
<tr>
<td>14</td>
<td>Systematic procedures are in place to monitor the residual effect of the insecticide used in bednets</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0.5</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>2.5</td>
<td>2.5</td>
<td>8.0^a</td>
<td>9.5</td>
<td>6.0</td>
</tr>
</tbody>
</table>

**Note:** 1 = Yes; 0 = No; 0.5 = Partial; N/A = not applicable.

*a. The total in Bolivia is based on 12 criteria given that the country does not retreat bednets (long-lasting bednets are used).

In the adequacy scale, two countries obtained an intermediate adequacy score and three of them a deficient rating. One of the national authorities who was interviewed explains the program’s difficulties as follows—
ITNs were purchased, but they were delivered without following established technical criteria. Political authorities deliver them during their visits to the towns and villages without taking into consideration the fact that the area was not targeted for the delivery of bednets.\(^\text{80}\)

**Table 12. Results of the Implementation of the ITN Strategy in Five Countries in the Adequacy Scale**

<table>
<thead>
<tr>
<th>Country</th>
<th>Score</th>
<th>Adequacy scale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bolivia</td>
<td>8.0</td>
<td>Intermediate</td>
</tr>
<tr>
<td>Colombia</td>
<td>9.5</td>
<td>Intermediate</td>
</tr>
<tr>
<td>Ecuador</td>
<td>2.5</td>
<td>Deficient</td>
</tr>
<tr>
<td>Guyana</td>
<td>6.0</td>
<td>Deficient</td>
</tr>
<tr>
<td>Peru</td>
<td>2.5</td>
<td>Deficient</td>
</tr>
</tbody>
</table>

**Timely Diagnosis**

The timely diagnosis strategy involves microscopic diagnosis as well as RDTs. In Guyana’s case, the country did not introduce rapid tests; therefore, the adequacy analysis was carried out for only the microscopic diagnosis criterion. Microscopic diagnosis has been the main strategy in the countries, and it was strengthened over the years. Therefore, all these countries have national guidelines and systems in place to monitor the quality of microscopic diagnosis.

PAHO’s general coordinator for AMI-RAVREDA explains that the capacity of microscopic diagnosis in the countries is as follows—

> We are familiar with the capacity of the diagnostic network in the countries and trust to a certain extent their good diagnostic capacity.\(^\text{81}\)

The RDT is relatively new. Even through it was introduced and distributed in all the countries (except Guyana), its introduction and use have not been systematically implemented. Some countries still have no national standards for the acquisition and use of rapid tests. In the countries where standards are in place, systematic processes have not yet been fully implemented to monitor compliance with the standards related to transportation, storage, and use of RDTs. Table 13 shows the level of compliance with each criterion in the countries, and table 14 shows their scores in the adequacy scale.

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\(^\text{80}\) Interview with the malaria national authority, Ecuador.

\(^\text{81}\) Interview with Keith Carter, PAHO’s general coordinator for AMI-RAVREDA.
Table 13. Evaluation Results of the Adequacy Criteria in the Implementation of the Timely Diagnosis Strategy in Five Countries

<table>
<thead>
<tr>
<th>No.</th>
<th>Criterion</th>
<th>Ecuador</th>
<th>Peru</th>
<th>Bolivia</th>
<th>Colombia</th>
<th>Guyana</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>At least 80 percent of all cases are diagnosed within the first 24 hours (time elapsed between taking the blood sample for the thick blood smear or samples for rapid tests and the delivery of results in endemic areas) after the onset of fever</td>
<td>1</td>
<td>0.5</td>
<td>0</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>2</td>
<td>No stock-outs of rapid tests have occurred in any facilities within the public network in endemic areas</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>N/A</td>
</tr>
<tr>
<td>3</td>
<td>A system is in place to monitor the quality of microscopic diagnosis in the public network</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>4</td>
<td>A system is in place to monitor the quality of RDTs</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>N/A</td>
</tr>
<tr>
<td>5</td>
<td>National standards are in place for RDT application, distribution, transportation, and storage</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>N/A</td>
</tr>
<tr>
<td>6</td>
<td>A systematic process is in place to monitor compliance with distribution, transportation, and storage standards</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0.5</td>
<td>N/A</td>
</tr>
<tr>
<td>7</td>
<td>A training and supervision program is in place for the staff in charge of applying RDTs</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td><strong>Total</strong></td>
<td>3.0</td>
<td>1.5</td>
<td>1.0</td>
<td>6.0</td>
<td>1.5</td>
</tr>
</tbody>
</table>

*Note: 1 = Yes; 0 = No; 0.5 = Partial; N/A = not applicable.*

*a. The evaluation in Guyana is based on only two criteria; rapid tests are not used in the country.*

Table 14. Results of the Implementation of the Timely Diagnosis Strategy in Five Countries in the Adequacy Scale

<table>
<thead>
<tr>
<th>Country</th>
<th>Score</th>
<th>Adequacy scale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bolivia</td>
<td>1.0</td>
<td>Deficient</td>
</tr>
<tr>
<td>Colombia</td>
<td>6.0</td>
<td>Adequate</td>
</tr>
<tr>
<td>Ecuador</td>
<td>3.0</td>
<td>Deficient</td>
</tr>
<tr>
<td>Peru</td>
<td>1.5</td>
<td>Deficient</td>
</tr>
<tr>
<td>Guyana</td>
<td>1.5</td>
<td>Only two criteria were evaluated; RDTs are not used</td>
</tr>
</tbody>
</table>
Artemisinin-Based Combination Therapy

ACT is the most recent strategy implemented by the countries of the Amazon region. It stands out because of its systematic implementation in all countries, as well as the level of collaboration among the countries in terms of conducting prior resistance and sensitivity studies as well as coverage and quality studies. The evidence collected shows that the systematic implementation is the result of the support provided by AMI-RAVREDA to the countries in the region. In addition to the documentary evidence (publications, reports on resistance and sensitivity studies, national guidelines), this result was also acknowledged by the officers who were interviewed in each country.

With respect to adequacy criteria, all the countries in the region complied with most of the expected criteria. A common problem for these countries is to ensure the continuous supply of ACTs, as well as the implementation of systematic processes to monitor the adequate application of standards and protocols. As a result of the strategy’s systematic implementation, all the countries obtained an “adequate implementation” rating for the strategy in accordance with the technical criteria established by WHO. Table 15 presents the scores obtained by the countries for each criterion, and table 16 includes the scores on the adequacy scale.

Table 15. Evaluation Results of Adequacy Criteria in the Implementation of ACT Strategy in Five Countries

<table>
<thead>
<tr>
<th>No.</th>
<th>Criterion</th>
<th>Ecuador</th>
<th>Peru</th>
<th>Bolivia</th>
<th>Colombia</th>
<th>Guyana</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>In vivo or in vitro <em>P. falciparum</em> resistance studies were carried out on medicines used in previous treatment regimens</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>In vivo or in vitro <em>P. falciparum</em> ACT sensitivity studies were carried out</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>3</td>
<td>At least 80 percent of <em>P. falciparum</em> cases receive ACT</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>4</td>
<td>No ACT stock-outs have occurred in the public network during the past three years</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0.5</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>The country’s treatment regimens have up-to-date ACT standards and protocols</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>6</td>
<td>A system is in place to monitor ACT’s therapeutic failures</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>7</td>
<td>According to current standards, ACT is delivered only when there is a positive test result (either microscopic or rapid test) for <em>P. falciparum</em></td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0.5</td>
<td>1</td>
</tr>
<tr>
<td>8</td>
<td>A systematic procedure is in place to monitor the adequate application of ACT standards and protocols</td>
<td>1</td>
<td>0.5</td>
<td>0.5</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td><strong>Total</strong></td>
<td>7.0</td>
<td>6.5</td>
<td>6.5</td>
<td>6.0</td>
<td>6.0</td>
</tr>
</tbody>
</table>

*Note: 1 = Yes; 0 = No; 0.5 = Partial.*
Findings

Table 16. Results of the Implementation of the ACT Strategy in Five Countries in the Adequacy Scale

<table>
<thead>
<tr>
<th>Country</th>
<th>Score</th>
<th>Adequacy scale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bolivia</td>
<td>6.5</td>
<td>Adequate</td>
</tr>
<tr>
<td>Colombia</td>
<td>6.0</td>
<td>Adequate</td>
</tr>
<tr>
<td>Ecuador</td>
<td>7.0</td>
<td>Adequate</td>
</tr>
<tr>
<td>Peru</td>
<td>6.5</td>
<td>Adequate</td>
</tr>
<tr>
<td>Guyana</td>
<td>6.0</td>
<td>Adequate</td>
</tr>
</tbody>
</table>

According to the collected data, ACT supply problems correspond to the complexity of implementing procurement processes for new medicines (Coartem and others), which must respond to national procurement standards. For example, a reduced number of suppliers has led the public procurement of ACTs to be declared void in several instances in Peru. Procurement procedures where units of the ministry of health are involved other than the malaria program have lengthened the process in other countries. This implies that ACT stock-outs in these countries do not directly correspond to the inaction of malaria authorities, but rather to these countries’ existing procurement processes and public contracts. A PAHO adviser who worked in several countries in the region explains this as follows—

Currently, one of the greatest weaknesses is linked to the management of medicines and other supplies. Peru and Ecuador have experienced serious stock-outs. These problems arise from the application of purchase and procurement laws in these countries, which affect malaria programs. Therefore, to make improvements in this area, work must be carried out at another level, that is, at the country level as well as with central finance authorities and others.82

Added to the preceding, decentralization and other health reforms have generated a new organizational architecture in these countries. Although previously the procurement of supplies was exclusively under the responsibility of malaria control programs, it currently involves other units from the ministries of health (procurement, decentralized authorities, etc.). The ways in which decentralization and health reforms have changed the units and actors involved in issues relevant to malaria control programs are discussed in a later section.

Summary of Control Strategies Implementation

Of the four control strategies that were analyzed, only ACT is adequately implemented. The other three are implemented with adequacy levels ranging from intermediate to deficient, and only one country attained an adequate level in timely diagnosis. The information that was gathered in the different countries reveals that research processes aimed at defining current guidelines and protocols have been successful in all these countries. Even though the ACT strategy has attained an adequate implementation level, some criteria still must be strengthened, such as medicine supply and the implementation of systematic processes to monitor the adequate application of standards and protocols.

82 Interview with Gustavo Bretas, PAHO’s local coordinator for AMI-RAVREDA-Ecuador.
Results and Impact of ACT Introduction in the Countries of the Amazon Basin

As explained in the “Methodology” section, PAHO’s annual reports contain information about malaria indices for all the countries in the region as well as information about morbidity and mortality rates associated with malaria. Therefore, this report focuses on analyzing information that was not included in the PAHO reports: *P. falciparum*’s trend between 1995 and 2008, and ACT coverage for the reported cases of *P. falciparum* as of the introduction of ACT in each country. This analysis follows, beginning with an analysis of the individual countries and followed by a joint analysis.

**Bolivia**

The trend of *P. falciparum* cases in the country shows an increase since 1995, peaking in 1998, when 11,414 cases were reported. As of 1999, a rapid drop in the number of cases began, and in 2000 only 2,536 cases were reported. The ACT strategy was introduced in 2001, and from 2002 onward 100 percent coverage of *P. falciparum* cases was reached with ACT treatment (represented in red in figure 1). Even though the number of cases increased between 2001 and 2008, this increase was relatively low, with the total remaining at less than 2,000 cases per year.

![Figure 1. Comparison of P. falciparum cases and cases treated with ACT in Bolivia, 1995–2008](image)

**Colombia**

*P. falciparum*’s trend in Colombia between 1995 and 2008 presents a different pattern from the rest of the region. Whereas in the other countries, only one episode involving a brisk rise and drop in the number of cases is observed, three episodes are identified in Colombia. These peaks are also quite abrupt. For example, from 98,460 cases registered in 1998, during the following year only 24,718 cases were registered, and two years later approximately 100,242 cases were registered once again. Only as of 2002 is it possible to observe a gradual decrease in the number of cases, which is similar to the behavior observed in the rest of the countries. It is important to note that the various sources of information for *P. falciparum* cases differ in Colombia, particularly between the data that are managed and reported by the provincial offices for control of vector-transmitted diseases and SIVIGILA (national public health surveillance system). Usually, SIVIGILA, which is the national source of official information, reports fewer cases than the provincial offices. Therefore, a significant probability exists that the particular trend presented by Colombia is influenced by the variability in registering the number of cases.

The country introduced the ACT strategy in 2006. During the three years that are compared, no relationship is seen between the registered number of cases and the reported cases treated with ACT (see figure 2). For example, between 2007 and 2008 the number of cases dropped to approximately 20,000 registered; however, more than 40,000 treated cases were reported during the same year. This discrepancy again indicates the likelihood that case records are not reliable. It also suggests the possibility that problems exist in terms of the registration of treated cases, given that no coincidence occurs with the number of cases reported during any of those years.

![Figure 2. Comparison of *P. falciparum* cases and cases treated with ACT in Colombia, 1995–2008](http://new.paho.org/hq/index.php?option=com_content&task=view&id=2632&Itemid=2049)

Ecuador

From 1995 to 1997, the trend of *P. falciparum* cases was dropping, and at least 5,000 cases were reported. As of 1998, a rapid rise occurred in the number of cases, reaching 49,252 cases in 1999 and 48,974 in 2000. As of 2001, a period of rapid and sustained descent occurred, and 5,891 cases were reported in 2004. From 2005 to 2008, the drop continued, and only 491 cases were reported in 2008. The ACT strategy was introduced in 2005, and consistency was evidenced between the number of reported *P. falciparum* cases and the cases treated with ACT in only two years. During 2007 and 2008, the country did not purchase medicines, and thus no data appear in the official records for these years. However, the national malaria program obtained supplies through donations. Therefore, even though medicines were not purchased, in practice, the country was able to continue delivering ACT from the donations received (see figure 3).

![Figure 3. Comparison of *P. falciparum* cases and cases treated with ACT in Ecuador, 1995–2008](image)


Guyana

The only two consecutive years that recorded a drop in the number of cases were 1999 and 2000. From 2001 to 2005, slight increases and drops occurred in the number of *P. falciparum* cases. Decreases in the number of cases occurred in 2006 and 2007; however, a slight rise in the number of cases was recorded in 2008 (see figure 4).

The ACT strategy was introduced in 2004. During that year, the coverage of cases treated with ACT was quite low; however, during 2005 all cases were covered, and in the following years coverage was maintained at approximately 90 percent of all cases.
Findings

**Peru**

Between 1995 and 1998, a rapid rise in the number of *P. falciparum* cases was recorded, and 84,289 cases were reported in 1998. As of that time a rapid descent in the number of cases began until 17,687 cases were registered in 2001. The following two years this figure remained stable, and fewer than 20,000 cases were reported. As of 2004, a gradual reduction in the number of cases occurred, and only 4,492 cases were reported in 2008 (see figure 5).

The ACT strategy was officially introduced in the country in 2001. In spite of that, no information sources indicate the number of treatments that were provided. Records become available in 2004. From 2005 to 2008, the records indicate a higher number of treated cases than the number of reported cases, which indicates a coverage rate exceeding 100 percent. This can be explained by the fact that no information available in Peru corresponding to the number of treatments provided to patients, and only the number of ACT treatments distributed to health facilities is recorded, which could be higher than the number of ACT treatments that were actually delivered to patients with confirmed *P. falciparum* malaria, given that health facilities try to maintain ACT inventories.

**Figure 4. Comparison of *P. falciparum* cases and cases treated with ACT in Guyana, 1995–2008**

Impact of ACT for Malaria in Various Countries and Implications for the Countries of the Amazon Basin: Final Report


Figure 5. Comparison of *P. falciparum* cases and cases treated with ACT in Peru, 1995–2008

Comparison of ACT Coverage in All Countries

PAHO’s reports, based on the countries’ information, indicate that between 95 percent and 100 percent of all *P. falciparum* cases are treated with ACT in the countries of the Amazon region. The analysis of annual *P. falciparum* cases and ACT treatments delivered to each country (presented in the previous section) revealed several years of discrepancies between the number of reported and treated cases. Therefore, a comparative analysis of all countries is relevant. This analysis is presented in table 17. The data for each country begin in the year that the ACT strategy was officially introduced. In a situation with adequate implementation of the strategy, one would expect that the countries would gradually increase coverage until they attain 100 percent coverage and maintain it. However, as can be appreciated in the table, only Ecuador and Bolivia approach an adequate level. The other countries present years with percentages exceeding the number of reported cases (for example, Colombia registered 207 percent coverage in 2008) or coverage percentages well below the number of reported *P. falciparum* cases (for example, Guyana’s 89 percent in 2008).

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83 PAHO. Malaria Day in the Americas 2009.
Findings

Table 17. Coverage of *P. falciparum* Cases Treated with ACT in Five Countries, after the Introduction of ACT in Each Country through 2008 (%)

<table>
<thead>
<tr>
<th></th>
<th></th>
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<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Peru</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>94</td>
<td>111</td>
<td>170</td>
<td>189</td>
<td>150</td>
</tr>
<tr>
<td>Bolivia</td>
<td>43</td>
<td>83</td>
<td>103</td>
<td>118</td>
<td>106</td>
<td>99</td>
<td>101</td>
<td>94</td>
</tr>
<tr>
<td>Guyana</td>
<td>81</td>
<td>108</td>
<td>106</td>
<td>97</td>
<td>89</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ecuador</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colombia</td>
<td>122</td>
<td>68</td>
<td>207</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The variability of ACT coverage can be better visualized in figure 6. One would expect the lines for each country to coincide at approximately 100 percent coverage; however, there is a broad dispersion. The incongruence between reported *P. falciparum* cases and ACT can have many explanations: (a) presumptive treatment is being prescribed, which is why in some countries more treatments are delivered than the actual number of confirmed cases; (b) countries are reporting the number of ACTs distributed to the health facilities as a synonym of treatments provided to confirmed patients, which is not equivalent; (c) problems are occurring with the registration of ACT delivered to confirmed patients.

The three explanations proposed are not mutually exclusive; therefore, it is most likely that a combination of all these factors occurred. In any case, the information that was analyzed suggests the need to improve the registration and analysis of ACT in these countries.

![Figure 6. ACT coverage of *P. falciparum* cases in five countries, 2001–2008](image)
Summary of Trend Analysis of P. falciparum Cases and ACT Coverage

The trend analysis identified that four countries had experienced a rapid drop in the number of cases before the introduction of ACT (Bolivia, Colombia, Ecuador, Peru). In Guyana, the descending trend of P. falciparum appeared recently, in line with introduction of ACT in the treatment protocol.

The preceding indicates one cannot reach clear conclusions about the relationship between the recent trend of P. falciparum cases and ACT coverage. The current descending cycle in the number of cases experienced by the countries may possibly be influenced not solely by ACT but also, to some extent, by the other control strategies that are being implemented, even with the identified deficiencies in their implementation. Several experts in the region who were interviewed referred to this aspect—

What we are currently observing, in some way or another, is not only the result of a single strategy, such as ACT, but a combination of the different strategies that the countries have been implementing. The “Roll Back Malaria” strategy fostered control programs, which have certainly contributed to the descending trend we are currently experiencing.84

Another official stated the following—

What we have learned is that to control malaria, diagnosis and treatment are essential because they affect the number of cases that occur. Therefore, even if the control strategies are not implemented with all the technical elements, it is possible to have an effect on the number of cases if there is at least a good diagnosis and treatment delivery network. The countries made much progress in terms of expanding the diagnostic network during the last years.85

If the countries are currently experiencing a descending cycle influenced by both external (climate related and ecological) and internal factors (the control strategies that are being implemented), a hypothesis can be proposed where the contribution of the ACT strategy has been to prevent the initiation of a new cycle of an increasing number of cases, similar to the cycles that occurred in the countries between 1995 and 1999.

Following the previously described hypothesis, a fundamental task is to ensure that both the ACT strategy and the other main strategies (residual spraying, ITNs, and timely diagnosis) are implemented in a technically adequate manner to attain the greatest possible potential to continue the decreasing cycle in the number of P. falciparum cases. For this reason, it is important to take into account that malaria control programs and the countries’ own health systems have been undergoing transformations. Such transformations create new challenges as well as the need to review the operational procedures that the countries have been implementing. The following section analyzes the transformation of the health systems in these countries.

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84 Interview with Keith Carter, PAHO’s general coordinator for AMI-RAVREDA.
85 Interview with Gustavo Bretas, PAHO’s local coordinator for AMI-RAVREDA-Ecuador.
Findings

The Changing Context of Countries’ Control Programs

During the last 15 years, most countries in the region have been implementing health system reform processes. These processes have introduced many changes into the structure, organization, funding, and management of health systems. These changes have also reached the malaria control programs. At the time data were collected for this study (January to July 2010), only Ecuador had not experienced major transformations. However, it was anticipated that major changes in the program’s structure and organization were about to become official by midyear 2010.

It is important to take into account that the adjustments that the programs made as a result of these changes can be relatively slow and pose several challenges. The global coordinator of AMI-RAVREDA visualizes it as follows—

During the reform processes, control programs underwent changes and became diagonal. We refer to them as diagonal because they are neither completely vertical nor horizontal or decentralized.86

The transformations that the programs experienced were significant, and they have affected the various components of malaria control. To exemplify this situation, Peru’s case is used. Figure 7 shows how the program was structured before the reforms in terms of five core components—

- Regulations and protocols
- Regulation and supervision of operational workers
- Planning, programming, and procurement of medicines and supplies
- Storage and distribution of medicines and supplies
- Information system

86 Interview with Keith Carter, PAHO’s General Coordinator for AMI-RAVREDA.
Figure 7, corresponding to the prereform structure, identifies that the program’s key components are under the national authority, which reflects a vertical control program. As of the implementation of system reform processes and other national reforms, such as decentralization, the national malaria program experienced substantial modifications. Figure 8 presents the program’s postreform structure.
Figure 8 clearly shows that only the regulations and protocols of the prereform structure remained under the direct responsibility of the national authority. In the remaining key components, the national authority assumes a technical and advisory role. Authority in the remaining components is shared with other directorates or units within the ministry of health or is directly under the responsibility of decentralized provincial governments. Also noteworthy is that several other actors are part of the control processes and activities. The most notable is the information system. Whereas in the prereform structure it was a direct competency of the national control program and its operational workers, in the current structure at least three actors participate in the information collection effort, while data analysis and reporting must be coordinated and agreed with six different directorates and departments within the Ministry of Public Health and Social Welfare.

The programs’ new structure in the countries has direct implications on the adequate implementation of control strategies. This could also explain why changes in treatment regimens
and national regulations were implemented at a relatively rapid pace whereas the implementation of processes and guidelines to improve pharmaceutical supply management has been more difficult. In the case of national regulations, AMI-RAVREDA had a clear counterpart: the national authority in each country. To implement the pharmaceutical management and supply processes and guidelines, several counterparts with different levels of technical management, authority, and priorities have to agree. Additionally, the countries continue reforming the planning processes, for example, the implementation of planning methodologies for the products.

Also important to note is that the preceding change processes continue taking place in these countries. For example, in Ecuador’s case, a program adviser stated—

Changes are still taking place within the countries’ health systems that directly affect the programs; for example, in Ecuador, there is no per diem for fieldwork. How do they expect to implement control programs without conducting fieldwork? How do they expect to implement active identification of cases?  

All the above present important challenges for control programs and AMI-RAVREDA. Some of the main advisers of AMI-RAVREDA have identified this situation. For example, since 2009, Jaime Chang, general coordinator of AMI/USAID, identified the need to implement a regional workshop with the aim of discussing how decentralization processes are affecting control programs.  

Both the health sector decentralization and reform processes in general pose challenges that demand review of the strategies that have been implemented to strengthen national programs, particularly to go from the establishment of national regulations to situations where the tools, processes, and routines are inserted in the countries’ health systems.

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87 Interview with Gustavo Bretas, PAHO’s local coordinator for AMI-RAVREDA-Ecuador.
CONCLUSIONS

The systematization and analysis of AMI-RAVREDA’s experience in terms of supporting the introduction of ACT in the countries reveal that the program has been successful in generating a network that systematically produces, shares, and analyzes scientific evidence related to antimalarial drug resistance. The evidence generated constituted one of the factors that contributed to the adoption of changes in treatment regimens in the countries of the Amazon region, as well as in the introduction of ACT into countries’ therapeutic regimens for those who did so after 2003.

Even though contributions have been successful to the point of adoption of national guidelines, the implementation of processes and activities to ensure the adequate implementation of the ACT strategy has been more difficult, mainly with respect to medicine supply management. Despite a number of analyses, regional workshops for the development of guidelines and processes, and technical assistance activities at the country level, ACT implementation has been slow and challenging because of the variety of actors (procurement, decentralized authorities, etc.) that are beyond the malaria control programs. This makes the tasks to ensure adequate medicine supply management substantially more complex than the stage when efforts were aimed at influencing a change in treatment regimens and regulations.

Health systems in these countries have changed in the past 15 years, and they are still undergoing changes. Until now, AMI-RAVREDA has emphasized control programs and not the other actors that are part of the health system, even though they are also decision makers responsible for key inputs for control strategies.

Concerning the rapid evaluation of adequacy levels in terms of the implementation of the four malaria control strategies, the analysis revealed that residual household spraying and ITN strategies are currently being implemented at a deficient level. This is relevant if one takes into account the findings of the literature review, which indicate that to implement sustainable malaria control initiatives, the combined effect of different strategies is needed. Additionally, the current scenario in the region, with countries presenting both high and low transmission rates, makes it necessary to have all the tools and technologies available to be able to adjust the strategies and activities to this new context.

The ACT strategy was considered adequate in most countries, given that almost all the technical criteria to implement the strategy were met. The criteria that have not been met yet are those related to the systems aimed at ensuring the continuous supply of ACT and the systems to supervise the quality of ACT implementation, including adherence to treatment.

With respect to the trend analysis of *P. falciparum* between 1995 and 2008, and the introduction of ACT, a clear conclusion cannot be reached concerning the drop in the number of *P. falciparum* cases in the countries and the introduction of ACT. This is because four countries had begun experiencing a rapid decrease in the number of cases before the introduction of ACT (Bolivia, Colombia, Ecuador, Peru). Only Guyana experienced a recent descending trend of *P. falciparum* cases as a result of the introduction of ACT in the country’s treatment regimen.
The preceding does not indicate that the introduction of ACT has not had an effect, but rather the difficulty of identifying a clear association. This also responds in part to the weaknesses that are still present in the countries’ information systems in terms of routine information. For example, the analysis of reported *P. falciparum* cases compared to ACT treatments delivered reveals serious inconsistencies in several countries. These weaknesses are related to the complexity and diversity of the actors that participate in data collection, analysis, and decision making at the level of each individual country. Such complexities are the result of health system reform processes as well as other state reforms affecting public organizations (for example, decentralization) that the countries have been implementing.

Finally, the paradigm of vertical health programs or a national authority that has total control over malaria programs is clearly no longer present in the region. This implies that AMI-RAVREDA must review its support strategies for control programs in the region, preferably using an approach aimed at strengthening health systems.
RECOMMENDATIONS

Systematic Approach to Strengthen Control Strategies

The analyses revealed that the other three control strategies implemented by the countries (household spraying, ITNs, and timely diagnosis) present some deficiencies. Therefore, it is recommended that AMI-RAVREDA expand the systematic approach it has been implementing for ACT to strengthen the remaining control strategies.

In addition, malaria incidence in the region clearly has been changing, and currently some geographical areas have different types of incidence: (a) areas where no cases were reported, but where there is a transmission risk; (b) low-incidence areas; and (c) high-incidence areas. This implies that to strengthen control strategies, a strategic approach should be implemented that recognizes and acts on the described situations. Through AMI/USAID’s leadership and coordination, the partners of this initiative have developed strategic orientation documents that will serve as a guide for each country so they can develop a multiannual plan to strengthen control strategies in high- and low-incidence regions.

Toward ACT Consolidation in the Region

As described in the preceding sections, even though implementation of the ACT strategy was considered adequate, weaknesses were identified in two criteria, which should be strengthened. These include (a) ensuring adequate medicine supply management, and (b) establishing systematic processes to monitor the adequate application of regulations and protocols.

Concerning medicine supply management, the general findings identified that adequate management presents several challenges because several actors and administrative procedures are involved in each country that are beyond the scope of the national malaria control programs. In addition to these general factors, a number of specific studies carried out by MSH’s Strengthening Pharmaceutical Systems Program documented that the medicine availability problems observed in the countries are the result of two main factors: (a) suppliers’ lack of interest in marketing the small volumes that are currently required as a result of the disease’s reduced incidence in the region, and (b) deficiencies in terms of programming needs and procurement-related issues.

Of these two factors, the programming deficiency is most relevant, given that adequate programming would allow identification of alternative procurement mechanisms for a context where the number of suppliers is reduced. A recent technical analysis exercise carried out by the

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90 Ibid.
countries identified specific variables that are associated with these programming deficiencies—

- Failure to consider a safety stock
- Failure to consider the supplier’s purchase and delivery times
- Failure to include strategic stocks for low-incidence areas
- Failure to plan purchases for special cases

On the basis of that analysis, the countries that benefitted from the technical support provided by AMI-RAVREDA have launched a process to standardize, as much as possible, the treatment regimens used in the region. Such standardization would have the advantage of allowing joint purchases by several countries, donations among countries in emergency situations, information exchanges regarding the medicine’s adverse effects, studies on treatment resistance and adherence, and treatment continuity for patients living along border zones.

The foregoing indicates that the countries that benefitted from the technical assistance provided by the partners of AMI-RAVREDA have already begun implementing decisive steps to strengthen medicine supply in the medium and long term. Moreover, each country has developed an action plan to implement the activities and processes required to standardize treatment regimens and consolidate purchases. Therefore, it is recommended that AMI-RAVREDA’s support focus on providing assistance and follow-up so the countries can implement these action plans.

With respect to strengthening supervision systems for the adequate application of regulations and protocols, the strengthening of routine information systems plays an important role. Because of the ongoing transformations throughout the region’s health systems, the information systems related to malaria do not fall under the exclusive competency of the national control programs, but rather are shared with other departments at the central level of the ministries as well as the provincial and municipal units. The issue of information systems is addressed below as part of the strengthening of health systems.

AMI-RAVREDA and Health Systems Strengthening in the Region

It is clear that the countries’ health systems have undergone transformations. These transformations are at different stages, and in most cases they require consolidation. Within this context, it is vital to apply an approach aimed at strengthening health systems, which implies that the processes occurring within the health systems are equally or more important than the specific activities. It also implies having a detailed and profound understanding of each country’s health system, which includes not only the formal components of the health system (laws, regulations,
protocols) but also informal mechanisms and incentives (clientelism, identification of priorities, etc.) that influence the governance of health systems. All this is vital to be able to identify effective processes, mechanisms, and strategies to strengthen malaria control interventions within health systems that have broader responsibilities.

To implement the above, it is suggested that AMI-RAVREDA conduct an analysis of processes of change that the countries have been experiencing and the implications for malaria control. This analysis must include a detailed mapping of the new processes related to the key components of a control program: (a) regulations and protocols; (b) regulation and supervision of operational workers; (c) planning, programming, and procurement of medicines and supplies; (d) storage and distribution of medicines and supplies; and (e) information system.

Following this analysis, AMI-RAVREDA should be capable of developing strategic technical assistance plans for each country. This step is of utmost relevance given that based on what was disclosed by the analysis, processes of change have generated specific particularities in each country. In addition to the general strategies, programs, and activities for all these countries, technical assistance plans must include actions consistent with each country’s specific context.

To strengthen the implementation of protocols and technical guidelines as well as their insertion into the health systems, AMI-RAVREDA must test innovative strategies and mechanisms. An example of this is implementation research that allows identification of management arrangements and effective incentives to improve the response capabilities of all the actors involved in controlling malaria, not only the traditional counterparts of AMI-RAVREDA, but also those that participate at the country level (decentralized authorities, procurement units of the ministries of health, etc.).

It is also recommended that AMI-RAVREDA define and implement actions to strengthen the countries’ information systems. The experience acquired in development and maintenance of the surveillance system to determine resistance to antimalarial medicines will be vital for this system. However, it should be clear that the strengthening of routine data collection, analysis, and decision making is a much more complex task that requires medium- and long-term actions.

Finally, this study developed and applied tools for the rapid analysis of performance of control programs in the countries using the analytical framework to evaluate public health interventions following adequacy, plausibility, and probability criteria. These types of tools have the flexibility to expand and adapt to implement continuous performance monitoring processes. Therefore, it is suggested that AMI-RAVREDA implement actions to make these types of tools available to countries to increase the arsenal of strategies, methodologies, and processes aimed at strengthening malaria control programs.
ANNEX A: DATA COLLECTION INSTRUMENTS FOR EACH OF THE FOUR ANTIMALARIA STRATEGIES

Instrument 1: Collection of Information on ACT

1. General information

Country: ____________________

Name of consultant who collects the information: ________________

E-mail: ____________________

1.1 Please fill out the following table with the official information corresponding to reported *P. falciparum* cases in the country.

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of cases reported</th>
<th>Distribution according to gender</th>
<th>Distribution of cases in high-risk groups</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Men</td>
<td>Women</td>
</tr>
<tr>
<td>1995</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1996</td>
<td></td>
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<tr>
<td>2009</td>
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</tbody>
</table>

Note: If the risk groups in the country/state/department differ from those indicated in the table, please prepare a table to accommodate these risk groups.

2. Efficacy studies of antimalarial medicines

2.1 Were in vivo or in vitro efficacy studies of antimalarial medicines for *P. falciparum* carried out in the country outside the RAVREDA project? If yes, please fill out the following table—
3. Introduction of ACT

3.1 What procedure was followed to determine what specific medicines and presentations would be part of the ACT regimen implemented in the country? Please, describe. If a report about the process is available, please attach it.

3.2 Was there any other reason, in addition to the studies conducted by RAVREDA, that influenced the introduction of ACT? If yes, please explain.

3.3 When was the regulation for ACT introduction approved?

3.4 When was the first distribution of ACT conducted?

3.5 Did the introduction of ACT occur simultaneously in the entire endemic region or was it phased? Please describe, and if it occurred in phases, describe the reasons behind this (e.g., medicine availability, cost, etc.).

4. National guidelines for ACT use

4.1 What is the current therapeutic regimen implemented in the country?

4.2 What are the medications’ presentations?

4.3 Who delivers the medications to the patients? (e.g., health promoters, nurses, physicians)

4.4 Is it a requirement to have one positive test result (either microscopic or rapid test) for *P. falciparum* to be eligible for a prescription of ACT? If the answer is yes, what procedure is implemented to ensure compliance? (e.g., forms to attach test results, etc.) If the answer is no, what is the estimated percentage of ACT delivered based on a presumptive malaria diagnosis? (attach information source)
4.5 Were studies conducted to evaluate the number of patients who receive ACT even though their test results were negative (either microscopic or rapid test)? If the answer is yes, please briefly explain the study and attach the full report. If the answer is no, are authorities concerned about the delivery of ACT to patients whose test results were negative? Please, describe.

4.6 Are any oral artemisinin-based medicines available as monotherapies that can be freely purchased in the private subsector? If the answer is yes, what are the health authorities’ policies or guidelines in this respect? (e.g., promote controlled sales, restrict imports, etc.)

5. **ACT procurement and distribution**

5.1 What process does the country implement to purchase medicines that are part of ACT (including the selection of suppliers)?

5.2 Please, fill out the following table (as of the year ACT was introduced)—

<table>
<thead>
<tr>
<th>Year</th>
<th>Unit price paid per treatment (including all related costs such as transportation and insurance)</th>
<th>Total number of treatments purchased</th>
<th>Total number of treatments delivered</th>
<th>Distribution of treatments among high-risk groups</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Children under 12 months</td>
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</tbody>
</table>

* The sum of all treatments delivered outside priority groups. The sum of the remaining treatments and the three priority groups must match the total quantity of medicines delivered.

5.3 What were the funding sources for each year that ACT was purchased? (e.g., ministry of health budget, international cooperation, etc.)

5.4 How is ACT distributed in endemic areas and particularly in remote regions?

**END OF INSTRUMENT**
Instrument 2: Collection of Information about ITNs

1. General Information

Country: ___________________

Name of consultant who collects the information: _______________

E-mail: ___________________

1.1 Please fill out the following table with official information corresponding to the reported cases of *P. vivax* in the country.

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of cases reported</th>
<th>Distribution according to gender</th>
<th>Distribution of cases in high-risk groups</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td>Men</td>
<td>Women</td>
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<td>1995</td>
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<td>2009</td>
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</tbody>
</table>

Note: If the risk groups in the country/state/department differ from those indicated in the table, please prepare a table to accommodate these risk groups.

2. Prior research/preparation phase and program startup

2.1 Was a stratification of the population at risk conducted based on disease burden and transmission epidemiology? If the answer is yes, please briefly explain the procedures that were implemented as well as the results obtained. Attach the respective reports if available.

2.2 Were the vector’s habits studied and verified? If the answer is yes, please briefly explain the studies that were carried out, the year they were conducted, and the main results. If there are reports concerning such studies, please obtain copies thereof and attach them.
2.3 Was susceptibility to prospective insecticides verified before selecting the insecticide(s) that yielded the best results? If the answer is yes, briefly describe the process that was followed.

3. Program launch and use of insecticides

3.1 When was the program officially launched?

3.2 Was the program launched in the entire endemic region or in phases? Please describe, and if it was implemented in phases, describe the reason for doing so (e.g., staff scarcity, etc.) and the estimated number of households/population covered during each phase.

3.3 What insecticide is currently used for retreatment of bednets? If several, please list them.

3.4 Were different insecticides used as of the year the program was launched and up to this date? If so, please list the names of the insecticides, and if one is no longer used, please briefly describe the reasons behind this decision.

3.5 What process is implemented in the country to purchase insecticides (and other key supplies) for retreatment?

3.6 Did stock-outs of insecticides used for retreatment occur in previous years? If so, please indicate the year or years when this happened, and the period of time the stock-out lasted.

4. National (or state/departmental/municipal) guidelines for ITNs and implementation processes

4.1 According to national guidelines, what population groups should use bednets?

4.2 What procedure is followed to retreat bednets with insecticide?

4.3 What is the recommended retreatment frequency?

4.4 Who is in charge of retreatment?

4.5 Are standards and programs in place for retreatment at the household or community levels? If so, describe them.

4.6 Is there a cost (even if subsidized) for the population to obtain ITNs through the program/ministry of health (or equivalent)? If the answer is yes, what is the average cost of a new ITN?

4.7 Is there a cost for the population for the retreatment of bednets through the program/ministry of health (or equivalent)? If the answer is yes, what is the average cost of each retreatment?
4.8 Are retreatment services available from the private sector? If the answer is yes, is there any information concerning the estimated percentage of people who retreat their bednets in the private sector?

**NOTE:** In addition to the preceding information, please submit to the attention of Walter Flores the national guidelines and protocols for the ITN program.

4.9 What process is implemented in the country to purchase ITNs (including the selection of suppliers)?

4.10 Did stock-outs occur of new bednets for distribution during previous years? If so, please indicate the year or years when stock-outs occurred and the period of time the stock-out lasted.

4.11 Please fill out the following table (as of the year when ITNs were introduced)—

<table>
<thead>
<tr>
<th>Year</th>
<th>Total population in risk areas</th>
<th>Total number of new bednets distributed by the program</th>
<th>Total number of bednets that were retreated by the program’s staff</th>
<th>Total number of bednets retreated through community-based campaigns (by family members or promoters)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1995</td>
<td></td>
<td></td>
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<td>1996</td>
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<td>2009</td>
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</tbody>
</table>

4.11 Does the country have long-lasting impregnated bednets? If the answer is yes, what year were they introduced, and what is the annual distribution percentage in the country in comparison to the bednets that require constant retreatment?

4.12 Is a systematic procedure in place to monitor whether the families that received the bednets are adequately using them (including retreatment and washing)? If so, please briefly describe and attach official protocols or documents corresponding to said procedures.
4.13 In the event there is no such procedure, were specific studies conducted to evaluate the families’ practices related to the use of bednets? If so, indicate the dates, and if possible, attach the reports corresponding to said studies.

5. Monitoring the progress and achievements of the ITN program

For the 1995–2009 period, please write down the program’s official indicators available from the following list—

NOTE: This is a comprehensive list of indicators recommended by WHO. It is possible that countries do not implement or monitor all the indicators included in the list. Some indicators were obtained from routine information, and others were drawn from specific studies. If an indicator is implemented in the country that is not included in the list, please add it.
<table>
<thead>
<tr>
<th>Indicators</th>
<th>Years</th>
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<tbody>
<tr>
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<td>95</td>
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<tr>
<td><strong>Operational indicators</strong></td>
<td></td>
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<tr>
<td>Dosage</td>
<td></td>
</tr>
<tr>
<td>Coverage</td>
<td></td>
</tr>
<tr>
<td>Residuality</td>
<td></td>
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<tr>
<td>Program’s annual cost</td>
<td></td>
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<tr>
<td><strong>Entomological Indicators</strong></td>
<td></td>
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<tr>
<td>Bite cycle related to the</td>
<td></td>
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<tr>
<td>population’s habits</td>
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<tr>
<td>Bite rate in human beings</td>
<td></td>
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<tr>
<td>Human blood ingestion index</td>
<td></td>
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<tr>
<td>Sensitivity to insecticides</td>
<td></td>
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<tr>
<td>Sporozoite rate</td>
<td></td>
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<tr>
<td>Adult mosquito density</td>
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<tr>
<td><strong>Results</strong></td>
<td></td>
</tr>
<tr>
<td>Total number of persons</td>
<td></td>
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<tr>
<td>using ITNs</td>
<td></td>
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<td>Number of persons that</td>
<td></td>
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<tr>
<td>live in homes where ITNs</td>
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<tr>
<td>are used</td>
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<tr>
<td>Percent of children under</td>
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<td>five in risk areas who</td>
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<tr>
<td>sleep under bednets</td>
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<tr>
<td>Percent of pregnant women in</td>
<td></td>
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<tr>
<td>risk areas who sleep under</td>
<td></td>
</tr>
<tr>
<td>bednets</td>
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<tr>
<td>Parasitemia index in areas</td>
<td></td>
</tr>
<tr>
<td>where bednets are used</td>
<td></td>
</tr>
<tr>
<td>Parasite rate among children in</td>
<td></td>
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<tr>
<td>endemic areas where bednets are</td>
<td></td>
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<tr>
<td>used</td>
<td></td>
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<tr>
<td>Splenic index in endemic</td>
<td></td>
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<tr>
<td>areas</td>
<td></td>
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<tr>
<td>Morbidity rate in protected/</td>
<td></td>
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<tr>
<td>intervention areas using bednets</td>
<td></td>
</tr>
<tr>
<td>Mortality rate in protected/</td>
<td></td>
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<tr>
<td>intervention areas using bednets</td>
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</tbody>
</table>

END OF INSTRUMENT
Instrument 3: Collection of Information on Residual Household Spraying

1. General Information

Country: ________________

Name of consultant who collects the information: ________________

E-mail: ________________

2. Previous research/preparation and program startup

2.1 Was a stratification of the population at risk conducted based on disease burden and transmission epidemiology? If the answer is yes, please briefly describe the procedures that were implemented and the results obtained. Attach the respective reports if available.

2.2 Were the vector’s habits studied and verified? If the answer is yes, please briefly describe the studies that were carried out, the year they were conducted, and the main results. If reports are available, please obtain copies thereof and attach them.

2.3 Was the susceptibility to prospective insecticides verified before selecting the insecticide(s) that yielded the best results? If the answer is yes, briefly describe the process that was followed.

3. Program launch and use of insecticides

3.1 When was the program officially launched?

3.2 Was the program launched in the entire endemic region or in phases? Please describe, and if it was implemented in phases, describe the reason for doing so (e.g., cost, staff scarcity, etc.) and the estimated number of households/population covered during each phase.

3.3 What insecticide is currently used for spraying? If several, please list them.

3.4 Were different insecticides used since 1995 and up to this date? If so, please list the insecticides, and if any of them is no longer used, please briefly describe the reasons behind this decision.

3.5 What process is implemented in the country to purchase insecticides?

3.6 Did stock-outs of insecticides used for spraying occur in previous years? If so, please write down the year or years when stock-outs occurred and the period of time the stock-out lasted.
4. National (or state/departmental/municipal) guidelines for residual indoor spraying

4.1 According to the guidelines, in what cases should residual indoor spraying be applied and how frequently?

4.2 Who is in charge of spraying?

4.3 Does spraying have any cost for the population? If the answer is yes, what is the cost per household?

4.4 Are residual indoor spraying services available in the private sector? If the answer is yes, is there any information concerning the estimated percentage of households in risk areas that engage services from the private sector? If the answer is yes, write down the percentage for each year since the intervention began.

**NOTE:** In addition to the preceding information, please submit to the attention of Walter Flores the national guidelines and protocols for residual household spraying.

5. Monitoring the progress and achievements of the residual household spraying program

For the 1995–2009 period, please write down the program’s official indicators available from the following list—

**NOTE:** This is a comprehensive list of indicators recommended by WHO. It is possible that countries do not implement or monitor all the indicators included in the list. Some indicators stem from routine information and others were drawn from specific studies. If an indicator is implemented in the country that is not included in the list, please add it.
## Annex A: Data Collection Instruments

### Operational indicators
- Dosage
- Coverage
- Timeliness
- Residuality
- Condition of equipment used in the program
- Program’s annual cost

### Entomological indicators
- Indoor daytime napping
- Bite rate in human beings
- Human blood ingestion index
- Reproduction rate
- Sporozoite rate
- Sensitivity to insecticides
- Adult mosquito density

### Results
- Total number of sprayed households
- Total number of persons who live in sprayed households
- Parasitemia index in spray-protected area
- Parasite rate among children within endemic areas
- Splenic index in endemic areas
- Morbidity rates in spray-protected/intervention areas
- Mortality rates in spray-protected/intervention areas

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**END OF INSTRUMENT**
Instrument 4: Collection of Information on Timely Diagnosis

1. General Information

Country: _________________

Name of consultant who collects the information: _________________

E-mail: _________________

2. Microscopic diagnosis

2.1 Please fill out the following table with official information—

<table>
<thead>
<tr>
<th>Year</th>
<th>Total number of suspected malaria patients reported</th>
<th>Total number of smears examined</th>
<th>Total number of positive smears</th>
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<tbody>
<tr>
<td>1995</td>
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<td>2009</td>
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</table>

2.2 What facilities or regions carry out microscopic tests? Please describe the area and population.

2.3 Did a study that estimate the average time elapsed between the thick blood smear and the delivery of test results in endemic areas? If the answer is yes, include the estimated time (in hours).

2.4 Is there a cost for patients (copayment) for microscopic tests at public network facilities? If the answer is yes, what is the cost per diagnosis that must be paid by the patients? (in USD)

2.5 Are microscopic tests carried out in the private subsector? If the answer is yes, is there an estimate of the total number of tests carried out in this subsector per year? Please include information for the years this information is available.
2.6 Is a system in place to monitor the quality of microscopic diagnosis in the public network? If so, please describe it in detail. If a document is at hand that explains the system, please attach it.

3. Rapid tests

3.1 In what month and year were the standards/guidelines for rapid tests introduced?

3.2 In what month and year did the application of rapid tests begin?

3.3 According to national regulations and protocols, who must apply rapid tests, and in what cases?

3.4 In what areas or localities are rapid tests carried out?

3.5 Is there a cost for the patients (copayment) for rapid test diagnosis? If the answer is yes, what is the cost per diagnosis? (USD equivalent)

3.6 Are rapid tests carried out in the private subsector? If the answer is yes, is there an estimate of the total number of tests carried out in this subsector per year? Please include information for the years that this information is available.

3.7 What process is implemented in the country to purchase rapid tests (including the selection of suppliers)?

3.8 Please fill out the following table (starting as of the year when rapid tests were introduced)—

<table>
<thead>
<tr>
<th>Year</th>
<th>Unit price paid for rapid tests (USD)</th>
<th>Total number of rapid tests purchased</th>
<th>Total number of rapid tests applied</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</tbody>
</table>

3.9 What were the funding sources for each year that rapid tests were purchased? (e.g., ministry of health budget, international cooperation, etc.)

3.10 Did stock-outs of rapid tests occur in previous years? If so, please indicate the year or years when stock-outs occurred and the period of time the stock-out lasted.

3.11 How are rapid tests distributed, particularly in remote areas?

3.12 Is the consistency between rapid tests results and microscopic diagnosis evaluated? If the answer is yes, what is the approximate percentage of rapid tests submitted to microscopic diagnosis?
3.13 Are rapid tests also included in the positive smear indicator?
3.14 Is a system in place to monitor the quality of rapid test use? If so, please describe it in detail. Is there a document that explains the system? Please attach it. Also indicate if the monitoring system reaches the private subsector.

3.15 What are the national regulations for distribution, transportation, and storage of rapid tests? Please list them.

3.16 Is a system or mechanism in place to monitor compliance with distribution, transportation, and storage regulations? If the answer is yes, describe the system or mechanism that is implemented and indicate if it also reaches the private subsector.

3.17 Is a staff training and supervision program in place for personnel who apply rapid tests? If the answer is yes, please describe the program in detail, the activities it carries out, and the results obtained. If there is written official documentation, please attach it.

END OF INSTRUMENT
ANNEX B: INTERVIEW GUIDELINES FOR KEY INFORMANTS

Interview: Coordinator of AMI-RAVREDA at the Regional Level (PAHO)

General Information

Respondent’s name:

Current position:

Brief description of the respondent’s relationship and functions within the coordination efforts of AMI-RAVREDA at the country level and years of experience in this area:

Date of interview:

Role played by technicians and authorities within AMI-RAVREDA

How and with what individuals are the plans and activities supported by AMI-RAVREDA defined? Please describe.

Who and how are the monitoring and evaluation activities for AMI-RAVREDA’s work plans carried out? Please describe.

NOTE FOR INTERVIEWER: If the respondent mentions the local authorities as key participants in the planning and implementation activities, ask the following question: What is the relevance of the national authorities’ involvement in network activities?

Country support modalities and strategies

What are the main support modalities that AMI-RAVREDA provides to the countries? (e.g., financing of staff members, scholarships for researchers, purchase of supplies and medications for studies, etc.)

Do you have information or any opinion with respect to the success of these modalities; are some of them more successful than others? If the answer is yes, please give concrete examples.

Are there any concrete implementation strategies that AMI-RAVREDA has implemented in the country? (e.g. workshops and capacity development processes as well as information for authorities and technicians of the malaria program, the publication of policy briefs and other materials, etc.)

Do you have any information or any opinion with respect to the success of these modalities; are some of them more successful than others? If the answer is yes, please give concrete examples.
Results obtained by AMI-RAVREDA at the country level

Several members of RAVREDA informed us that the sensitivity and resistance studies were the main reason behind the countries’ decision to adopt changes in their treatment guidelines and introduce ACT. The difficulty for scientific evidence to exercise an immediate influence on public health policies is well known in the literature. Do you think that other factors were present in addition to the evidence of resistance and sensitivity studies? (e.g., AMI-RAVREDA’s technical and financial support for the countries, the fact that health authorities responsible for treatment guidelines had the technical background and training to understand the relevance of the evidence, etc.)

Through the support of MSH/AMI several diagnostic studies were implemented concerning the supply of antimalarial medicines in the country. A number of suggestions, concrete activities, and plans to improve medicine supply management in the country emerged from these studies. Until now, the advances attained in these activities and plans have been slow and limited in the countries if compared with the rapid changes implemented in terms of treatment guidelines based on the resistance and sensitivity studies. In your opinion, what factors are responsible for these differences?

AMI-RAVREDA’s technical and financial sustainability

AMI-RAVREDA has been characterized for making available high-level technical assistance and financial resources to implement different processes at the country level. In your opinion, is it feasible for the countries to continue working with their own technical and financial resources?

In the event the respondent considers that such feasibility is low, ask the following question: What type of achievements and processes do you think are exposed to greater risk in the event that technical and financial sustainability fail to be ensured?

In your opinion, what types of processes can help promote technical and financial sustainability?

Final comments

Would like to discuss any issues that were not covered in the interview with respect to your experience as national coordinator for AMI-RAVREDA? If the answer is yes, please let us discuss those issues.
Interview: AMI-RAVREDA’s Former Official at the Regional Level (Roberto Montoya)

General Information

Current position:

Brief description of the respondent’s relationship and functions within the coordination of AMI-RAVREDA at the country level, and years of experience in this area:

Date of interview:

Role of technicians and authorities within AMI-RAVREDA

What role did domestic technicians and authorities play within AMI-RAVREDA during the period you worked for the institution?

Support modalities and strategies at the country level

What were the main support modalities that AMI-RAVREDA provided to the countries during the period you worked for the network? (e.g., financing of staff members, scholarships for researchers, purchase of supplies and medications for studies, publications and policy briefs, etc.)

In your opinion, were some of these modalities more successful than others? If the answer is yes, please give concrete examples to illustrate this.

AMI-RAVREDA’s results at the country level

Several members of RAVREDA informed us that the sensitivity and resistance studies were the reason behind the different countries’ decision to adopt changes in their treatment guidelines and introduce ACT. The difficulty for scientific evidence to exercise an immediate influence on public health policies is well known in the literature. Do you think that in this particular case other factors existed besides the evidence stemming from the resistance and sensitivity studies? (e.g., technical and financial support provided by AMI-RAVREDA to the countries, the fact that the health authorities responsible for treatment guidelines had the technical background and training to understand the relevance of such evidence, etc.)

Thanks to the support provided by MSH/AMI, several diagnostic studies were implemented concerning countries’ prevailing antimalarial medicine supply management situation. A number of suggestions, concrete activities, and plans to improve medicine supply in countries stemmed from these studies. Until now, the progress attained in these activities and plans have been quite slow and limited in the countries if compared with the rapid changes that have been implemented in terms of treatment guidelines based on the results of the resistance and sensitivity studies. In your opinion, what factors are these differences attributable to?
AMI-RAVREDA’s technical and financial sustainability

AMI-RAVREDA has been characterized by making available to countries high-level technical assistance and financial resources to implement the different processes. In your opinion, what is the likelihood that these countries can continue this work with their own technical and financial resources?

In the event the respondent considers that the feasibility is low, ask the following question: What type of achievements and processes do you think are at greater risk if technical and financial sustainability fails to be ensured?

In your opinion, what types of processes can help promote technical and financial sustainability?

Final comments

Would like to discuss any issues that were not covered in the interview with respect to your past experience as regional coordinator for AMI-RAVREDA? If the answer is yes, please let us discuss those issues.

Interview A: Technicians/Experts Who Participated in the Countries’ RAVEDRA-Financed In Vivo/In Vitro Studies (Resistance and Sensitivity)

General Information

Respondent’s name:

Current position:

Brief description of the relationship with RAVREDA and years of experience:

Date of interview:

Relevance of resistance and sensitivity studies

Did you participate in some of the resistance and/or sensitivity studies that were carried out in the country with RAVREDA’s support? If the answer is yes, please describe the study or studies in which you participated as well as the role you played.

Were the studies in which you participated published in a scientific journal? If the answer is yes, please provide a complete reference for such publication. In the event it was not published, why was a scientific publication of the study not made? Do you think it is relevant to make a publication of this type? If the answer is yes, why do you consider it relevant?

In your opinion, what is the relevance of the studies in which you participated? Please give examples.
Several members of RAVREDA informed us that the sensitivity and resistance studies were the reason behind the countries’ decision to adopt changes in their treatment guidelines and introduce ACT. The difficulty for scientific evidence to exercise an immediate influence on public health policies is well known in the literature. Do you think that in addition to the evidence stemming from the resistance and sensitivity studies there were also other factors? (e.g., technical and financial support provided by AMI-RAVREDA, the fact that health authorities in charge of treatment guidelines had the technical background and training to understand the relevance of the evidence, etc.)

**Strategies to communicate the evidence to decision makers**

Were you involved in the presentation of the studies’ results to health authorities? If the answer is yes, please explain how the results were presented (technical workshops, research reports, publications, etc.).

To what other actors and sectors were the studies’ results presented?

**Technical and financial support provided by RAVREDA**

What type of technical support did you and your colleagues receive from RAVREDA to carry out the study or studies? Please describe.

Did any other technical assistance activities fail to be implemented that you would have preferred? If the answer is yes, please describe them.

What type of financial support did you and your colleagues receive from RAVREDA to carry out the study or studies? Please describe (purchase of materials, equipment, support to cover researchers’ salaries, etc.).

Were any other financial assistance activities not implemented that you would have preferred? If the answer is yes, please describe them.

**Final comments**

Would like to discuss any other issues that were not covered by the preceding questions with respect to your experience at AMI-RAVREDA? If the answer is yes, please let us discuss such issues.
Interview B: Health Authorities Responsible for Malaria Treatment Guidelines

General Information

Respondent’s name:

Current position:

Brief description of the respondent’s relationship and functions within the department/unit in charge of issuing treatment guidelines and years of experience:

Date of interview:

Factors that influenced the decision to change treatment guidelines

In your opinion, what factors had an influence in the country’s decision to adopt changes in malaria treatment guidelines, particularly in *P. falciparum* cases? (NOTE FOR INTERVIEWER: If the respondent mentions factors in addition to the resistance and sensitivity studies [e.g., the person in charge of the program was a malaria expert, USAID offered funding, etc.], continue asking about these factors and request him or her to provide concrete examples about how these factors influenced the outcome.)

For those respondents who mentioned the results of the resistance and sensitivity studies carried out by AMI-RAVREDA, ask the following question:

The difficulty for scientific evidence to exercise an immediate influence on public health policies is well known in the literature. The particular case of resistance and sensitivity studies and how they influenced the policies and treatment guidelines is unusual. In your opinion, why did they have this relatively rapid and direct effect on treatment policies and guidelines? Please describe the reasons and give concrete examples.

Guideline dissemination and training, and challenges identified during the treatment guidelines change process

Were any difficulties or challenges faced during the process of changing/updating treatment guidelines? If the answer is yes, please describe them and provide concrete examples, and explain how these difficulties/challenges were addressed/overcome (especially those that were resolved).

What were the procedures and strategies followed to disseminate the new guidelines and train new staff? Please describe.

What challenges did you find in the guideline dissemination and training processes? How were these challenges addressed/overcome?
Do any challenges or difficulties still exist up to this date? If the answer is yes, please describe them.

**Support received from AMI-RAVREDA for the treatment guidelines change process**

What technical support did you and your colleagues receive from AMI-RAVREDA to update treatment guidelines? Please describe it.

Were other technical assistance activities not implemented that you would have preferred? If the answer is yes, please describe them.

What financial support did you and your colleagues receive from AMI-RAVREDA to update treatment guidelines? Please describe it (technical/informative workshops, printing the guidelines, communication campaigns, etc.).

Were any other financial assistance activities not implemented that you would have preferred? If the answer is yes, please describe them.

**Final comments**

Would like to discuss any issues that were not covered in the preceding questions, concerning your experience within AMI-RAVREDA? If the answer is yes, please let us talk about those issues.

**Interview C: Health Authorities in Charge of Medicine Supply Management**

**General information**

Respondent’s name:

Current position:

Brief description of the respondent’s relationship and functions within the department/unit in charge of medicine supply:

Date of interview:

**ACT Procurement**

As we are aware, ACT has a higher cost than the medications that were purchased before changing the treatment guidelines.

Did you have any difficulties with the authority that allocates financial resources justifying the purchase of new medications at a higher cost? If the answer is yes, please explain these
difficulties and how they were addressed/overcome. If the answer is no, explain the strategies or justifications that were used so this would not to become a limiting factor.

**Rapid diagnostic tests**

As we are aware, rapid tests constitute new supplies that were recently included in the program. Did you have any difficulties with the procurement, distribution, and quality control of rapid tests? If the answer is yes, please describe those difficulties.

**Progress attained in the plans and activities to improve medicine supply management**

With the support of MSH/AMI, several studies were conducted to diagnose the situation of antimalarial medicine supply management in the country. A number of suggestions, concrete activities, and plans to improve medicine supply management in the country were derived from those studies. *(NOTE FOR INTERVIEWER: Show the activities and plans for the country where the interview is carried out.)*

Could you please tell me about the progress attained to date with respect to each suggestion, plan, and activity? *(NOTE FOR INTERVIEWER: For those activities or plans that are reportedly completed, ask the respondent to provide verification, such as reports, pictures of the new warehouse, etc.)*

If any activities or plans were successfully accomplished, ask the following question: What factors influenced the execution of the plans and activities whose completion you reported? *(e.g., the authorities’ commitment, allocation of specific funds, etc.)* Please give concrete examples.

**Challenges identified in the implementation of plans and activities**

If progress was slow for any plans and activities, ask the following question:

Could you please explain the reasons or limitations that affected the plans and activities whose progress was slow? Please give concrete examples of the limitations. *(NOTE FOR INTERVIEWER: if the respondent mentions any reasons to explain the absence of financing, unavailability of personnel to carry out the plan, or the unwillingness of the authorities in charge of the implementation, etc., ask him or her to provide concrete examples concerning how these factors influence the outcome.)*

Do you believe that AMI/USAID/PAHO/MSH can support the advancement of these issues in any way? If the answer is yes, please give concrete examples.

**Final comments**

Would like to talk about any issues that were not covered by the preceding questions with respect to your experience implementing activities and plans to improve the supply of antimalarial medicines? If the answer is yes, please let us discuss those issues.
Interview D: Authorities in Charge of Allocating Financial Resources (as Well as Other Resources) to the Malaria Control Program and Specifically ACT

General information

Respondent’s name:

Current position:

Brief description of the respondent’s relationship and functions within the department/unit in charge of allocating resources to treat malaria:

Date of interview:

Priority level of malaria control in the public budget

Please describe briefly the methodology and the people who make decisions with respect to the amount of financial resources allocated to the malaria program (e.g., the finance ministry, based on the historical budget, or an allowance ceiling, etc.).

In your opinion, are the resources allocated to the malaria program sufficient? If the answer is yes, explain why you think so. If the answer is no, please explain why these resources are insufficient.

Show the respondent the figure/table that details the resources allocated to the program between 1995 and 2009, and ask him or her the following question: In your opinion, what factors explain the funding trend of the malaria program?

Effects of the introduction of ACT and rapid tests into the budget

The cost of the medications in the new treatment regimen is higher than the cost of the medicines that were previously purchased. How was the budget affected by the purchase of more expensive medications?

Rapid diagnostic tests are supplies that did not exist in previous years. How was the budget affected by the purchase of rapid tests?

Both ACTs and rapid tests are supplies that did not exist prior to the program’s implementation. How were the resources for the malaria program negotiated/planned with the central authorities of the ministry of health?
Current challenges presented by the allocation of resources (e.g., financial, technical capacity, deficit of human resources) for the malaria and ACT programs

In your opinion, what are the current challenges presented by the allocation of resources for the malaria program, and specifically for ACT? NOTE FOR INTERVIEWER: Inquire about each challenge mentioned by the respondent, and ask him or her to provide concrete examples.

Do you believe AMI/USAID/PAHO/MSH can provide support to address the aforementioned challenges? If the answer is yes, please provide concrete examples.

Final comments

Would like to talk about any issues that were not covered by the preceding questions with respect to your experience with the allocation of resources for the malaria program? If the answer is yes, please let us discuss these issues.

Interview E: Technician in Charge of AMI-RAVREDA at the Country Level

General information

Respondent’s name:

Current position:

Brief description of respondent’s relationship and functions within the coordination of AMI-RAVREDA at the country level and years of experience in this area:

Date of interview:

Role of technicians and national authorities within AMI-RAVREDA

How and with what individuals are the plans and activities supported by AMI-RAVREDA defined? Please describe.

Who carries out and how are monitoring and evaluation activities carried out within AMI-RAVREDA’s work plans? Please describe.

NOTE FOR INTERVIEWER: If the respondent mentions the local authorities as key actors in the areas of planning and implementation, ask the following question: What is the relevance of national authorities’ involvement in the network’s activities?

Support modalities and strategies at the country level

What are the main support modalities that AMI-RAVREDA provides to the countries? (e.g., financing of staff members, scholarships for researchers, purchase of supplies and medications for studies, etc.)
Do you have any information or opinion concerning these modalities; are some of them more successful than others? If the answer is yes, please give concrete examples.

Has AMI-RAVREDA implemented any concrete implementation strategies in the country? (e.g., workshops and capacity development processes, information for authorities and technicians of the malaria program, publication of policy briefs and other materials, etc.)

Do you have any information or opinion with respect to these modalities; are some of them more successful than others? If the answer is yes, please give concrete examples.

Results obtained by AMI-RAVREDA at the country level

Several members of RAVREDA informed us that the sensitivity and resistance studies were the reason behind the changes implemented by the countries with respect to treatment guidelines and the introduction of ACT. The difficulty for scientific evidence to exercise an immediate influence on public health policies is well known in the literature. Do you think that in addition to the evidence obtained from the resistance and sensitivity studies there were other factors? (e.g., technical and financial support provided by AMI-RAVREDA to the countries, the fact that health authorities responsible for treatment guidelines had the technical background and training to understand the relevance of the evidence, etc.)

Through the support provided by MSH/AMI, several studies were conducted to diagnose the situation of antimalarial medicine supply management in countries. A number of suggestions, concrete activities, and plans to improve countries’ medicine supply management were derived from those studies. Until now, the progress attained by these activities and plans in the countries has been quite slow and limited if compared with the rapid changes implemented in treatment guidelines based on the results of the resistance and sensitivity studies. In your opinion, what factors are these differences attributable to?

Final comments

Would like to talk about any issues that were not covered by the preceding questions with respect to your experience as national coordinator of AMI-RAVREDA? If the answer is yes, please let us discuss those issues.
ANNEX C: INFORMATION REQUIRED TO ESTIMATE THE IMPACT OF ACT ON MALARIA

As described in the “Literature Review” section, sufficient documentation exists about the relationship between the introduction of ACT and the reduction of malaria cases in different regions around the world. This information aroused interest in implementing studies to determine the impact of ACT on malaria control. This is an enormous task because it implies separating the relative effects of ACT from those of the other control interventions implemented by countries (e.g., ITNs, timely diagnosis, residual indoor spraying).

In recent years, the publication of studies that use mathematical and/or epidemiological models to study transmittable diseases, including malaria, has increased dramatically.\(^9^5\) Given the complexity of \textit{P. falciparum}’s transmission cycle, recent studies used models to predict the epidemiology of such transmission.\(^9^6\) These models are necessary to forecast the epidemiological results generated by the different malaria control strategies, including ACT.\(^9^7\)

Among the models that were published, there are at least three groups of variables: (a) malaria transmission cycle, (b) treatment provided to the population, and (c) vector behavior. Each of these components is in turn disaggregated into subvariables. For example, the structure of one of the models that was published is summarized here—\(^9^8\)

Transmission in humans:
The transmission of parasites in humans and among the mosquito population was structured based on a compartmental and deterministic model. Given the absence of treatment, the human population in each age group of interest is situated in three different states: susceptible, latent, or infected. The model requires information about mosquito density, mosquito bite rate in humans, and prevalence of infections among the mosquito population. In addition, the latency period is divided in two different stages, and the infectious period is divided in four different stages. These stages respond to the trends observed in longitudinal studies of malaria transmission.

Stratification in accordance with age groups and the heterogeneity of exposure:
The different population groups are stratified. In this model, which is used as an example, stratification was carried out in three groups (0–4 years, 5–14 years, and older than 15 years). These groups are once again stratified in connection with the level of exposure to mosquito bites. The model also estimates the population’s immunity levels and the proportion of the population that is infected and will present symptoms. The model adjusts the levels of exposure to mosquito bites in relation to age, assuming that adults have a larger physical area exposed to bites. Based on this information, the contribution of each age group to maintaining the reservoirs is estimated.

Vectors’ dynamics:
Transmission among mosquitoes responds to the changes in infection prevalence among humans. Mosquitoes are born in a susceptible state, and if they become infected, they enter a latent state before they have the capacity to infect humans.

Table C-1 presents an example of some of the variables that must be used to apply the model described.

Table C-1. Examples of Variables Used in ACT Impact Studies

<table>
<thead>
<tr>
<th>Transmission cycle</th>
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</thead>
<tbody>
<tr>
<td>Ratio of female mosquitoes to humans</td>
</tr>
<tr>
<td>Feeding events with human blood per mosquito per day</td>
</tr>
<tr>
<td>Probability that human blood is in the infectious stage as a result of each infected mosquito bite</td>
</tr>
<tr>
<td>Duration of the latency period in mosquitoes (as of the ingestion of gametocytes until the appearance of sporozoites in salivary glands)</td>
</tr>
<tr>
<td>Mosquitoes’ life span</td>
</tr>
<tr>
<td>Proportion of human population in the high-exposure stratum that receives X proportion of mosquito bites</td>
</tr>
<tr>
<td>Percentage of all mosquito bites received by the human population in the high-exposure stratum</td>
</tr>
<tr>
<td>Mean duration of infectious period in humans who do not receive treatment</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Variation by age groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of the infectious period in humans who do not receive treatment, disaggregated by age groups</td>
</tr>
<tr>
<td>Probability of transmission of an infected human without treatment to a mosquito through a bite</td>
</tr>
<tr>
<td>Level of relative infection in each age group</td>
</tr>
<tr>
<td>Relative rate of mosquito bites in each age group related to the exposed area of the human body</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Treatment</th>
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</thead>
<tbody>
<tr>
<td>Probability of developing symptoms upon being infected</td>
</tr>
<tr>
<td>Duration of symptomatic period</td>
</tr>
<tr>
<td>Proportion of symptomatic cases treated with antimalarial medicines</td>
</tr>
<tr>
<td>Proportion of treatments corresponding to ACT</td>
</tr>
<tr>
<td>Duration of gametocytemia in infections treated with ACT</td>
</tr>
<tr>
<td>Duration of gametocytemia in infections treated without ACT</td>
</tr>
<tr>
<td>Relative infection capacity in individuals treated with ACT compared with untreated cases or those treated without ACT</td>
</tr>
<tr>
<td>Efficacy level of medications other than ACT (therapeutic failure before the introduction of ACT)</td>
</tr>
<tr>
<td>Presumptive treatment rate among the general population by age groups</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Demographic variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>Life expectancy</td>
</tr>
<tr>
<td>Mortality rate by age group</td>
</tr>
<tr>
<td>Proportion of total population for each age group</td>
</tr>
</tbody>
</table>


In addition to the aforementioned variables, a study that intends to estimate the impact of ACT must also include a description of the prevailing situation before the introduction of ACT. Table C-2 presents an example of the variables included in the characterization of the situation prior to ACT introduction.
Table C-2. Examples of Variables Used to Characterize the Situation before ACT Introduction

<table>
<thead>
<tr>
<th>Region of the country</th>
<th>Height in meters and population distribution by age groups</th>
<th>Positive smears (%)</th>
<th>Prevalence of symptomatic infected persons among the population surveyed (% of population)</th>
<th>Gametocyte density</th>
<th>Use of antimalarial medicines 14 days prior to the survey (%)</th>
</tr>
</thead>
</table>


Note: The information was obtained from parasitemia surveys at the community level.

Several published studies use the values obtained from other previously published studies because of the unavailability of local information for some variables. However, some of these variables, such as the vectors’ dynamics, are very specific to the different contexts and necessarily require entomological information generated at the local level.

The possibility of using mathematical models is undoubtedly an important tool. However, the identification and collection of reliable data, as well as its calibration in the models, constitutes an enormous challenge, given that the accuracy of the models’ estimations depends on the quantity and quality of available data.  

The summarized description of one of the models that was published and the table with the variables that these studies must include is relevant information to identify whether the countries supported by AMI-RAVREDA have the required information to carry out studies like the one that was previously described and possess the reliability and certainty that is required in these cases. During this study it was evidenced that most of the information that is usually required for such a significant study is not available in the countries. A country may have information corresponding to small geographical areas (district, province, and municipality) related to the above-described variables. Conducting a study using such information would be a first step. However, the findings of these studies cannot be extrapolated to the rest of the country and much less to the rest of the region.  


Impact of ACT for Malaria in Various Countries and Implications for the Countries of the Amazon Basin:
Final Report