
External Evaluation of the Amazon Malaria
Initiative (AMI) and the Amazon Network for the
Surveillance of Resistance to Antimalarial Drugs
(RAVREDA)

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1. Acronyms and abbreviations

AMI	Amazon Malaria Initiative
ACT	Artemisinin-based combination therapy
CIDEIM	Centro Internacional de Entrenamiento e Investigaciones Médicas
ICEMR	International Centers of Excellence for Malaria Research
INS	Instituto Nacional de Salud (Colombia)
IRS	Indoor residual spraying
ITN	Insecticide-treated bed net
LLIN	Long-lasting insecticidal mosquito net
MSH	Management Sciences for Health
NCM	Nitrocellulose membrane
PAHO	Pan American Health Organization
PAMAFRO	Global Fund financed project for malaria control in the cross border areas of 4 countries (Colombia, Ecuador, Peru and Venezuela) of the Andean Region.
QC	Quality control
QA	Quality assurance
RAVREDA	Amazon Network for the Surveillance of Antimalarial Drug Resistance
RDT	Rapid diagnostic tests
RTI	Research Triangle Institute
SNEM	National Service for Malaria eradication
USAID	United States Agency for International Development
USP	United States Pharmacopeia
WHO	World Health Organization

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2. Executive summary

This is the report of an external evaluation of the following coordinated initiatives for the period 2007-2010:

The [Amazon Malaria Initiative](#) (AMI) includes Bolivia, Brazil, Colombia, Ecuador, Guyana, Peru, and Suriname. It is a [United States Agency for International Development](#) (USAID) supported initiative funded under the United States [President's Malaria Initiative \(PMI\)](#), and managed from USAID/Washington from 2001 to 2008 and then by [USAID/Peru](#), as part of its South American Regional Infectious Diseases Program (SARI).

The Amazon network for surveillance of resistance to antimalarial drugs (Red Amazónica de Vigilancia de la Resistencia a los Antimaláricos or [RAVREDA](#) (from its Spanish acronym) is a network of Amazon countries' national malaria control programs coordinated by the [Pan American Health Organization](#) (PAHO) and also supported by USAID. At the onset, this network emphasized support to participating countries to revise their antimalarial drug treatment policies based on scientific evidence obtained through clinical efficacy trials in sentinel sites. It also promotes the implementation of malaria control policies based on that information.

As progress towards those objectives was achieved, AMI supported a more comprehensive approach to malaria prevention and control, as defined by its expected results: 1) Reliable and standardized surveillance information on malaria drug resistance and vector control used to monitor trends and target effective control efforts; 2) Diagnosis of malaria improved; and 3) Tools and approaches developed, adapted, tested in local settings, and disseminated.

In order to support participating countries, AMI amalgamated technical partners: the Pan American Health Organization; USAID/Latin America and the Caribbean (LAC) and USAID/Peru; the United States [Centers for Disease Control and Prevention](#) (CDC); the [United States Pharmacopeia's](#) Drug Quality Initiative (USP/DQI); [Management Sciences for Health](#) (MSH); [Links Media](#), and the [Research Triangle Institute](#) (RTI), which just recently joined as a partner in the Initiative.

Technical partners provide their expertise within a subregional approach to promote evidence based decision-making, and foster south-to-south collaboration to implement the following lines of work (participating partners in each line of work indicated in parenthesis):

1. Surveillance of resistance to antimalarial drugs in vivo and in vitro, using standard protocols and identifying molecular markers of resistance (PAHO/WHO and CDC).

2. Improvement of drug procurement mechanisms; use of formulations based on best treatment practices, dispensation and adherence. Promoting the design and implementation of a supervision strategy for diagnosis and treatment (PAHO and MSH).
3. Use of quality antimalarial drugs. Promote policies for drug evaluation, and provide equipment for drug quality testing (minilabs) (PAHO and USP).
4. Access to quality diagnosis. Promoting the standardization and improvement of malaria diagnosis by developing a QC/QA system for microscopy, rapid diagnostic tests, and protocol development to characterize *Plasmodium falciparum* strains regarding HRP2 and HRP3 presence (PAHO, CDC, and MSH).
5. Entomology and integrated vector control. Institutionalization of high impact vector control interventions. Includes tool development to disseminate information on the selected control strategy; carry out agreed upon entomological activities; coordinate the development of routines for analysis and dissemination of entomological information; develop training on and discussion of the use of CDC bottles and colorimetric tests, as well as the taxonomy agenda; promote the use of alternative methods for human bait captures; testing of window traps; and document experiences of long-lasting insecticide nets (LLINs) and develop techniques for measuring residual insecticides and longevity of the LLINs (PAHO, CDC, and RTI).
6. Epidemiology and information systems and information management. Implementing routines for information analysis and use; carrying out the analysis plan of main indicators and parameters for the management of diagnosis, treatment and vector control (PAHO and CDC).
7. Communications and dissemination. To identify countries that conducted a larger number of studies and had more experiences supported by AMI, and assist in the publication of their results. To participate in the development of digital versions of tutorials on strategies promoted by AMI addressed to public health workers (PAHO/Links Media).

Purpose of the evaluation

The results of this evaluation will be used to assess the effectiveness of the approach used in the design and evolution of AMI in reference to the achievement of its expected results, while responding to country and regional needs; and to guide AMI management and implementation through 2015.

Due to the importance of antimalarial drug resistance in the Region, and the need to implement drug treatment policies accordingly, this evaluation will be used to determine whether to expand the scope

of the Initiative to include surveillance of antimalarial drug resistance, which was the focus of RAVREDA, to Central America.

Participants in this evaluation had to verify that activities planned and implemented contributed to the expected results and lines of work agreed upon, and collect information on improvements and progress achieved in each line of work.

The evaluators were to visit Brazil, Colombia and Ecuador; they also obtained information on other AMI countries through data, records, norms, regulations, official guidelines, and other documents used in program revisions and implementation that provide evidence of institutionalization.

Accomplishments within AMI/RAVREDA

- **The creation of a monitoring system for antimalarial drug efficacy.** Data provided by this system was used to devise evidence-based antimalarial drug policies (with special emphasis on treatment of uncomplicated falciparum malaria) in the countries of the Amazon subregion. As a result, each country modified its official malaria treatment regimens to more effective combination therapies; drug efficacy monitoring continues through the surveillance network, in search of new forms of resistance. In Ecuador for example, following efficacy studies in humans carried out between 2002 and 2006, a Coartem® became the treatment of choice for uncomplicated falciparum malaria; the policy was fully implemented throughout the country in 2007.
- **Countries have reliable software and personnel trained in its use.** Standardization of the information system for malaria surveillance, treatment, drug resistance, and vector control has been achieved. The software is available at the central level (Ministry of Health) and/or at the departmental level, and is used to monitor trends and to target disease control efforts more effectively.
- **Laboratory diagnosis of malaria has improved** through the use of guidelines and recommendations on diagnostic quality control and quality assurance (QC/QA) systems developed within the Initiative. Training to improve the diagnostic proficiency of microscopy technicians was implemented; and proficiency testing was introduced as a component of diagnostic QC/QA systems to improve the efficiency of diagnostic performance monitoring.
- **Tools and approaches for malaria control, diagnosis and prevention were developed, adapted, tested in local settings, and disseminated.** Studies of drug efficacy allowed for the selection of effective treatments, which combined with the aforementioned improvements in diagnosis and

increased access to rapid diagnostic tests (RDT), facilitated early diagnosis and treatment of human cases.

Vector control by environmental management, use of larvicides and indoor residual household spraying were the strategies for vector control. These, together with insecticide impregnated bed nets, were the basic tools available to combat malaria. All or some of the above are in use in the countries of the Amazon basin; protocols are jointly discussed in order to select the best strategy. An insecticide resistance surveillance program has been established in most countries, and guidelines for vector and malaria control have been developed. Policies and strategy documents were written for the implementation of a national bed net distribution program that includes a monitoring component.

- **Antimalarial drug quality.** Sustainable systems for ensuring the availability of high quality antimalarial medications were adopted, and proper quality assurance and drug quality control systems for medicines used in national malaria control programs were strengthened. The initiative has contributed to the improvement of the official drug control laboratory in each AMI partner country by a) providing guidance on good laboratory practices and systems for quality management, as well as training in analytical techniques, and the provision of analytical instrumentation; b) implementing, through the use of portable minilabs, a decentralized method to monitor and control drug quality in endemic area conditions (storage and distribution); and c) documenting shortcomings in quality assurance systems.

Suitability/success of AMI in increasing the efficiency and efficacy of USAID's investment in the fight against malaria

Personnel at all levels of the malaria control programs, health authorities and collaborating research and training institutions in the three countries visited recognized the very important contribution of AMI/RAVREDA to the improvement of malaria control in their respective country. This appreciation was shared by the Military Health Service in Colombia, which deals with malaria in war zones and isolated areas that often are the main foci of drug resistance. The success of the Initiative has resulted from modest investments. It can, therefore, be concluded that the investment in AMI/RAVREDA has been both effective and efficient in general terms. In addition, national authorities gratefully recognized the support of PAHO personnel in the countries, for their support in developing proposals to the Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM or Global Fund). Five-year proposals from each of the three countries visited were approved by the Global Fund.

Is the AMI model effective and replicable?

Without exaggeration, and at least in terms of improvement of antimalarial treatment and access to diagnosis and treatment, AMI/RAVREDA has achieved more substantial and likely more sustainable results than in the previous 30 years of trying to cope with antimalarial drug resistance in South America. The manner in which countries joined and maintained their participation in the Initiative, as well as the willingness of the countries of Central America to become part of it, provide a strong indication that the model is replicable.

Value added by the AMI model

A map of sentinel sites of the AMI/RAVREDA surveillance system for antimalarial drug resistance illustrates just how such a network can perform effective surveillance of the parasite's response to antimalarial drugs in different epidemiological situations. This could never have been possible in previous programs. Within the AMI model it became possible due to a collaborative approach to management and implementation by USAID-Peru, USAID and PAHO in Washington DC, the AMI /RAVREDA Coordinator, and country staff. Besides widening the field of observation and the exchange of information, the work of the AMI/RAVREDA coordinator, and periodic stakeholders meetings provided a rapid and efficient way to analyze and validate results.

Areas that AMI/RAVREDA should address in upcoming years

Drug resistance monitoring should continue, and explore the possibility of using fewer test subjects and/or combining results of different testing sites using the WHO protocol.

Microscopy diagnosis strengthening should also continue. The results of efforts to develop a QC/QA system that is effective, accurate, and timely have been insufficient. Laboratories should be further strengthened to improve staff competency and performance in malaria diagnosis.

Quality of medicines: activities in this area should continue to provide guidance on quality management systems and training in pharmacopeial techniques; to implement methods to monitor and control conditions in which antimalarial drugs are stored and distributed in endemic areas; as well as to increase awareness of these issues as a matter of patient safety.

Epidemiological surveillance. A review of information systems and data analysis should be conducted to incorporate geographical information that allows geographical analysis of case distribution, as well as epidemiological studies in localities presenting case clusters. In addition, stratification of problem areas (or areas where outbreaks occurred) based on ecological and social characteristics should be carried out.

Review of guidelines for entomological studies to ensure a clear distinction between:

- completion of basic data on vector distribution and behavior, after collecting all existing information on the subject;
- assessment of the contribution of different interventions in use towards the control of transmission, in terms of time and space;
- monitoring the continued efficacy of vector control measures in use;
- contribution to the epidemiological investigation of localities and problem areas, taking into account the possible changes from the time of onset of cases and the time of investigation;
- work on these different points will require prioritizing based on degree of urgency.

Integration of epidemiology and entomology in addressing problems or impending risks:

- There is a need to establish a strong epidemiological/entomological surveillance system capable of detecting the potential spread of *Plasmodium falciparum* throughout the Amazon area.
- Monitoring is also needed to detect the emergence and spread of the mosquito *Anopheles darlingi* in the Amazon areas of Colombia and Ecuador, which may precede the epidemic spread of *P. falciparum*. Emphasis should be on potential points of entry for *P. falciparum* and/or *An. darlingi*, such as those with important boat or land traffic within infected areas; new settlements; points of attraction for the exploitation of resources or for laborers, and others where sentinel posts could be established.
- GPS analysis should be incorporated into epidemiological and entomological surveillance, and maps developed on vector resistance to insecticides;
- Quality assurance of the techniques being implemented needs to be addressed.

Review approaches to the use of diagnostic facilities for disease case management, including:

- optimizing case detection, concentrating on passive case detection, locality investigations and fever surveys in the study of outbreaks;
- addressing the management of malaria-negative cases by:
 - o broadening the competence of microscopy technicians to identify other parasites and perform other simple diagnostic tests, such as tuberculosis, as is being done in Cruzeiro do Sul, Brazil, as well as monitoring quality assurance and performance evaluation of these technicians.
 - o improving the advice to patients and their acceptance within the referral system (hospitals or health centers)
 - o Review approaches to case management for marginalized and illegal populations.

Development of realistic guidelines for various programmatic levels, including a review of existing manuals as sources of material. It is necessary to clearly state the tasks to be performed at each

operational level, and review training courses and materials for all technical personnel.

Background

The III Meeting of the Network for Surveillance of Emerging Infectious Diseases in the Amazon Countries laid the cornerstone on which AMI and RAVREDA were established. The meeting took place in Salvador, Bahia, Brazil, in March 2001,^a with the participation of public health professionals, representatives of international institutions and governmental cooperation agencies. Antimalarial drug policy and the then current state of drug resistance in participating countries were analyzed. Within the framework of Roll Back Malaria, emphasis was placed on the importance of early diagnosis and timely treatment of the disease, and the need for strategies and implementation of multiple prevention activities based on local requirements; and the need for coordination among distinct groups and organizations involved in prevention and control. Additionally, the importance of conducting operational research to find ways to clear bottlenecks observed in several national programs was underlined.

A summary of the epidemiology of malaria in the Americas showed that malaria transmission occurred in 21 countries of the Region, all of which had programs to prevent and control the disease. Due to the importance of monitoring antimalarial drug resistance in the Region, information on the experience on the subject in other continents was considered useful. Information was also shared on activities in East African countries, and USAID supported activities in the Mekong, Southeast Asia Region.

Countries of the Amazon region reported on their national situations with regard to antimalarial drug resistance and drug treatment policies. In turn, each country committed to jointly undertake monitoring of resistance and to use the information thus generated as the basis for rational malaria treatment policies. The U.S. Agency for International Development, the World Health Organization, and PAHO were committed to supporting those efforts. Following are the recommendations of the meeting.

Regarding malarial drug policy in the Amazon countries—monitoring drug resistance

1. To countries

Each country will have a national coordinator to monitor drug resistance; a common protocol developed by PAHO/WHO and adapted to the Region of the Americas will be used to monitor *Plasmodium vivax* and *P. falciparum* resistance to drugs. Databases for resistance studies will be shared among all countries, which will discuss and agree on their structure (Brazil already has a database and will share it

^a <http://www.paho.org/english/ad/dpc/cd/reunion2001.htm>).

with the rest of the countries for analysis and potential use); Steering Committees at the national and subregional levels will be created to supervise the studies and sentinel sites. Tests will be monitored in order to establish the efficacy of antimalarial drugs.

2. To PAHO and WHO (Roll Back Malaria)

That they support the organization of the national and subregional networks for monitoring antimalarial drug resistance.

3. To the U.S. Agency for International Development

That it provides financial support so that the activities of the network can be undertaken.

As a result of the meeting, the Amazon Network for the Surveillance of Antimalarial Drug Resistance (RAVREDA) was established. At that time, the Network was considered part of the Roll Back Malaria (RBM) Initiative, as well as a partnership that included Bolivia, Brazil, Colombia, Ecuador, Guyana, Peru, Suriname, and Venezuela, with French Guiana as observer. Technical support to the network was going to be provided by PAHO and WHO. The network's goal was to continuously monitor antimalarial drug resistance, and promote the implementation of malaria control policies based on surveillance information.

3. Statement of work

Purpose of the evaluation

This is an external evaluation of two independent but closely coordinated initiatives. First, the [Amazon Malaria Initiative](#) (AMI), is a [USAID](#) program funded under the [President's Malaria Initiative \(PMI\)](#), and managed from [USAID/Peru](#), as part of its South American Regional Infectious Diseases Program (SARI). The second is a network of national malaria control programs coordinated by the [Pan American Health Organization](#) known as the Amazon Network for the Surveillance of Resistance to Antimalarial Drugs ([RAVREDA](#)).

The results of the evaluation will be used to assess the effectiveness of the approach used in the design and evolution of AMI in reference to the achievement of its expected results while responding to country and regional needs; and to guide AMI management and implementation through 2015.

Therefore, in respect of AMI, the evaluation would have to,:

1. Assess AMI's suitability and success in increasing the efficiency and efficacy of USAID investments in the fight against malaria by answering the following questions:
 - a. Is the AMI model effective? (Does it achieve results?)
 - b. Is the AMI model efficient? (Does it make good use of resources?)

- c. Is the AMI model replicable in other regions and/or to address other health problems?
 - d. What is the value added by the AMI model?
 - e. What are the results achieved by AMI vis-à-vis those expected (see below)?
 - f. Has AMI served to leverage resources from other sources (e.g. national governments, the Global Fund)?
2. Assess the rationale, quality, outcomes and results of activities not originally planned or expected, but implemented by technical assistance partners in connection to or as a consequence of planned activities and work in the field.
 3. Discuss the current situation and future of AMI around the following questions:
 - a. What has worked well within the Initiative?
 - b. Who else will be supporting the Initiative?
 - c. What challenges or obstacles remain that require further tuning?
 - d. Has AMI evolved to build effectively on previous progress, and has it responded adequately to changes in the malaria context at regional and country levels?
 - e. What are the areas in malaria prevention and control (and other factors related to or influencing prevention and control) that AMI should address in upcoming years?
 - f. What is the importance of expanding to other subregions in the Americas, beyond the Amazon?
 4. Discuss the sustainability of the initiative:
 - a. Are changes in policies, strategies and activities institutionalized and sustainable?
 - b. Have policies, strategies, methodologies, and processes promoted by AMI been implemented by countries?
 - c. If implemented, have such policies, strategies methodologies, and processes been sustained? Examples: policies for treating falciparum malaria; vector control strategies; methods for assessing the efficacy of antimalarial drugs; processes for assessing vector susceptibility to insecticides.
 - d. Provide recommendations regarding criteria to apply in decreasing, and eventually terminating assistance provided to countries under AMI.

Regarding RAVREDA, the results of the evaluation will be used to:

1. Assess the effectiveness of the network while responding to national and regional needs, including South-to-South collaboration.
2. Assess the contribution of RAVREDA toward achieving AMI expected results.
3. Guide RAVREDA coordination and implementation through 2015.

4. Strengthen malaria prevention programs and expand activities to Central America.

The evaluators verified that activities planned and implemented under AMI respond to the expected results and lines of work described in the introduction below, and collected information on improvements achieved in each of these areas by the countries. An assessment was also made of progress achieved in each line of work, with special emphasis on the period 2008-2011. In addition, the evaluators determined whether AMI has been an effective and efficient way to support malaria prevention and control.

The evaluators visited Brazil, Colombia and Ecuador, and obtained information on other countries through data, records, and phone interviews with staff from national malaria control programs. Norms, regulations, official guidelines, and other documents were used as evidence of institutionalization.

4. Introduction

The Amazon Malaria Initiative was launched by the United States Agency for International Development in 2001 to improve the control and treatment of malaria by the Ministries of Health and national malaria control programs of the Amazon Basin, i.e. those from Bolivia, Brazil, Colombia, Ecuador, Guyana, Peru, Suriname, and Venezuela. These partner countries collaborate with one another and maintain an ongoing exchange of information, experiences and expertise. In the early 2000s, despite the experience gained in the fight against malaria by these countries (especially in preventive measures, such as indoor residual insecticide spraying, insecticide treated mosquito nets, and effective antimalarial treatment), several drawbacks still influenced malaria prevention and control programs, namely:

- Emergence of plasmodia resistant to antimalarial drugs, as well as treatment policies not based on efficacy studies.
- Limited access to diagnosis and/or inadequate quality assurance/quality control (QC/QA) of diagnosis.
- Insufficient availability of or access to antimalarial drugs; inappropriate drug use, and/or deficiencies in QC/QA systems for antimalarial drugs, or ineffective implementation of appropriate corrective measures.
- The use of non-selective and/or non-integrated, and sometimes ineffective, vector control measures; or delays in testing or implementing new approaches of proven effectiveness in areas of participating countries.

AMI began as a collaborative effort by PAHO and USAID to complement the Roll Back Malaria Partnership. Coordinated by PAHO in Latin America and the Caribbean, the purpose of AMI was to

overcome the aforementioned drawbacks. AMI’s initial emphasis was on providing support to participating countries to revise antimalarial drug treatment policies based on scientific evidence obtained through efficacy trials. As progress was made towards that purpose, a more comprehensive approach to drug efficacy was implemented, including issues of drug quality assurance, adherence to treatment, supply chain management, and others. Also, activities related to evidence based integrated vector management were undertaken.

The partnership approach emerged in response to the need to invest in targeted activities to improve malaria control in the Amazon Basin, where, according to PAHO, 88% of cases reported in Latin America originate; it was also meant to complement country specific activities with a regional approach. For this to happen, a highly coordinated effort was needed. USAID leads a portfolio of activities that is also closely coordinated with partners in each participating country, mostly national malaria control programs and other entities within Ministries of Health. For AMI, USAID joined forces with technical partners, i.e., the Pan American Health Organization, USAID/Latin America and the Caribbean (LAC) and USAID/Peru, CDC, U.S. Pharmacopeia, Management Sciences for Health, Links Media, and the Research Triangle Institute as of 2010, to ensure that selected best practices and evidence based policy changes in the partner countries were implemented.

4.1 Lines of work

Table 1, below, lists the activities carried out by each partner agency under the Initiative’s lines of work.

Table 1. Activities carried out within AMI/RAVREDA, by line of work, and partner agency

Line of Work	Activity
Partner Agency	
Line of Work 1: Surveillance of resistance to antimalarial drugs	
PAHO	
<ul style="list-style-type: none"> •Coordinates the regional agenda in support of studies of therapeutic efficacy and related topics, both at the technical and administrative levels (e.g., protocol review by PAHO’s ethical committee; financial tools, such as preparing letters of agreement, contracts, and grants). •Coordinates the development of regional review mechanisms for the network, and the involvement of CDC to develop the sampling protocol for <i>P. falciparum</i> molecular markers studies, and methods for drug serum level determination; •Coordinates the participation of experts to support reference laboratories in Bolivia, Brazil and Colombia, and for the standardization of in vitro techniques. 	
CDC	
<ul style="list-style-type: none"> •Develops protocols for molecular characterization of <i>P. falciparum</i> strains with three objectives: studies of HRP2 genes, resistance molecular markers for sulphadoxine/pyrimethamine and mefloquine, and studies of genetic variability in <i>P. falciparum</i> strains. •supports genotyping studies in the countries, as well as the determination of drug serum levels for efficacy studies. 	
Line of Work 2: Access to and use of antimalarial drugs	
PAHO	

-
- Supports countries with procurement mechanisms through the PAHO Strategic Fund to guarantee the availability of medicine stocks, as well as in the use of formulations associated with the best administration of and adherence to treatment.
 - Promotes the institutionalization of a supervision strategy for diagnosis and treatment posts.
 - Coordinates with MSH the implementation of regional workshops.
-

MSH

- Supports countries by designing and developing workshops on drug, rapid diagnostic tests and other supplies management.
 - Supports the institutionalization of the supervision strategy for diagnosis and treatment posts.
-

Links Media

- Provides supports by editing technical reports about best practices related to the supervision of diagnosis and treatment posts.
-

Line of Work 3: Quality of antimalarial drugs

PAHO

- Promotes the analysis and implementation of USP recommendations with national regulatory authorities and reference laboratories regarding the development of a management system for drug quality and the use of basic tests.
-

USP

- Supports training in analytical techniques and good laboratory practices;
 - Supplies analytical instrumentation.
 - Develops workshops on the use of minilabs.
 - Supports countries by disseminating the three-level approach model.
 - Promotes studies on counterfeit drugs;
 - Coordinates with PAHO for the development of workshops for drug quality, with the countries official laboratories.
 - Coordinates with PAHO south-to-south cooperation activities among regional reference laboratories.
-

Line of Work 4: Diagnosis access and quality

PAHO

- Promotes the development of national guidelines to improve the management of quality control systems for diagnosis the quality assurance of diagnosis, based on WHO recommendations. This involves both microscopy and RDTs.
-

MSH

- Supports the development of national guidelines, and management of RDT supplies.
-

CDC

- Supports protocol development to characterize *P. falciparum* strains regarding the HRP2 and HRP3 presence, as well the analysis of samples, in coordination with national laboratories. Also, in coordination with PAHO, CDC supports regional laboratories on batch quality control.
-

Line of Work 5. Entomology and integrated vector control

PAHO

- Promotes institutionalization of high impact vector control interventions.
 - Supports countries in their development of tools to disseminate the strategy following the model discussed and agreed upon in 2006.^b
 - Coordinates with countries the implementation of vector control activities following agreements reached in 2008.^c
-

^b Reunión Anual de Evaluación de RAVREDA-AMI Quito, Ecuador, 25–27 abril 2006
<http://www.paho.org/Spanish/AD/DPC/CD/ravreda-V-quito.pdf>.

-
- Coordinates the development of periodic analyses and dissemination of entomological information.
 - Coordinates with CDC to develop training and discuss the use of the CDC bottle and colorimetric tests, as well as the taxonomy agenda (since 2008).
 - Promotes, together with CDC, alternative methods to human bait captures, and for testing window traps.
 - Supports countries in documenting experiences regarding the use of long-lasting insecticide nets (LLINs), in coordination with Links Media, which edits technical documents.
 - Guides countries in the development of techniques for measuring residual insecticides in bed nets, and LLIN longevity.
-

CDC and RTI (since 2010 is a partner of AMI/RAVREDA).

- Coordinates with PAHO the development of workshops for national staff on the use of the CDC bottle method for insecticide resistance surveillance, the use of colorimetric tests for insecticide residuality in mosquito nets, and internal quality control for said methods.
 - Analyzes the work with experimental huts.
 - Supports the analysis and decision making process for surveillance and policy, as well as technical algorithms for resistance management.
 - Provides support to develop protocols to evaluate LLIN coverage, usage and duration monitoring.
-

Links Media

Supports the dissemination of information on national experiences regarding LLINs.

Line of Work 6. Epidemiology and information systems, and information management

PAHO

- Supports the national implementation of routines for information analysis and use in different levels, following the analysis plan for the main indicators and parameters for diagnosis, treatment and vector control management.
 - Supports the use of data bases of individual records.
-

Line of Work 7. Communication and dissemination

PAHO

- Identifies countries with studies and experiences supported by AMI that warrant publication.
- Participates with Links Media in the development of digital versions of tutorials for use by public health workers on strategies promoted by AMI (stratification, information management, entomology, and supervision).
- Reviews guidelines developed by Links Media.
- Defines mechanisms to improve and update the contents of the [RAVREDA](#) Web page in PAHO's Internet site, as well as links with the [AMI Web](#) page developed by [Links Media](#).

Links Media

- Supports the preparation of scientific papers and technical reports of AMI products.
 - Develops and maintains the AMI web site.
 - Updates and improves the RAVREDA page in the PAHO web site.
 - Develops documental about AMI.
-

PAHO has a preponderant role as an AMI partner; it serves as a channel for AMI support to individual countries, and provides guidance and support not solely to RAVREDA members, but to all countries in

^c Guayaquil: Meeting for evaluation decision-making strategy in vector control and entomological surveillance in malaria

[http://new.paho.org/hq/index.php?option=com_docman&task=doc_download&gid=7662&Itemid=.](http://new.paho.org/hq/index.php?option=com_docman&task=doc_download&gid=7662&Itemid=)

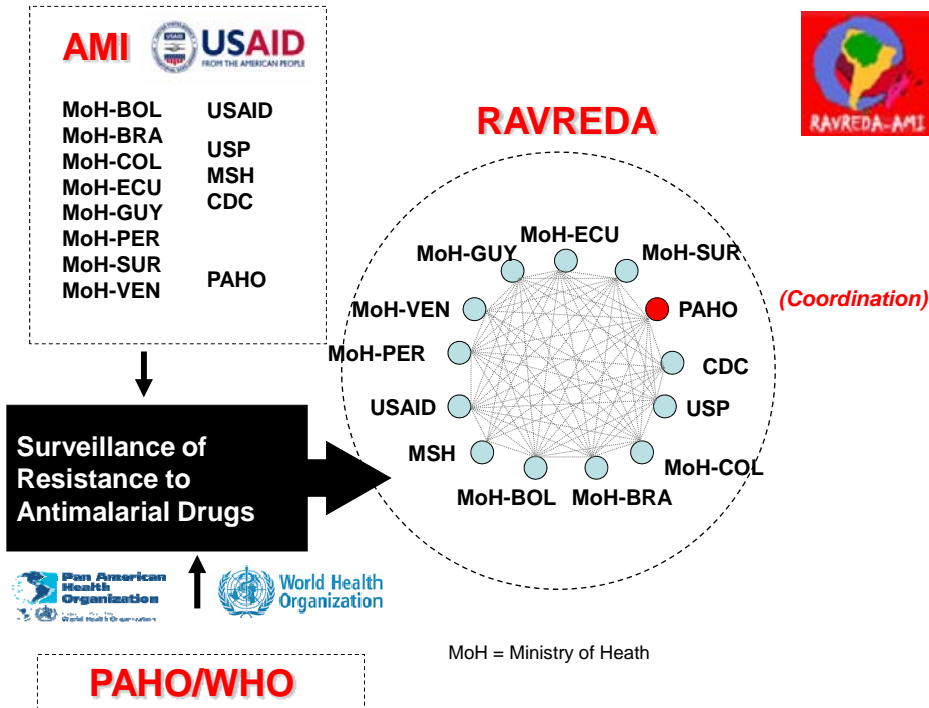
the Americas regarding malaria prevention and control. In fulfilling the latter role, PAHO finalized a Strategy and Plan of Action for Malaria in the Americas for 2011-2015 with input from a number of stakeholders, including USAID. The strategy and action plan were presented to and approved by all countries of the Americas in the 51st Meeting of the Directing Council of the Organization ([CD51/11](#)). The document will provide input in planning the 2011-2015 phase of AMI.

5. AMI evolution: from 2007 to 2011

With AMI, USAID developed and implemented a novel approach that combines complementary sources of technical assistance organized in, and coordinated by, a steering committee. The approach proved more effective and efficient than the more conventional paths to program management. The AMI strategy of working within a network of national malaria control programs coordinated by PAHO addresses issues of actual common interests, as opposed to an externally imposed agenda. Collaboration is essentially provided through technical assistance, with a very low proportion of resources going to commodities. AMI has been essential to the development of the most functional existing network of national malaria control programs worldwide. In addition to consistent and continuous participation of all Amazon member countries since 2002 (except for Venezuela, which has not participated since 2007 for reasons external to AMI), the network includes now 5 Central American countries (Belize, Guatemala, Honduras, Nicaragua and Panama).

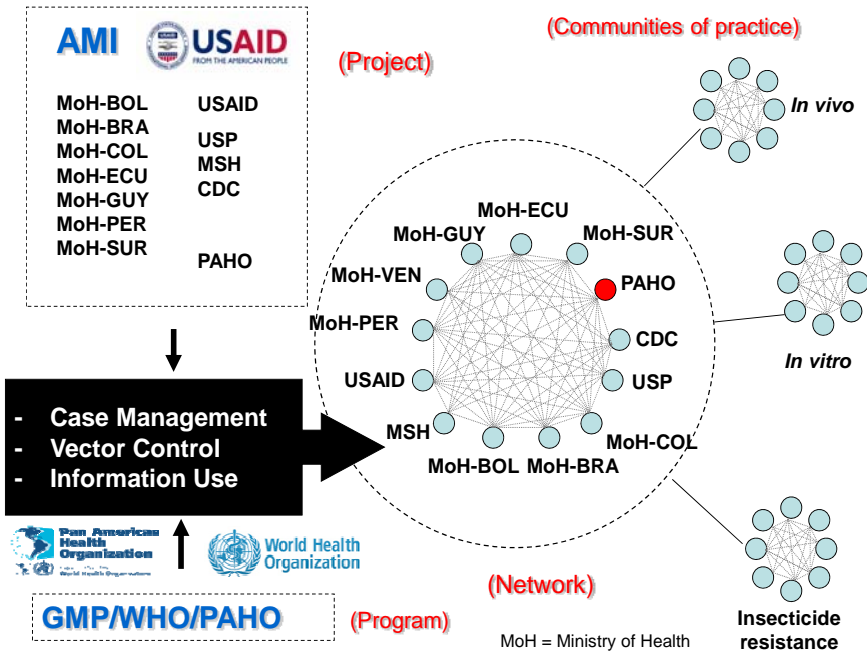
On the technical side, AMI has had a comprehensive vision of and approach to malaria prevention and control. Nonetheless, its initial purpose was to gain the evidence to support the introduction of artemisinin-based combination therapy (ACT) for falciparum malaria in all Amazon basin countries, and to improve the access to malaria diagnosis and its quality. Figures 1 and 2 illustrate the configuration and functions, respectively, of RAVREDA and AMI, and the relationship between the two initiatives.

Figure 1. Configuration of the Amazon Malaria Initiative and the Amazon Network for the Surveillance of Antimalarial Drug Resistance (RAVREDA)



Source: PAHO/WHO 2001 and up

Figure 2. Functions of the Amazon Malaria Initiative and the Amazon Network for the Surveillance of Antimalarial Drug Resistance



Source: PAHO/WHO, 2007- 2008.

As progress in the introduction of ACT became evident, epidemiological surveillance and vector control received more attention (Figure 3).

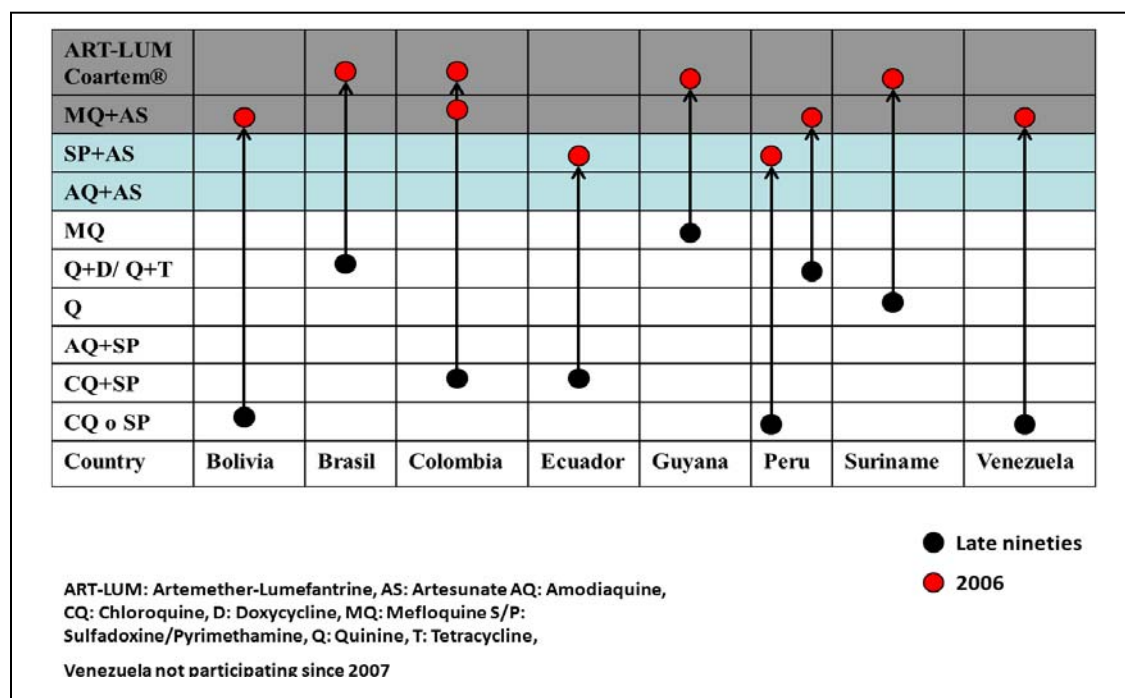
6. AMI expected results

The expected results established for the Amazon Malaria Initiative are:

1. Reliable and standardized surveillance information on malaria drug resistance and vector control used to monitor trends and more effectively target disease control efforts.
2. Laboratory diagnosis of malaria improved.
3. Tools and approaches developed, adapted, tested in local settings, and disseminated.

Activities that should lead to achieving these results are detailed under the corresponding line of work in the Introduction section of this document.

Figure 3. Changes in treatment policy for non-complicated falciparum malaria in the countries of the Amazon Malaria Initiative, 2000-2006*



Note: Ecuador is changing to ART-LUM and Brazil maintains MQ-AS for non-endemic States.

* Source: PAHO/WHO

7. Achievements and challenges

The most important impact of AMI on malaria control in the Amazon Basin subregion is measured in lives saved and illness prevented. In fact, since 2000-2001, the status of malaria improved, albeit in different degrees, in the Amazon basin countries. In Brazil, 14% of cases were prevented when compared to 2001, while in Colombia this proportion was 49%, and in Ecuador, 98% (Table 2).

Although the decrease in the number of malaria cases may or may not be attributed to RAVREDA-AMI activities, it is a welcome development. At the same time, it has become more difficult to recruit cases to monitor and to conduct drug efficacy testing.

Table 2. Total number of cases of malaria and cases by *Plasmodium falciparum* in countries visited for the evaluation, 2001-2010

Year Country	2001			2010			Cases averted
	All cases	<i>Plasmodium falciparum</i> cases		All cases	<i>P. falciparum</i> cases*		
		No.	%		No.	%	
Brazil	388,303	81,833	21	334,618	51,050	15	53,685
Colombia	231,233	100,242	43	117,637	34,334	29	137,596
Ecuador	108,903	37,491	34	1,888	258	14	107,015

* Includes cases by more than one species.

Source: Annual country report to PAHO/WHO

Malaria cases fluctuate through time, influenced by social, environmental, epidemiological and economic factors. Additionally, simultaneous implementation of several control strategies (e.g., household spraying, insecticide-treated bed nets; timely diagnosis, and artemisinin combination therapy) makes it impossible to attribute potential success to any specific control measure.

Resistance to antimalarial drugs

AMI established collaboration with RAVREDA's network of sentinel sites, where standardized protocols are being used for ongoing in vivo surveillance of malarial drug efficacy. Figure 4 shows the location of sentinel sites where in vivo drug testing was conducted. Refer to figure 3 for treatment policies by country up to 2006. Two countries adopted new policies since 2007.

Figure 4. Network of sentinel sites for drug susceptibility testing, Amazon countries



Source: PAHO/ WHO

Drug resistance surveillance provides AMI partner countries with reliable information on the distribution and intensity of resistance to antimalarial medicines. Treatment policies have been tested and adopted by local governments about a year after completion of efficacy studies, reflecting unusually quick decision-making, and the importance of the issue in affected countries.

All countries participating in RAVREDA have now modified their official malaria treatment regimens to more effective combination therapies; drug efficacy monitoring continues, and provides ongoing means of detecting new forms of resistance. Ecuador provides a good example of activities at country level since the inception of RAVREDA. In that country, efficacy studies of antimalarial drugs (Table 3) moved the Ministry of Health in 2006 to make drug policy changes regarding the treatment of uncomplicated malaria. Treatment with Coartem had been fully implemented throughout the country by 2007, and continues until today.

Table 3. Summary of antimalarial drug efficacy studies, Ecuador, 2002 to 2005, by sentinel site

Sentinel site	<i>Plasmodium</i> species	Drugs used	Number of patients evaluated	Treatment failure		Status
				Number	%	
Machala	<i>falciparum</i>	AS+SP	50	0	0	Completed
	<i>falciparum</i>	CQ	15	12	80	Completed
Milagro	<i>falciparum</i>	SP	49	0	0	Completed
Portoviejo	<i>falciparum</i>	CQ	22	18	82	Completed
	<i>falciparum</i>	SP	29	0	0	Completed
Santo Domingo	<i>Falciparum</i> 2004	AQ	64	21	41	Completed
	<i>vivax</i>	AQ	22	0	0	Completed
	<i>vivax</i>	CQ	60	0	0	Completed
Esmeraldas	<i>falciparum</i>	CQ	21	19	90	Completed
	<i>falciparum</i>	SP	41	7	17	Completed
	<i>Falciparum</i> 2004	AQ+SP	34	0	0	Completed
	<i>Falciparum</i> 2004	AS+SP	61	0	0	Completed
	<i>Falciparum</i> 2003	CQ+SP	50	0	0	Completed
Esmeraldas, Santo Domingo, Milagro	<i>Falciparum</i> 2005-2006	Coartem	60	0	0	Completed

Source: Ministerio de Salud Pública. Política nacional de medicamentos para el tratamiento y control de la malaria en el Ecuador. 2006.

AQ: amodiaquine; AS: artesunate; CQ: chloroquine; SP: sulfadoxine-pyrimethamine;

Diagnosis: quality assurance and access

The diagnostic process. Clinical diagnosis of malaria is neither sensitive nor specific enough to accurately confirm a true case of malaria. In general, malaria suffers of over diagnosis, which generates poor management of non-malaria febrile illness, and an overuse or misuse of antimalarial drugs. Up to now, the gold standard for malaria diagnosis continues to be light microscopy of thin or thick blood smear. It is used for early diagnosis and treatment, and its importance cannot be overemphasized, as it is vital for reducing malaria morbidity and mortality. Detection of malaria parasites prior to treatment administration is the norm for malaria prevention and control programs in Amazon countries. On the other hand, microscopy diagnosis of malaria may be inadequate, as those performing the task are not competent or motivated enough to do it correctly. In the three countries visited for the current

evaluation, microscopy diagnosis is made mostly by malaria prevention and control programs, which also may provide free treatment following a positive diagnosis. In most countries, one technician prepares the slides, which are then stained and interpreted by microscopy technicians. All positive and negative slides are sent for confirmation to supervisors who reexamine all positive slides, and 10% of randomly selected negative slides. Slides forwarded to the supervisory level are washed, dried and reused, except for those kept for training purposes.

Activities aimed at improving malaria diagnosis

- AMI/RAVREDA provided support for training of microscopy technicians of several AMI countries, whose performance improved following training.
- AMI also led the development of guidelines and recommendations for improving diagnostic QC/QA systems in the Amazon Basin subregion. To facilitate the implementation of these guidelines, AMI engaged in technical collaboration and provided funding for a number of activities in partner countries, including training to improve competency in laboratory diagnosis; efforts to introduce proficiency testing as a component of diagnostic QC/QA systems; and efforts to improve the efficiency of diagnostic performance monitoring.
- With RAVREDA/AMI support, workshops and courses have been conducted leading to an overall improvement in malaria diagnosis. AMI also recommended that countries adopt proficiency testing and performance monitoring methods.
- Improved diagnostic QC/QA systems in the Amazon countries will allow public health laboratories to train personnel, provide supervision and monitoring, carry out operations research, contribute to evidence based decision-making, and participate in the design of interventions to improve malaria diagnosis and treatment.

In spite of the above contributions from technical partners, in some endemic areas (Acre and Manaus in Brazil, and Buenaventura and Choco in Colombia) visited as part of this evaluation, no activities were found to have taken place to implement a QC/QA system or performance evaluation to assure staff competency and performance in malaria microscopy. On the other hand, health authorities in the state of Acre deserve credit for implementing, in collaboration with the State University, a diploma on tropical diseases, whose curriculum includes light microscopy of malaria, tuberculosis and *Trypanosoma cruzi*.

Strengthening QC/QA systems of malaria microscopy by using regional reference laboratories in the preparation of slide panels (as is being done in Honduras) and monitoring performance evaluation may open further possibilities for south-to-south collaboration.^{1, 2,3 4, 5}

Quality of antimalarial medicines. AMI has generated increased awareness of the importance of quality regarding antimalarial medicines, and has encouraged the strengthening of proper quality assurance and quality control systems for drugs used in national malaria control programs, given their relevance to malaria control and drug efficacy. Specifically, the Initiative has contributed to:

- Strengthening the official medicine control laboratory in each AMI partner country by providing guidance on quality management systems and training in pharmaceutical techniques;
- Implementing a decentralized methodology to monitor and control drug quality under storage and distribution conditions, in endemic area, as well as testing in portable laboratories (minilabs); and
- increasing awareness of the need for quality antimalarial medicines, by documenting shortcomings in QA systems. Numerous AMI supported training activities in analytical techniques and good laboratory practices; analytical tools were also supplied. Staff of several laboratories in all AMI countries are now better trained and equipped to ensure the quality of antimalarial medicines. In addition, all AMI partner countries have agreed to implement portable laboratories as an inexpensive, rapid, and efficient approach for continuous assessment of antimalarial drug quality. The equipment is already available in Colombia and Ecuador. Training was also provided in procurement of antimalarial medicines, quality control, and storage and distribution.⁶

RAVREDA provides AMI with a means to achieve its goal of monitoring antimalarial drug quality, and to promote, in turn, drug efficacy throughout the area. AMI provides RAVREDA with the additional expertise and resources of its AMI technical partners to strengthen the Ministry of Health of each participating country. Table 4 lists the expected results, corresponding line of work, and a summary of achievements, and future challenges.

Table 4. Achievements and challenges of AMI-RAVREDA, by expected result and line of work

Line of Work	Achievement	Challenge
Expected result 1. Reliable and standardized surveillance information on malaria drug resistance and vector control used to monitor trends and more effectively target disease control efforts.		
Surveillance of antimalarial resistance a. In vivo b. In vitro c. Molecular markers	A network of sentinel sites for ongoing surveillance of drug efficacy using standardized protocols has been established. This surveillance provides countries with reliable information on the distribution and intensity of resistance to antimalarial drugs.	To continue in vivo surveillance and expand it to include in vitro surveillance. It has been an excellent endeavor for which all partners ought to be congratulated.
Drug policy implementation	Antimalarial drug resistance assessed, drug policies defined, use of efficacious antimalarial drugs promoted; policies tested and adopted by local governments about one year after completion of efficacy studies.	Because of the decrease in the number of <i>Plasmodium falciparum</i> infections, the possibility of using fewer subjects and combining results from different testing sites must be tried following the WHO protocol. Surveillance of resistance should be expanded to include in vitro testing.
Expected result 2. Access to quality diagnosis and treatment		
Improve access to diagnosis (RDTs)	RDTs are available in all RAVREDA-AMI countries.	Kits are now paid for with monies from the Global Fund. Before the kits are released to users, they must be controlled and checked to determine whether they still meet specifications.
Quality of microscopy diagnosis	Laboratory diagnosis of malaria has improved because of increased training and supervision. RAVREDA – AMI has supported training for microscopy technicians in several AMI countries. AMI also provided funding for a number of other activities in partner countries, including: <ul style="list-style-type: none"> • training to improve competency in laboratory diagnosis; • efforts to introduce proficiency testing as a component of diagnostic QA/QC systems; and • efforts to improve the efficiency of diagnostic performance monitoring. There have been demonstrated improvements in competence following training. Also, proficiency testing and performance monitoring methods recommended by RAVREDA–AMI have been promoted among AMI partner countries.	National efforts to implement an effective, accurate and timely QC/QA system for malaria microscopy have been insufficient. Country reference laboratories should be strengthened to meet this challenge.
Drug quality	The situation improved significantly. AMI provided: guidance on quality management systems and training in pharmacopeia techniques; application of methods to monitor and control the quality of medicines under endemic area storage and distribution conditions through the use of portable laboratories; and increase awareness about the issue of antimalarial medicine	Continue with drug QC/QA, and periodic evaluations by AMI. It is imperative that the same approach be in place for insecticides.

	quality among Amazon countries by documenting shortcomings in QA systems.	
Drug availability and use	Sustainable systems for ensuring the availability of high-quality antimalarial medications have been adopted and implemented. As a result of numerous AMI-supported trainings in analytical techniques and good laboratory practices, other forms of technical assistance, and the supply of analytical instrumentation, laboratory personnel in all AMI countries is now better trained and equipped to ensure the quality of antimalarial medicines. In addition, all AMI partner countries have agreed to implement portable laboratories as an inexpensive, rapid, and efficient approach to continuously assess antimalarial medicine quality.	The activities under this line of work should continue to guarantee quality drugs and protect patient safety.
Expected result 3. Tools and approaches for malaria control, diagnosis, and prevention developed and adapted, tested in local settings, and disseminated.		
Evidence-based vector control	Entomological information is now available to guide control activities and integrated vector management. An impressive number of routine activities took place in which strategies, tools, achievements, and lessons learned were shared with other participating countries, other countries in Latin America and the Caribbean, and other stakeholders in malaria control efforts in other regions (e.g. the President's Malaria Initiative, Mekong Regional Initiative, Andean Malaria control project financed by the Global Fund).	Integrated vector management and its related information system need to be strengthened. There needs to be further integration of vector control and epidemiology; and maps of resistance to insecticides should be developed.
Epidemiological stratification	Countries have staff trained in the use of, and are using reliable software for malaria surveillance, treatment, drug resistance and vector control. The software is available at the central level (Ministry of Health and/or departmental level), and is used to monitor trends and to target disease control efforts more effectively.	Incorporate epidemiologists in program activities. Train lower level personnel on the use of the software chosen by PAHO or similar.

8. Evaluators' responses to specific questions on statement of work

8.1. Assess the suitability and success of AMI in increasing efficiency and efficacy of USAID's investment in the fight against malaria

The main feature of the AMI/RAVREDA model is the implementation of a collaborative network of countries supported by national and international institutions and concerned agencies, to address all aspects of malaria. Central to that implementation is the provision of mechanisms for coordinated planning, exchange, validation and consolidation of experiences, leading to the development of policy proposals, in contrast to prior loosely coordinated institutional or national attempts to address problems, often from separate disciplinary perspectives.

Antimalarial programs, health authorities and collaborating research and training institutions visited in the three countries concur in recognizing the important contribution of AMI/RAVREDA to the improvement of malaria control in their country. This positive perception was shared by the Military Health Service in Colombia, which faces malaria related problems in war zones and isolated areas, often the main foci of drug resistance.

The Initiative's success has taken what is obviously a rather modest investment vis-à-vis national malaria budgets and historical USAID investments in the fight against the disease. It can therefore be concluded that, in general terms, the investment in AMI/RAVREDA has been both effective and efficient.

On the other hand, at least in Brazil, Colombia,^{dd} and Ecuador, malaria program managers as well as lower ranked staff, when interviewed by the evaluation team, appeared unable to clearly distinguish between AMI and RAVREDA, which are both perceived as mutually reinforcing the support to a strong inter-country collaboration in the Amazon subregion. It was the joint success of RAVREDA and AMI that generated a demand for continuing and expanding functions to the broader field of malaria control. Beyond the subregion, there seems to be no clear distinction between both initiatives either; this is evident in the fact that the requested expansion of AMI/RAVREDA to Central America indicates that AMI is not perceived as limited to the Amazon basin. This general perception has persisted in spite of the recommendation by USAID's External Evaluation of AMI and SAIDI (South American Infectious Disease Initiative) of July 2007, to "clarify RAVREDA's identity as distinct from AMI (no longer use the term RAVREDA-AMI)." Perhaps, as the program expands to Central America, it would be advisable to consider that extension as pertaining to RAVREDA, while AMI remains an Amazon initiative that seeks exchanges and collaboration with the developing Mesoamerican Malaria Initiative.

Because of the lack of distinction between AMI and RAVREDA in those countries visited for the evaluation, it was not possible to attribute to either initiative the success or problems encountered.

All public health authorities interviewed, from Secretaries of Health at the country or state levels in Brazil and Ecuador, as well as the Director of National Service for Malaria Eradication from Ecuador (Section 19 of this document), field workers' supervisors of the municipality of Manaus (Amazon), or the municipality of Rio Grande do Sul (Acre), to researchers in Brazil and Colombia, were pleased and

^{dd} Colombia does not have a national malaria control program. Malaria activities are managed by the Vector Control Program, which includes malaria, Chagas' disease, leishmaniasis, and other vector-borne diseases.

thankful for the role that AMI/RAVREDA had in the fight against malaria. Although funds provided by USAID through PAHO were small when compared to national investments in malaria prevention and control, said funds were crucial and made a difference on whether a project/activity could be carried out or not. Authorities gratefully acknowledged the support of PAHO staff for the assistance provided in developing proposals to the Global Fund. Table 5, shows the amount of funding available for malaria activities, by source, in 2010. Ecuador was awarded US\$ 6.9 million from the Global Fund for Phase I of a project commencing in 2009. The government has traditionally provided most funding for malaria

control (US\$ 2.4 million in 2009), indicating strong national commitment to malaria control.⁷

Table 5. Sources and amount of funding¹ for malaria activities in Brazil and Colombia, 2010 (US\$)

Country	Source of funding	Amount (US\$)
Brazil (2010)	Ministry of Health	106,000,000
	USAID	227,000
	Global Fund	13,968,815
Colombia (2011)	Ministry of Health ¹	32,526,772
	USAID	120,000
	Global Fund	8,125,525

¹ Does not include funds provided by departments or states nor national level staff salaries.

8.2. Effectiveness and replicability of the AMI model

The first two evaluation questions under this item were *is the AMI model effective?* and *is the AMI model replicable in other regions and/or for addressing other problems?* Both questions are somewhat related. It can be said without exaggeration that, at least in regard to improving antimalarial treatment and access to diagnosis and treatment, AMI/RAVREDA achieved more substantial and, probably, more sustainable progress than in the previous 30 years in reference to antimalarial drug resistance in South America.

Countries having joined and maintained their participation in the Initiative, as well as the willingness of Central American health authorities to become part of the Initiative are strong indications that the model is replicable.

Moreover, the model, which was originally conceived to address a single concrete problem, i.e., mapping drug resistance, has evolved to deal quite successfully with the whole issue of accessibility to diagnosis and treatment; selection, training, qualification and performance monitoring of microscopy technicians; storage and logistics of drugs and insecticides. Furthermore, it is now addressing the issues of epidemiological surveillance and information systems, as well as the integration of entomology into epidemiological surveillance. This evolution is strong evidence that the approach may be also suitable for addressing other health problems (e.g. antimicrobial resistance). However, there is room for improvement, particularly, regarding the quality of each and every procedure carried out by malaria prevention and control personnel, from household spraying to quality control of RDTs, QC/QA, and performance evaluation of thin/thick smear microscopy.

8.3. Value added by the AMI model

The AMI/RAVREDA sentinel site map for antimalarial drug resistance surveillance (see figure 2) illustrates how such a network can perform effective surveillance of parasite response to antimalarial drugs in a variety of epidemiological situations. This would never have been possible within previously existing programs. The broad field of observation, exchange of information, performance of the AMI/RAVREDA coordinator, and periodic meetings afforded the opportunity to conduct rapid and efficient analyses and validation of results.

9. Comments on results reported by AMI

As mentioned above, RAVREDA's original purpose was to establish a surveillance network for malaria parasite resistance to antimalarial drugs in South America, and to identify the best course of treatment for the disease. The main purpose of the network was not just to map the distribution of resistance, but to routinely evaluate the therapeutic efficacy of antimalarial treatments and use the results in policy decision making.

9.1. Selection of effective first-line antimalarial drug combinations

Based on clinical efficacy trials coordinated by RAVREDA in participating countries, and in spite of some good response to drug combinations, such as mefloquine-sulphadoxine-pyrimethamine in specific areas, it became obvious that *P. falciparum* infections would require artemisinin-based combination therapy (ACT). This conclusion emerged from trials conducted to assess the efficacy of different antimalarial drugs and combinations in Bolivia, Brazil, Colombia, Ecuador, Guyana, Peru, Suriname and Venezuela, between 2002 and 2008. In total, 2 535 tests were completed for *P. falciparum* (of those,

1152 were in Colombia, and 560 in Brazil), and 1,609 on *P. vivax* (930 in Brazil and 175 in Colombia). After the trials, artemether-lumefantrine was the combination most widely adopted, based on results obtained in Brazil, Ecuador, Guyana (5 treatment failures), Suriname (2 treatment failures) and Venezuela.

Consequently, ACT combinations were progressively adopted since 2006. These drug policy changes, together with efforts to improve access to diagnosis and treatment, have made an important contribution to remarkable improvements in the epidemiological situation of malaria in most countries in the subregion, including the decline in the proportion of cases of *P. falciparum* malaria in the three countries visited for this evaluation.

In Ecuador, artesunate-sulphadoxine-pyrimethamine was adopted as first line treatment of *P. falciparum* malaria in 2006, but due to increasing resistance to sulphadoxine-pyrimethamine, a decision was made to change to artemether-lumefantrine. In Colombia, the response to the combination mefloquine-sulphadoxine-pyrimethamine was good, but a decision was made to adopt artemether-lumefantrine instead.

In Brazil, artemether-lumefantrine was adopted as the first line treatment for *P. falciparum* malaria, and artesunate-mefloquine as second line treatment; this same combination will be used for treatment in non-endemic areas (outside the legal Amazonia). Artesunate-mefloquine was also used as first line treatment in the State of Acre, but it was later decided to adopt artemether-lumefantrine, which is consistent with the national policy.

In Brazil, since 2005, *P. vivax* resistance to chloroquine has been documented with a prevalence of 6%-10% in clinical efficacy trials. A similar frequency of treatment failure occurred with chloroquine-primaquine, showing no synergistic effect between the two drugs. These results have been reported in several congresses and published in the scientific literature since 2007. The search for alternative treatments for *P. vivax* malaria is now being pursued.

In recent years, due to the considerable decrease in malaria incidence, it has become apparent that proper *in vivo* studies will be increasingly more difficult to carry out, although some avenues may be opened for monitoring and reporting treatment response.

RAVREDA has been supporting laboratory and field studies, particularly in Brazil and Colombia, aimed at identifying potential molecular markers of resistance to the main drugs, which could be used for *in vitro* studies

9.2. Access and acceptability of diagnosis and treatment

Soon it was recognized that improving treatment would require not only effective drugs, but also considerable improvements in access and acceptability of diagnosis and treatment. Therefore, AMI/RAVREDA collected existing information, and stimulated and supported the necessary studies to provide scientific evidence for improving malaria diagnosis and treatment, as well as the required epidemiological information for translating this evidence into policy changes.

9.3. Microscopy diagnosis

All countries made important investments in training and refresher training of microscopy technicians, as well as in extending the coverage of basic laboratories, supported by a network of reference laboratories. AMI/RAVREDA assisted countries in implementing recommendations of a PAHO consultation meeting held in Caracas in 2004, i.e., to follow training or retraining with proficiency testing consisting of an external evaluation of laboratories and the continued assessment of microscopy technicians by direct and indirect slide validation. Although training and retraining of these technicians were implemented in all countries, follow up steps to implement QC/QA, including proficiency testing, were not in place in some of the sites visited by the current evaluation team (Buenaventura, Choco, EL Oro, Guayaquil, Cruzeiro do Sul, Manaus).

9.4. Rapid diagnostic tests (RDT)⁶RDTs have been used at least since 2007, and all countries recognize them as a valid alternative in areas where it is not possible to maintain an adequate network of properly trained microscopy technicians, as well as for isolated groups or for the rapid evaluation of epidemic outbreaks.

However, country reports for 2010 seem to indicate that RDTs have not been fully incorporated into the epidemiological surveillance system. Data for Ecuador in the [World Malaria Report 2010](#) indicates that 2,758 and 4,992 rapid diagnostic tests were performed in 2008 and 2009, respectively. However, the report does not include any RDT positive results; furthermore, the number reported under “total confirmed cases (microscopy + RDT)” is the same as that reported under “microscopy positive”. (One field staff using the test in Ecuador remarked that it is not rapid [no less than 15-20 minutes]; time for the different steps must be strictly followed, and this makes it very difficult to conduct more than two tests at a time.)

In Colombia, RDTs have been widely used with PAMAFRO^e support since 2005, and through 2007 (25,000 tests) and 2008 (22,754 tests). Information gathered by the current evaluation team indicates a decreasing number of positive cases detected by RDTs in 2008 (1,329) and 2009 (13) .

In 2011, Colombia acquired and distributed some 200,000 RDTs for activities within a Global Fund project in the Pacific area, where two RDT field operators from Buenaventura, Cali, indicated the need to ensure that RDT kits are in good working condition when leaving storage. Thus, QC is specially needed regarding RDTs, as it is important to avert mistakes and minimize errors. Performance of the test depends on characteristics of the test itself, such as the migration rate of the drop of blood on the nitrocellulose membrane (NCM) or the binding of captured antibodies to the NCM. Other factors may also affect the kits' quality; there are different manufacturers and brands, and RDTs may deteriorate during transport and storage because of high humidity and heat (> than 30 °C). Thus, a strict system of quality control must be in place for product, lot and point of use testing. The International Center for Training and Medical Research (Centro Internacional de Entrenamiento e Investigaciones Médicas, [CIDEIM](#)) in Colombia has offered to collaborate in this matter.

Data for Brazil published in the [World Malaria Report for 2011](#) does not include RDTs performed in 2008, 2009 or 2010. Nevertheless, RDTs are introduced in the Operational Manuals for Malaria Diagnosis of the three countries visited. Furthermore, Ecuador issued a *Guía Operacional para Uso de Pruebas Rápidas para el Diagnóstico de Paludismo en El Ecuador (2010)*.

9.5. Human resources development

AMI/RAVREDA promoted the establishment of highly motivated teams within malaria programs, to address the main concern of improving diagnosis and treatment, and conducting *in vivo* studies of response to treatment. Since the beginning, the Initiative involved the higher echelons of program management, which facilitated eventual changes in treatment policies, once supportive data had been gathered. Eventually these teams expanded their interest to the epidemiology and control of malaria, becoming concerned with entomology, as a guide to vector control operations, as well as with the analysis of epidemiological information. In turn, the system offers refresher training, competence assessment, and qualification at all service levels.

^e PAMAFRO was a project financed by the Global Fund for malaria control in the cross border areas of 4 Andean countries (.Colombia, Ecuador, Peru, and Venezuela).

9.6. Communication, public information and education

In improving diagnosis and treatment, continued effort to inform and educate the public have been essential to promote timely use of health services, and projecting those services to the communities. To this end, training was provided to all health agents who have contact with the public, particularly those working at community level. These efforts have been accompanied by media messages and appropriate communications to all levels of society, emphasizing that malaria is everybody's problem. In Colombia, an interesting information campaign, "*mucho cuidado*" ("be very careful"), included messages addressed to school children, plus a board game that underlined the need for bed nets and prompt seeking of treatment in cases of fever.

The success of these efforts is evaluated by calculating, from individual case management reports, the time elapsed between the onset of symptoms and initiation of treatment, particularly the proportion of cases initiating treatment within 72 hours of onset of symptoms, which is increasing in most countries.

9.7. Procurement, storage and distribution of drugs

The Initiative has guided and supported the development of appropriate management systems to ensure availability of high quality antimalarial drugs and laboratory reagents at all levels of the health services. This has included setting up suitable storage, and a process to monitor the system's level of development, and circulating systems' reports to stimulate the correction of deficiencies. The system has improved and works well in the three countries visited as part of this evaluation, and staff in charge were proud of the results. A similar system needs to be set up for insecticides used in vector control activities for all vector borne diseases, to ensure their safe storage, distribution and use.

9.8. Epidemiological surveillance

AMI/RAVREDA has contributed to the improvement of epidemiological surveillance; joint analysis of RAVREDA data has led to the adoption of a powerful relational database (Tableau) for common use, to consolidate and analyze all epidemiological information. This, in turn, has promoted the exchange of multiple analyses of program information at all levels, in tabular and graphic form, particularly as countries adopt similar forms for data entry. Furthermore, countries have adopted a similar form for case reporting. However, some important differences among countries regarding recorded information remain, especially data related to treatment, occupation, and probable origin of the infection.

The epidemiological surveillance system does not yet include geographic information, which will be increasingly necessary as transmission becomes progressively focalized. Geographic information will facilitate the identification and delimitation of foci of transmission across administrative localities,

defining with greater precision the true epidemiological sites, leading eventually to the identification of important ecological and other epidemiological determinants of persistence or reemergence of transmission.

Finally, the use of geographic positioning systems for the identification of points of confirmed or suspected transmission or clusters of positive cases may provide a more precise tool than the current fitting of sketch maps from epidemiological site surveys.

9.9. Entomological studies

In the last few years, AMI/RAVREDA developed guidelines for entomological studies, which have translated into national manuals, staff training, and the establishment of entomological teams.

As a first step, support was provided for the study of resistance to insecticides by introducing and promoting the use of the “bottle bioassay,” to determine the presence of potential resistance to a given insecticide (vector mortality <80% indicative of potential resistance). The WHO indicator of insecticide resistance for impregnated paper is a vector mortality <80% as well. A detailed analysis of the entomological work carried out in Ecuador and Colombia is presented in the Entomology and Vector Control section of this report.

9.10. Publication of operations manuals and guidelines

An important objective of AMI/RAVREDA has been the publication of national operational guidelines for the main activities of malaria control; the following were made available to the team in the countries visited:

Epidemiological surveillance: *Guía protocolo para la vigilancia en salud pública de malaria* (Protocol Guideline for Public Health Surveillance in Malaria) Plan Nacional de Salud Pública. Ministerio de Protección Social, Instituto Nacional de Salud, Organización Panamericana de la Salud. 24 pp., Colombia.

Drug policy: (IN SPANISH) USAID, PAHO, RAVREDA-AMI, 56 pages, Ecuador.

STORAGE: *Manual para la aplicación de buenas prácticas de almacenamiento en las bodegas del SNEM* (Manual for the implementation of good storage practices in SNEM stock rooms). Ministerio de Salud Pública (2007). Ecuador. USAID, OPS, RAVREDA-AMI, 41 pp.

Diagnosis and treatment

Malária. Tratamento com COARTEM (Treatment with Coartem). Fundação de Vigilância em Saúde do Estado do Amazonas. 2ª Edição revisada, Brazil.

Guía para la atención clínica integral del paciente con malaria (Guidelines for malaria patient comprehensive care). Plan Nacional de Salud Pública. Ministerio de Protección Social, Instituto Nacional de Salud, Organización Panamericana de la Salud. 129 pp., Colombia.

Guia para gestão local do controle da malaria. Diagnóstico e tratamento (Guidelines for local malaria control management. Diagnosis and treatment). (2008) Serie B. Textos Básicos de Saúde. Ministerio da Saúde. Brasilia, DF, 30 pp., Brazil.

Microscopy

Manual de Diagnóstico Laboratorial da Malária (Malaria laboratory diagnosis manual) (2009), Série A. Normas e Manuais Técnicos. Secretaria de Vigilância em Saúde. Brasilia, 2ª Edição, 116 pp., Brazil.

Guia para microscopia de malária humana (Guidelines for human malaria microscopy) (2008). Álbum. Série A. Normas e Manuais Técnicos. Secretaria de Vigilância em Saúde. Brasilia, 27 pp., Brazil.

Pruebas de diagnóstico rápido (Rapid diagnostic tests). Ministerio de Salud Pública (2010). Guía Operacional para el Uso de Pruebas Rápidas para el Diagnóstico de Paludismo en el Ecuador. USAID, OPS, RAVREDA-AMI, 50 pp., Ecuador.

Entomology and vector control

Gestión para la Vigilancia Entomológica y Control de la Transmisión de Malaria (Entomological surveillance and malaria transmission control management). Plan Nacional de Salud Pública. Ministerio de Protección Social, Instituto Nacional de Salud, Organización Panamericana de la Salud. 130 pages, Colombia.

Guia para Gestão Local do Controle da Malária (Guidelines for local malaria control). Controle Vetorial (2009) Serie B. Textos Básicos de Saúde. Ministerio da Saúde. Brasilia, DF, 59 pp., Brazil.

10. Assessment of the rationale, quality and outcomes/results of activities not originally planned that technical assistance partners have carried out in connection with or as a consequence of planned activities and work/presence in the field

AMI/RAVREDA expanded activities to deal with other priority problems not addressed under the stated expected results; it also provided assistance when programs manifested a desire to improve their organization and performance. In addition, programs used AMI/RAVREDA as a model for review and analysis of other problems, as well as a channel for international contacts. For example, AMI/RAVREDA was of great help in revitalizing the Malaria Control Program of the State of Acre, Brazil, following a

worsening of the epidemiological situation during the first half of the past decade.⁸ The Initiative generated continuous flow and exchange of information and other products among AMI participating countries. For example, while the evaluation team was in El Oro, on the border between Ecuador and the city of Tumbes, Peru, and following a meeting of malaria staff of both countries, the SNEM (Ecuador) provided drugs and other inputs to their colleagues in Peru. The malaria clinic in El Oro extended its daily hours of operations to provide diagnosis and treatment to Peruvian patients. Also, AMI/RAVREDA, through PAHO, assisted the three countries visited in the preparation of funding proposals for the Global Fund, all of which were approved for a period of five years.

11. Entomology and Vector Control

Vector control programs in Ecuador and Colombia were evaluated against the expected results of AMI and RAVREDA. In particular, the reliability and standardization of vector surveillance, and evidence based vector control activities were examined.

In general, entomological programs at the department or provincial and local levels in evaluated countries are in their infancy. There is a critical lack of effective and efficient use of data collected from evaluations to determine success and implementation of changes in protocol and control strategy. Collection of biological information relies on standard/historical methods, with little insight into its meaning and use.

Three main areas of surveillance and monitoring were evaluated: vector biology; decision making related to insecticide resistance; and vector control (e.g. impregnated bed nets usage, integrated vector control). Following are the main observations of the evaluation.

Colombia

AMI/RAVREDA supported several programs that had an entomological component. These programs strengthened entomology laboratories at the central and provincial levels with workshops, training, equipment, and consumables, as well as hiring entomologists, who brought about the evaluation of resistance to insecticides and of insecticide residual effects on bed nets. Also, along with PAHO staff, they participated in the development of guidelines for vector control. One major strategy in this cooperation is to prioritize, stratify, and focus control efforts based on epidemiological data and vector characteristics. Entomologists at the department level have been trained by the Instituto Nacional de Salud (INS)/Ministry of Health; 31 of the 32 departments have an entomologist as well as approximately eight entomology technicians.

Vector biology

Epidemiologically, mosquito species primarily incriminated in malaria transmission in Colombia are *An. darlingi*, *An. albimanus*, and *An. nuneztovari*. Other local and regional anophelines are suspected of being associated with malaria transmission, including *An. pseudopunctipennis*, *An. punctimacula*, *An. calderoni*, *An. neomaculipalpus*, *An. lepidotus*, *An. neivai*, *An. rangeli*, and *An. oswaldoi*. Of these, several are considered species complexes, and efforts are ongoing to sort out their taxonomic differences, biology, and vector potential. Taxonomic keys were being updated taking into consideration the species complexes. These factors make decisions on vector control more difficult.^f

Vector distribution maps are being developed with MOSQMAP in cooperation with the [Smithsonian Institution](#) of the United States of America.

Site visit: The evaluators visited Choco to review the entomology laboratory. A general vector distribution map has been developed, and sentinel sites selected to study the three primary vectors. CDC/AMI/RAVREDA guidelines were followed to study mosquitos indoors and outdoors; collecting indoor resting mosquitoes; and determining female age using parity. During the evaluation visit, results of the observation of *An. darlingi* biting habits in 2007 and 2008 were presented. Major seasonal differences were found, with a larger number of mosquitoes collected during the month of June. Biting activity was highest outdoors. *An. darlingi* showed a bimodal peak, being more abundant at dusk and dawn. Parity data showed no trends.

Insecticide resistance

A national level surveillance network was established to monitor insecticide resistance. As of this date, 65% of all departments have trained personnel in evaluating insecticide resistance, focused on *An. darlingi*, *An. albimanus*, and *An. nuneztovari*. So far, the CDC bottle method has been standardized; diagnostic doses for insecticides used in malaria control to evaluate vector susceptibility have been determined; biochemical standards to determine mechanisms of insecticide resistance have been established; and the judicious use of insecticides at the local level has been facilitated. Results of studies from 2004 to 2007 are presented in table 6.

^f Note: A review of malaria vector biology in Colombia was recently published in Montoya-Lerma et al., *Malaria Vector Species in Colombia: a Review*, Mem. Oswaldo Cruz, in press.

In Choco, fenitrothion (50 µg) was tested against *An. albimanus*, with 100% mortality for both the CDC bottle and WHO impregnated paper tests. The effect of permethrin was tested by the bottle method, and mosquito mortality was 100% as well.

Impregnated mosquito nets

National level workshops have been conducted on the distribution and installation of impregnated bed nets. Priority locations for implementation were selected, and activity plans developed for each department. There have been some difficulties related to staff hiring, coordination among institutions, and insufficient field personnel to distribute nets in some departments. One goal of the INS is to guarantee that bed net implementation is a priority.

As part of a pilot study conducted in Choco in 2008, impregnated mosquito nets were distributed to every household (2 410 in total) in the locality of Pizzaro, municipality of Bajo Baudó; an education program was part of the activity. The primary vector in this area is *An. albimanus*. The study measured entomological parameters, including abundance indoors and outdoors; indoor mosquito resting; parity; and mosquito net residual insecticide duration. Results for abundance and parity were variable before and after the intervention, and showed no trends. The number of mosquitoes resting indoors decreased significantly after the introduction of bed nets. This may be the best indication of the insecticides' potential repellence effect. Six post-implementation evaluations took place, the last one in December 2009. The number of malaria cases fell over the study period, but no study was conducted to determine whether bed nets were the primary reason for the decrease in malaria incidence.

Testing bed nets for insecticide residual effect followed established protocol. In October 2008, mosquito mortality on two bed nets was 43% and 20%. Washing the nets decreased mortality even further; by March 2009, mortality was down to <4%. Activation increased mortality, but decreased again after washing.

The absence of window and door wire mesh for protection from mosquito bites indoors caught the evaluators' attention. This situation was observed in suburban areas of Rio Grande do Sul, Brazil, in homes where mosquito nets are being used.

The malaria program in Choco plans to expand its bed net program to other priority communities.

Other vector control interventions

Indoor residual spraying (IRS) is used in Colombia for malaria vector control. The exact extent of the program is unknown. In Choco (Boco de Pune, Medio Atrato), where *An. darlingi* was the main vector, a study was conducted in September 2007 using fenitrothion (40%). A total of 58 out of 63 houses were sprayed. Indoor and outdoor biting rates decreased between June 2007 and June 2008. The residual

effect of fenitrothion was evaluated and showed >90% mosquito mortality up to seven months after application. No integrated vector control management programs are in place at the time of the visit.

Summary

In Colombia, the vector situation has been described. *An. darlingi*, *An. albimanus*, and *An. nuneztovari* are the primary vectors for malaria. Efforts to get a better understanding of the taxonomy of species complexes are ongoing, and vector biology studies are underway in a few locations. Vector distribution maps have been developed and are being updated as information is collected. An insecticide resistance surveillance program has been implemented, and tested with primary vectors in priority regions. Internal conflicts make it difficult to implement vector control in the Amazon and other localities.

Guidelines for vector and disease surveillance have been developed by the Ministry of Health in cooperation with the INS and PAHO/WHO. Policies and strategy documents were available for the implementation of a national bed net distribution program, including a monitoring component. No information was provided on the number of bed nets distributed, community involvement, or a timetable and number of bed nets to be distributed over the next five years. Indoor residual spraying is part of the national vector control program, but exact details of national and departmental strategies were not provided. A well-designed IRS impact evaluation was shared with the evaluators in the Department of Choco. The study followed WHO protocols and was conducted in a high priority site. No evidence of larval control or integrated vector management programs was observed.

Recommendations

1. AMI/RAVEDA should determine the value of routine collection of parity data.
2. The use of indoor resting collections of anophelines before and after implementation of bed nets should be the primary entomological impact evaluation method. A protocol should be developed, perhaps using short-term knockdown insecticides. Other entomological parameters show considerable variability over time and space, and may not show the impact of bed nets on the vector.
3. Department level entomologists should be trained in the analysis and interpretation of data collected during surveillance and control interventions.
4. Professional training in mosquito identification should take place periodically, due to the ever changing classification of malaria vectors in Colombia.
5. Training in vector control management should be provided, and a review and update on the biology, control, and taxonomy of malaria vectors in the Americas should be conducted, as there have been very few reviews on these subjects in recent years. The last one was done in 1992.^{9,10}

Ecuador

Each province in Ecuador has a SNEM office. Twelve sentinel localities in seven provinces were part of AMI/RAVEDA. Five sites were activated and four are functioning as planned. The sentinel site in the Amazon locality is not yet operational. Ten professionals were trained in entomology, but at present, only four are actually working as entomologists of the SNEM at the provincial level.

During this evaluation, entomology program activities were presented by entomologists from two SNEM Zones, VII and VIII (Las Esmeraldas and El Oro, respectively) in a meeting with the National Malaria Control Program, PAHO's technical advisor, external consultants and others. The meeting was held in Guayaquil on 31 May 2011. A subsequent field visit was made to Zone VIII.

Vector biology

Vector species and their distribution in Ecuador are not well understood, except for the main coastal vector, *Anopheles albimanus*. No long term studies have been conducted in the Sierra (mountain) Region or the Amazon Basin. Historic data, surveys, and unpublished data on the regions' vectors indicate that *An. pseudopunctipennis* is the main vector in the foothill and Sierra areas, and a range of other vectors, except for *An. darlingi*, are found in the Amazon region.

Anopheles albimanus and *An. punctimacula* have been surveyed in Zone VIII, and *An. albimanus*, in Zone VII, from 2008 to 2011. Entomology laboratories of both Zones VII and VIII have followed AMI/RAVEDA guidelines, by selecting sentinel sites based on epidemiological information. Baseline data on mosquito biting habits, activity periods, and population age (parity) have been collected. With a few exceptions, *An. albimanus* showed a bimodal behavior, with a large peak in biting activity between 6.00 and 10.00 in the evening, and a smaller peak between 6.00 and 7.00 in the morning; biting activity did occur all night long. Outdoor biting density was greater than indoor biting density in most cases. Monthly parity data did not show seasonal trends. Overall, mosquito abundance increased after rainfall. *Anopheles punctimacula* was most abundant in Zone VIII, Canton El Guabo, locality of Barbones. Few studies have been conducted on the vector's biology and behavior. No information was available on *An. calderoni* and *An. pseudopunctipennis*, potential vectors that have been previously recorded in coastal Ecuador. Larval habitats of anophelines are being examined in Zone VIII, and the information collected was mapped for potential larval control interventions.

Resistance to insecticides^{11,12}

Resistance threatens the success of mosquito control. As a consequence, AMI/RAVEDA Ecuador began a program of early detection, surveillance, and decision making related to the selection and use of insecticides. The SNEM used two methods to determine adult mosquito response to a given pesticide

and potential insecticide resistance, i.e., the bottle bioassay, and the WHO impregnated paper. The bottle method was used to detect potential resistance to a given insecticide, determined by <80% vector mortality. The WHO impregnated paper also used a vector mortality of <80% as indicator of resistance.

Zone VII: deltamethrin, permethrin, and malathion were tested from 2009 to 2010 on *An. albimanus*. Results of the bottle test in one assessment of deltamethrin showed 100% susceptibility to the insecticide; however, other tests using the WHO impregnated paper suggested resistance to deltamethrin (72%-79.9% mortality). Mosquitos of the *Anopheles albimanus* species were susceptible to both permethrin and malathion (100%).

Zone VIII: In this zone (province of El Oro), a series of susceptibility tests were conducted from 2009 to 2011 (Table 6) with malathion, fenitrothion and deltamethrin. *Anopheles albimanus* showed resistance to deltamethrin in the Canton of Huaquillas, locality of Primero Mayo, by both the bottle test method (32.5%), and the WHO impregnated paper test (28.7%, 33%). In the Machala Canton, locality of Los Angeles, *An. albimanus* showed resistance to fenitrothion (56%).

Insecticide resistance monitoring continues in selected localities (e.g., El Oro). No clear strategy has been defined to decrease the risk of resistance. Data from other sentinel provinces were neither presented nor discussed, therefore, it is unknown at this time whether susceptibility testing for insecticides was conducted.

Impregnated mosquito nets

Studies were underway in Zones VII and VIII to implement community-based net distribution, training, education, and insecticide application monitoring. In the Amazon region, a plan was available for massive distribution of bed nets. In Zone VIII, 11 localities in two cantons were selected for implementation of impregnated mosquito nets in 2008 (Table 7). Residual effects of insecticides were monitored on three occasions. In 2010, residual effects dropped to 54% and 34% in the two cantons. Efforts were ongoing to train and educate communities on the use and care of nets; however, the impact of using impregnated nets on malaria transmission has not been evaluated.

Table 6. Results of Insecticide Susceptibility Testing, El Oro Province, Zone VIII, Ecuador, 2009-2011

Canton	Locality	Month of Test	Testing Method	Species	Insecticide	Doses	Mortality (%)	
							At 30 min	At 60 min
2009								

Machala	Los Angeles	June	Bottle	Albimanus	Deltamethrin	12.5 µg/ml	93.3	98.30%
Huaquillas	Primero Mayo	June	Bottle	Albimanus	Deltamethrin	12.5 µg/ml	32.5	81.25%
		June	Bottle	Albimanus	Malathion		76.3	91.56%
El Guabo	Barbones	June	Bottle	Puntimacula	Deltamethrin	12.5 µg/ml	82.5	93.75%
2010								
Machala	Los Angeles	May	WHO	Albimanus	Deltamethrin	0.05%	81.3	
		May	WHO	Albimanus	Malathion	5.0%	96.6	
		June	WHO	Albimanus	Malathion	5.0%	82.6	
Santa Rosa		June	WHO	Albimanus	Fenitrothion	1.0%	66.6	
		June	WHO	Albimanus	Deltamethrin	0.05%	86.6	
		October	WHO	Albimanus	Deltamethrin	0.05%	28.7	
Huaquillas	Primero Mayo	October	WHO	Albimanus	Deltamethrin	0.05%	33.0	
		October	WHO	Albimanus	Malathion	5.0%	85.0	
		October	WHO	Puntimacula	Fenitrothion	1.0%	100.0	
El Guabo	Barbones	October	WHO	Puntimacula	Deltamethrin	0.05%	87.5	
		October	WHO	Puntimacula	Malathion	5.0%	100.0	
		October	WHO	Albimanus	Fenitrothion	1.0%	98.0	
Machala	Los Angeles	October	WHO	Albimanus	Deltamethrin	0.05%	93.3	
		October	WHO	Albimanus	Malathion	5.0%	93.0	
Huaquillas	Primero Mayo	March	WHO	Albimanus	Malathion	5.0%	98.0	
		March	WHO	Albimanus	Fenitrothion	1.0%	80.0	
Machala	Los Angeles	April	WHO	Albimanus	Malathion	5.0%	93.0	
		April	WHO	Albimanus	Fenitrothion	1.0%	56.0	
Arenillas	Carcabon	April	WHO	Albimanus	Malathion	5.0%	85.0	

Table 7. Mosquito net implementation, Province of Oro, Zone VIII, Ecuador, 2008-2009

Canton	Parish	Date	Locality	No. of nets distributed	Monitor -ing events	Average No. of Washes	Residuality (%) Feb. 2010
Machala	9 de Mayo	30 Oct. 2008	San Fernando	69	3		
		20 Nov. 2008	San Luis	73	3	8	54
		22 Dec. 2008	Los Angeles	148	3
		Jan. 2009	Veinte de Noviembre		3
El Guabo	Barbones	Jun. 2008	Kuwait	104	3		
		May 2008	Samuel Quimi	94	3	13	34
			Brisas				
		May 2008	Barboneñas	180	3		
		Jun. 2008	Mariscal Sucre	156	3		
		May 2008	Buenos Aires	451	3		
	Jun. 2008	5 de Junio	162	3			

Other vector control interventions

Indoor residual household spraying is sporadic, depending on the region and the need (once or twice a year). For example, in Zone VIII, residual house spraying was done in the locality of Barbones, where indoor resting anophelines were found. When entomological surveillance indicated that the vector did not rest indoors, no IRS was used; rather, biological control and environmental management for larval control was applied, mainly in brick makers' burrow pits (Figure 1) and abandoned shrimp ponds. Entomology maps are used to monitor breeding sites. Entomological surveillance data were incorporated into the decision making process for malaria control. In the Amazon region, space spraying appeared to be used when needed. Information on vector biology and surveillance activities in the latter region was unavailable.

Summary

Personnel have been trained and performed high quality and accurate data collection on vector biology, insecticide resistance monitoring, and residual effect of insecticides on mosquito nets. No evidence of an established larval control program or integrated vector management program was observed other than that for Zone VIII.

With the potential risk of a huge malaria outbreak occurring during an El Niño event, a national and regional plan to prevent and intervene against *An. albimanus* should be developed in preparation for the next such event. The plan would help prevent a rapid increase in the number of cases of malaria along the coast of Ecuador. It would be a tragic blow to the last 10 year achievements in malaria control in the coastal region of Ecuador, if preventive and emergency control measures were not in place.

There is a potential risk of *An. darlingi*, the primary vector of *Plasmodium falciparum* in the Amazon Basin, reaching the Amazon region of Ecuador from its present northern distribution in the Peruvian Amazon. This risk should be evaluated.

Recommendations

1. Monitoring and surveillance programs should be implemented in other localities in the coastal region (e.g. coastal border with Colombia), the Sierra region, and in the Amazon Basin.
2. The role of *An. calderoni*, *An. punctimacula*, and *An. pseudopunctipennis* as potential vectors along coastal Ecuador should be evaluated.
3. The biology of *An. pseudopunctipennis* in the Sierra region needs to be reviewed, and a baseline study of Amazonian vectors should be initiated.

4. Entomology staff should be trained in each zone, in particular, on the analysis and interpretation of data they collected themselves.
5. Training in vector control management should be provided, and a review and update on the biology, control, and taxonomy of malaria vectors in the Americas should be conducted.
6. SNEM and AMI/RAVREDA should determine the true value of routine collection of parity data, and the need to continue intensive collection of *An. albimanus*, which has shown the same characteristics throughout its territorial range.
7. Vector monitoring should address other vector species and the study of parameters that would lead to integrated vector control in areas where such monitoring would be feasible.
8. Indoor resting collection of anophelines before and after implementation of bed nets should be considered the primary method for evaluating entomological impact. A protocol should be developed, perhaps including the use of short-term knockdown insecticides. Other entomological parameters showed considerable variability over time and space, and may not be able to show the impact of using bed nets on vectors.
9. A national and regional plan to prevent a potential malaria outbreak along the Pacific Coast caused by *An. albimanus* should be developed in preparation for El Niño events.
10. A vector control and surveillance program should be implemented in the Amazon region of Ecuador.

Figure 1. Picture of brick makers' burrow pit in Ecuador.



12. Current situation and future needs of AMI

Even with the shortcomings described in previous paragraphs, which may indicate that malaria prevention and control programs in countries of the Amazon basin are works in progress, AMI has evidently achieved its expected results in Brazil, Colombia, and Ecuador, as it has: documented the extent of parasite resistance to antimalarial drugs; proposed and achieved modifications of malaria treatment guidelines and policies, and established a system for monitoring future developments and guide change. In addition, AMI contributed to:

- improvements in training of malaria microscopy technicians; the development of guidelines and improved quality control of microscopy work; and the establishment of a foundation for a QC/QA and performance evaluation system for microscopy;
- improvements in storage and distribution systems for drugs and insecticides;
- development of operational guidelines for the main program activities.

As for malaria control effectiveness, activities in Ecuador have been quite effective, considering the significant decline in the number of malaria cases, as it has in the Brazilian Amazon. In Colombia, multiple problems have prevented similar successes; nevertheless, the situation is currently being focalized and, with Global Fund resources for the Pacific areas, the program seems to be on the right path.

Efficiency, on the other hand, is very difficult to judge, since several interventions are being implemented without adequate evaluation or clear technical justification. It may be argued that most of the positive effects observed during the past few years could be attributed mainly to improvements in treatment policy and a shorter interval between onset of symptoms and appropriate treatment, given the increased access to diagnosis and the use of effective drugs. It should be noted that in remote Amazon areas of Colombia and Ecuador, the interval between onset and treatment of malaria has not decreased, and treatment delays are usual.

The actual contribution of indoor residual spraying to malaria control as applied today in many areas is being questioned, particularly, where transmission seems to occur predominantly outdoors and where the quality of spraying may be well below standards. The effectiveness of measures such as fogging and various forms of larval control is even more questionable.

Efforts should be made to evaluate the impact of introducing insecticide treated mosquito nets, which seem perhaps the most effective vector control intervention in AMI countries. Procurement of long-lasting insecticidal mosquito nets for the Global Fund project in the Pacific area of Colombia has been

based on an assessment of requirements in different areas of nets of various types (single, double, extra-double and hammock), depending on ecological and socio-demographic characteristics. For example, extra-double nets are required for areas of very high temperature or for some indigenous populations who sleep in groups in rather small huts, while others require hammock nets. A preliminary small scale study in Colombia's Pacific area seems to indicate that the main effect of ITNs on *A. albimanus* was preventing mosquito entry into the personal sleeping space under an impregnated net, and not on mosquito mortality.

13. What has worked well within the Initiative?

As highlighted in the preceding analysis, most activities under the original AMI/RAVREDA program were aimed at improving diagnosis and treatment, and have been or are being implemented satisfactorily, from policy development to field application. Broadening the Initiative to incorporate other supportive activities, such as laboratory diagnosis quality assurance or drug delivery logistics, developed progressively. The expansion responds to the Initiative's holistic approach to the goal of improving diagnosis and treatment.

The addition of entomology interventions is also relatively new. However, in spite of the fact that said activities do not appear to have been fully mainstreamed into AMI/RAVREDA, at least in Ecuador and Colombia, malaria control programs have deployed well trained teams that have started a coordinated mapping of insecticide resistance and the collection of baseline data on vector biology and behavior. Unfortunately in spite of their discipline and dedication, they face logistic problems and financial difficulties that have slowed down their deployment.

14. Other support for the Initiative

AMI/RAVREDA has been quite successful at the international and national levels in attracting the support of organizations and institutions concerned with malaria as a health problem. It has also, as mentioned above, supported countries in securing funding from the Global Fund to improve malaria control in problem areas.

As control programs become stronger and gain success in interrupting transmission among relatively stable populations, malaria will be progressively more focalized among totally or partially isolated population groups due to ecological, social, political or cultural barriers. Malaria control in those situations will require novel and diverse approaches, as well as reformulation of program policies. In preparation for those needs, AMI/RAVREDA could strengthen its contacts and consider the

establishment of formal collaborative projects with other organizations working in the Amazon, not necessarily in malaria, but also on development or welfare programs for isolated populations. Examples of such programs are *Desarrollo Sostenible en el Estado de Acre* (Sustainable Development in the State of Acre, Brazil); research councils of the countries participating in AMI/RAVREDA; the Agency for Financing Studies and Projects from Brazil; countries participating in the *Convenio Hipolito Unanue*, and multilateral development banks.

15. Problems or obstacles within the Initiative that require further tuning

Coordination

It appears that AMI/RAVREDA's capacity to coordinate the follow-up of agreements reached in annual meetings has diminished, so that the more recent program expansions have not been as harmoniously developed. For example, new activities, such as the production of operational guidelines, do not seem coordinated, a situation similar to that of earlier times in the implementation of AMI/RAVREDA. The guidelines themselves give the impression of being early drafts that still need to benefit from a joint critical review and revision to improve their adaptation to the various operational levels where they may be needed. At least in part, this may be attributed to the fact that the post of RAVREDA coordinator remained vacant for 2 years. (The post has now been filled). It is also true that the newly added fields of entomology and epidemiological surveillance, as well as new interests in researching more basic aspects of resistance and pharmacology, are much broader and, therefore, less concrete and standardized than the original purpose of improving diagnosis and treatment.

Since 2006, a number of operational guidelines and manuals have been developed with the support of AMI/RAVREDA. There are considerable conceptual differences among these documents. Some of them are addressed to field workers, while many others don't seem to have a clear readership, reflecting instead a collection of suggestions by groups of specialists. Particularly confusing is the proliferation of documents and guidelines on entomology and vector control,^g which contrasts with the slow deployment of entomological teams in the field. These documents include:

^g Sample documents: Reunión sobre el uso adecuado de la entomología en los programas de control de malaria de las Américas (Ciudad de Panamá, 1-4 agosto 2006); Estrategia para la toma de decisiones en control racional de vectores de malaria en la Región de las Américas (20 pages + 38 pages of anexes); Anexo 11: Procedimientos e

Another concern regarding the above documents is their rather theoretical approach, which depicts the role of entomology as essential for the development of rational malaria control strategies. For example, there is emphasis on the need to base the selection of vector control interventions on prior studies of vector biology and behavior. The current situation in most circumstances is that control programs are using vector control interventions based on tradition and availability of human and material resources (IRS), empirical extrapolation of outside experiences (ITNs), popular and political demand for visible action (fogging) or the empirical reasoning that, if there are large mosquito breeding sites, the use of larvicides should be indicated. Under these circumstances, the main challenge is trying to estimate the value of each measure for control of transmission in each relevant locality.

As vector control has to be implemented in the context of consistent improvements in diagnosis and treatment, a decline in parasite rates is not a simple indicator of success for vector control. It is therefore necessary to look for intermediate results. For example, in order to monitor the effect of larvicide application, monitoring larval mortality is not very useful; rather, monitoring the impact on adult mosquito density would be indicated (man biting rates and resting densities); also the area where this effect is achieved needs to be determined.

The document *Gestión para la Vigilancia Entomológica de la Transmisión de Malaria* (Management for Entomological Surveillance in Malaria Transmission) goes a step further in its theoretical approach. Aside from quoting 61 bibliographical references, it proposes the stratification of malaria areas according to risk factors (relative and attributable risks and risk ratio), based on some PAHO proposals of the late 1980s and early 1990s that tried to adopt methods developed for the multifactorial etiology of chronic diseases for the study of malaria epidemiology.

In the field, entomological teams seem to follow a work plan that is independent of the requirements of epidemiological surveillance, and, as indicated in the entomological section of this document, accumulated a long list of routine observations (all night captures and parity) that confirm well known facts. In addition to the teams' weaknesses (only two teams seem to be fully operational in Ecuador, and

indicadores entomológicos para toma de decisiones en control vectorial en malaria en localidades seleccionadas; Gestión para la vigilancia entomológica y control de la transmisión de malaria. Plan Nacional de Salud Pública, Colombia; Estrategia para racionalizar la toma de decisiones en control vectorial en malaria. Red Amazónica de Vigilancia de la Resistencia a los antimaláricos (39 slides).

none in the Amazon area of either Colombia or Ecuador), their possible isolation, and lack of transportation and per diem support, are further obstacles to field work.

The dissociation of entomology and program evaluation was also evident in a presentation (May 2011) on the experience with LLINs in Acre, in which only data on distribution and acceptance were described, without any entomological information.⁸

It may be suggested that the amount of practical guidance is inversely proportional to the number of guidelines. This was well pointed out in a stakeholders meeting: "From the handout on pilot experiences that we received at the meeting, it appears that many countries are routinely collecting a variety of information that is of little or no practical value for making vector control decisions, e.g., data on parity, so countries also need to understand what value additional, more specific variables, might have and when that data should be collected" .

Epidemiological surveillance

This area suffers not only from an apparent dissociation from entomology, but also from its almost exclusive concern with the quantification of positive cases, and the calculation of traditional indices of malaria eradication campaigns. Most documents dealing with epidemiological stratification propose the use of ecological and social factors to characterize problem areas in terms which may guide the selection of intervention approaches, conceptually more or less in line with eco-epidemiological typing as recommended by the malaria control strategy (WHO, [Technical Report Series No. 936](#)). However, all stratification systems in use are based on different forms of grouping administrative areas based on the number of malaria cases detected. It is interesting to note that, as an exception, Ecuador is proposing a stratification of malaria based on major national ecological characteristics, i.e., riverine areas in Amazonia; piedmont towards the Amazonia (axes of road penetration); coastal piedmont and plains of the Esmeralda river (northern Pacific coastal area), and dry coastal area.

Ideally, characterizing eco-epidemiological differences should be pursued to more peripheral levels. Most descriptions of epidemiological situations, including a recent outbreak in the spring of 2010, in the area of the Global Fund project in Colombia, are incomplete, as was evident in the report of two foci in the departments of Antioquia and Choco. In that report, the outbreak investigation goes no further than a simple description of cases by species, and the number of complicated cases and death, by municipality, without any discussion of the differences between the two main foci. For example, the difference in the proportion of cases by *P. falciparum*: about 25% in the main focus of Antioquia, and about 50% in Choco. Such variation may very well be related to the proportion of population of African descent in each focus, but it would have been interesting to know whether there were also differences

in the vectors involved. Similarly there was no attempt to relate the outbreak to any changes in meteorological variables. In addition, the report uses the endemic-epidemic channels with certain methodological errors.

16. Areas in malaria prevention and control that AMI should address in upcoming years

The same mechanisms influencing AMI/RAVREDA's success in the improvement of malaria case management in partner countries should be revitalized and focused to address major remaining obstacles in malaria control in the subregion. Essential mechanisms of that past success were: the thorough study of the problem at hand throughout the established network of collaborating countries; an open exchange of ideas and experiences energized and supported by an active coordinator; and a periodic joint critical analysis in face-to-face meetings of main stakeholders to review progress and adjust plans.

The revival in full force of AMI/RAVREDA is not only feasible and desirable; it should be the most effective and efficient way to attain the best results in the most recent initiatives of AMI/RAVREDA, which appear to have lacked coordination in different countries.

The main areas in which AMI/RAVREDA should concentrate in upcoming years should include:

1. **Monitoring of resistance.**¹³ This area of work should continue in Amazon countries. The possibility of using fewer test subjects and/or combining results of different testing sites as per the WHO protocol should be explored. Surveillance of antimalarial drug resistance in Central America should be consolidated.
2. **Microscopy diagnosis.** To continue. There needs to be a new way of thinking about quality control. Efforts to develop an effective, accurate, and timely QC/QA system have been insufficient. Laboratories should be further strengthened to improve staff competency and performance regarding malaria diagnosis.
3. **Quality of medicines.** Continue to provide guidance on quality management systems and training in pharmacopeial techniques; implement methods to monitor and control storage and distribution conditions for antimalarial drugs endemic areas; and increase awareness of drug quality as a matter of patient safety.
4. **Epidemiological surveillance.** Modify information systems and analysis to:
 - Integrate epidemiological and entomological surveillance.
 - incorporate geographical information to allow geographical analysis of case distribution;

- conduct epidemiological surveys in localities presenting case clusters;
- stratify problem areas (or areas where outbreaks occurred) according to ecological and social characteristics.

5. Review guidelines for entomological studies to ensure a clear distinction between:

- completion of basic data on vector distribution and behavior, after collecting all existing information on the subject;
- assessment of the contribution of various interventions towards control of transmission in time and space;
- monitoring continued efficacy of vector control measures in use; and develop maps of insecticide resistance;
- contribution to epidemiological investigation of localities and problem areas, taking into account possible changes from the time of onset of cases and the time of investigation;

Work on the above points will require prioritization based on degree of urgency.

6. Integration of epidemiology and entomology^{14,15,16}

- there needs to be a strong epidemiological/entomological surveillance system throughout the Amazon area capable of detecting the potential spread of *P. falciparum*, which has not yet reached the Amazon areas of Colombia and Ecuador. GPS should be adopted to address problems or impending risks.
- the emergence and spread of *An. darlingi* in the Amazon area of Colombia and Ecuador needs to be monitored, given that it may precede the epidemic spread of *P. falciparum*. Monitoring should be implemented in potential points of entry of *P. falciparum* or *An. darlingi*, such as those with significant boat or land traffic between infected areas, new settlements, points of attraction for laborers or exploitation of resources, and others, where sentinel posts could be established.

7. Review approaches to integrate the use of diagnostic facilities for disease case management, including:

- optimization of case detection systems, concentrating on passive case detection, locality investigations, and fever surveys in the study of outbreaks;
- addressing the management of malaria-negative cases by a) widening the competence of microscopy technicians to identify other parasites and perform other simple diagnostic tests, e.g., tuberculosis, as is being done in Cruzeiro do Sul, Brazil; as well as stressing quality assurance and performance evaluation of microscopy technicians; b) improving patient

counseling and acceptance within the referral system (hospitals or health centers); c) review approaches to case management for marginalized and illegal populations.

8. Develop realistic guidelines for different operational levels:

- review existing manuals as sources of material to clarify what each operational group or level should do;
- review training courses and materials for all technical personnel assigned to malaria programs;

17. Relevant research on malaria in participating AMI/RAVREDA countries: the example of Brazil and Colombia

Through the years, the relationship among academic institutions and Ministries of Health from the Amazon basin countries has strengthened. Although not new, this relationship was nurtured and energized by AMI/RAVREDA, as seen in Brazil and Colombia. The research community's support to the goals and objectives of AMI/RAVREDA was evident in the research topics chosen by institutions from participating countries, whether or not supported by Initiative partners, CDC or PAHO. Research on the following topics was carried out in participating countries:

- selection of suitable antimalarial drugs to prevent morbidity and/or mortality from malaria. Research in this area is of paramount importance, and should, therefore, continue, especially in regard to treatment effectiveness and safety of combined anti-malarial drugs against uncomplicated *P. falciparum* in vivo;
- evaluation of *P. vivax* resistance to antimalarial drugs;
- plasmodia in vitro resistance;
- identification of molecular markers of resistance in different geographical areas;
- malaria complications in human pregnancy; and
- protection provided by impregnated bed nets. (The results of this activity were not presented to the evaluators)

Given the remoteness of areas where malaria is present, the gold standard for diagnosis (parasite identification in Giemsa-stained blood smears by microscopy) cannot be applied, because either trained personnel and/or equipment are not available. This has led to development of rapid diagnostic tests that assure a quick diagnosis and eventually antimalarial treatment. RDTs are immunochromatographic tests that detect specific parasite antigens through antibody capture. The main antigens detected by RDTs are

lactate dehydrogenase, aldolase (panspecific, which is present in all *Plasmodium* species), and histidine-rich protein 2 (HRP2), which is specific to *Plasmodium falciparum*. Most RDTs available use HRP2 as a target. However, it has been reported that sequence variations of this antigen, particularly the types and number of specific amino acid repeats, can affect the sensitivity of HRP2-based RDTs at low parasitemia. Currently, in the Americas, there is insufficient evidence of HRP2 variability in isolates from different geographical areas, and its relationship with RDT performance. Because of this, research is needed in order to evaluate the amount of HRP2 in *P. falciparum* isolates from different malaria-endemic regions, and its relation to parasitemia, and at the end, to establish the suitability (sensitivity and specificity) of RDTs currently available.

In Brazil, research at the Evandro Chagas Institute (not visited for this evaluation) and the Foundation for Tropical Medicine of the Amazon State make significant contributions to the malaria control program. The coordination between the CDC and Brazilian researchers seems much closer than that with researchers in Colombia. Following is a list of research projects conducted in Brazil and published as a result of the Initiative.

- Malaria diagnosis and hospitalization trends, Brazil. Santos-Ciminera et al., Emerg Infect Dis, 13:1597-1600, 2007.
- Chloroquine resistant *Plasmodium vivax*. Brazilian Amazon. Santana Filho et al.. Emerg Infect Dis 13:1125-1126, 2007 (supported in part by USAID).
- Malaria is associated with poor school performance in an endemic area of the Brazilian Amazon. Victor-Silva et al., Malaria J, <http://www.malariajournal.com>. Content /8/1/230, 2009.
- Glucose-6-phosphate dehydrogenase deficiency in an endemic area for malaria in Manaus: A cross sectional survey in the Brazilian Amazon. Santana et al., Plos One 4:2009.
- Determination of blood concentration of chloroquine (CQ) and of desetilchloroquine (DCQ) in patients with malaria vivax seen the Foundation of Tropical Medicine of the Amazon State. (Supported in part by RAVREDA). Mater thesis by Marly Marques de Melo.
- Malaria in Brazil: an overview. Oliveira- Ferreira et al., Malaria J 9:115, 2010.
- Severe *Plasmodium vivax* malaria, Brazilian Amazon. Alexandre et al., Emerg Infect Dis 16:1611, 2010.

In Colombia, there are several research institutions that contribute to RAVREDA goals. In Cali, the evaluation team visited the CIDEIM, which reported late in the 1990s data on drug resistant malaria.

Among the following studies, the first two preceded RAVREDA, and provided crucial information from experience gathered at sentinel sites.

- “Assessment of therapeutic response of *Plasmodium falciparum* to chloroquine and sulfadoxine-pyrimethamine in an area of low malaria transmission in Colombia.” Osorio et al., Am J Trop Med Hyg, 61:968, 1999.
- Effects of chloroquine and sulfadoxine/pyrimethamine on gametocytes in patients with uncomplicated *Plasmodium falciparum* malaria in Colombia. Osorio et al. Mem Inst Oswaldo Cruz 97:1221, 2002.
- Assessment of therapeutic response of *Plasmodium vivax* and *P. falciparum* to chloroquine in a malaria transmission free area in Colombia. 2002 (Partially funded by PAHO), Mem Inst Oswaldo Cruz, 97: 559, 2002.
- Efficacy of amodiaquine and sulfadoxine/pirimetamine in the treatment of non-complicated malaria by *P. falciparum* in Nariño, Colombia, 1999-2002. (supported in part by TDR/WHO) Gonzalez et al Biomedica, 23:38-43, 2003.
- Evaluation of the efficacy of antimalarial treatment in Tarapacá, Colombian, Amazonas (In Spanish) By Osorio et al . Biomedica; 27:133, 2007. (This study received advisory planning from Trenton K Ruebush AMI/ RAVREDA.)

During the evaluation visit to CIDEIM, malaria researchers were enthusiastic, but raised the issue of increasing difficulties in enrolling patients with *P. falciparum* infection for in vivo efficacy studies, and the cost of such studies, which is beyond their reach. Therefore, those studies would be partially replaced by *P. falciparum* resistant studies in vitro, as well as studies to detect histidine-rich protein in *Plasmodium falciparum* isolates from Colombia. A paper on the first topic is already in press (first bullet bellow) and a second has already been published (second bullet):

- Sentinel network for monitoring *in vitro* susceptibility of *Plasmodium falciparum* to antimalarial drugs in Colombia: A proof of concept. Aponte et al., Mem Inst Oswaldo Cruz, 2011.
- Large variation in detection of histidine-rich protein 2 in *Plasmodium falciparum* isolates from Colombia. Pava, et al. Am. J. Trop. Med. Hyg, 83:834, 2010.

The United States National Institutes of Health recently designated an International Center of Excellence for Malaria Research (ICEMR) in Cali, Colombia, led by the Caucesco Scientific Research Center. This institution is proposing to collaborate with AMI / RAVREDA in the analysis of *P. falciparum* genome-wide variation in parasite populations in South America. This type of study will reveal how the history of drug

selection and different levels of spatial isolation affect distribution patterns of mutations. Genetic parameters, such as degree of gene diversity, extent of linkage disequilibrium, multilocus associations and recombination in different populations, as well as demographic parameters, such as human migration patterns and human and mosquito population densities, will allow an understanding of how drug resistance genotypes arise and disseminate under conditions of low intensity of transmission. Epidemiological models can thereafter be built and intervention measures planned.

The University of Antioquia, in Medellin, Colombia, also has a strong group conducting malaria research, and has a long record of publications. Those relevant to RAVREDA are listed below .

- Gametocyte levels in response to differing malaria treatments in two municipalities of Colombia. Arango et al , *Biomédica*;24:79, 2004. .
- Efficacy of three chloroquine-primaquine regimens for treatment of *Plasmodium vivax* malaria in Colombia. Alvarez et al *Am. J Trop Med Hyg*, 75:605, 2006.
- In vitro susceptibility of Colombian *Plasmodium falciparum* isolates to different antimalarial Drugs. Arango et al. *Biomedica*. 28:213, 2008.
- Dynamics of *Plasmodium falciparum* parasitemia regarding combined treatment regimens for acute uncomplicated malaria, Antioquia, Colombia. Alvarez et al. *Am. J Trop Med Hyg*, 83:90, 2010.
- Resistance to chloroquine is not associated to plasma levels of the drug, year 2000, Blair et al. *Rev Epidemiol Antioquia* 26:31,2000.
- “Resistencia de *Plasmodium falciparum* a tres fármacos antimaláricos in Turbo (Antioquia, Colombia), 1998. Blair et al., *Rev Panam Salud Publica / Pan Am J Public Health* 9: 23, 2001.
- Therapeutic efficacy of three treatment schemes in uncomplicated *Plasmodium falciparum* malaria in Antioquia, Colombia 2002. Blair et al., *Biomedica*, 23:318, 2003.
- Therapeutic efficacy test in malaria *falciparum* in Antioquia, Colombia. Blair et al., *Mal J*, 5: 14, 2006.
- Treatment with amodiaquine-sulfadoxine pyrimethamine is 98% effective against uncomplicated *falciparum* malaria. (Supported in part by USAID through PAHO). Carmona-Fonseca et al., *IATRENIA* 18: 26, 2005.
- Blood concentration of sulfadoxine-pyrimethamine according to the antimalarial therapeutic response in 2 municipalities of Antioquia, Colombia. Carmona et al., *Rev Panam Salud Publica*.18:75, 2005.

- “*Plasmodium vivax* malaria: treatment of primary attacks with primaquine, in three different doses, and a fixed dose of chloroquine, Antioquia, Colombia, 2003-2004”. Carmona et al., *Biomédica*; 26:353, 2006.
- Gametocytemia in falciparum malaria treated with amodiaquine or artesunate was also by Carmona-Fonseca et al., *Biomédica* 28:195, 2008.
- Therapeutic efficacy of a regimen of artesunate-mefloquine-primaquine treatment for *Plasmodium falciparum* malaria and treatment effects on gametocytic development. Vazquez et al., *Biomedica* 29:307, 2009.
- *Plasmodium falciparum*: diversity studies of isolates from two Colombian regions with different endemicity. Montoya et al. *Exp Parasit* 104:14, 2003.
- Polymorphisms of the *pfmdr1* gene in field samples of *Plasmodium falciparum* and their association with therapeutic response to antimalarial drugs and severe malaria in Colombia. Montoya et al., *Biomedica* 27:204, 2007.
- Clinical and laboratory findings of *Plasmodium vivax* malaria in Colombia, 2001. Echeverry et al. *Rev Inst Med Trop Sao Paulo*, 45:29, 2003.
- The epidemiology of complicated *falciparum* malaria: case and control study in Tumaco and Turbo, Colombia, 2003. Tobon et al., *Rev Brasil Epidemiol* 9:283, 2006.
- Danger signs in the malaria patient. Tobon A, *Biomedica*, 29:320, 2009.
- Intrauterine growth retardation, low birth weight and prematurity in neonates of pregnant women with malaria in Colombia. Tobon-Castano et al, (Partially supported by PAHO). *Rev Soc Brasil Med Trop* in press 2011.

18. Sustainability of the Initiative. Are changes in policies, strategies and activities institutionalized and sustainable?

Changes in drug policy, improvements in diagnosis, treatment and facilities are well institutionalized and have generated sufficient demand to be easily sustainable. Similarly, the involvement of researchers and academic institutions in technical guidance and training seems to be of such mutual interest that it would be sustainable. The strong interaction among AMI/RAVREDA and academic groups in Brazil and Colombia are examples that also support the sustainability of the Initiative.

Competence and performance quality assessment systems, as well as systems for drug and insecticide logistics, are such useful managerial instruments that it seems logical that programs would be interested in their further improvement and development. AMI/RAVREDA and participating countries must define

and provide recommendations regarding criteria to be used in graduating of assistance. In fact, Brazil already formally announced that it will not request further support from the Global Fund.

Last but not least, and as indicated in the recommendations, the need to improve the efficacy and effectiveness of entomological activities remains. This must be achieved through training in vector control management, ideally, based on the document *Estrategia para la toma de decisiones en control racional de vectores de malaria en la Región de las Américas*. Training must take into account the fact that its success rests on the training methods applied, specifically a change in training strategy to include experiential learning and problem solving. In addition, quality assurance issues regarding methodologies and techniques being implemented need to be addressed.

Decision making regarding vector control management must be based on knowledge of the vectors, not only local vectors, but those present at national and Regional levels.

19. Participants in meetings or interviewed by the evaluation team

Name	Affiliation
BRAZIL	
Maria Das Gracias Alecrin	President, Fundacao de Medicina Tropical, Manaus
Wilson Duarte Alecrin	State Secretary of Health, Amazonas, Manaus
Ana Ruth Arcanjo	LACEN Amazonas
Jarbas Barbosa	Health Secretary, Ministry of Health, Brasilia
Fabiana Bianchet	Municipal Advisor, Rio Preto da Eva, Proyecto Fondo Mundial
Estelita Castilho	Municipal Advisor, Fundação de Vigilância em Saúde do Amazonas, Rio Preto Municipality
Simone Daniel da Silva	Municipal Manager, Cruzeiro do Sul Municipality, Acre
Izanelda Batista Magalhães	Director, Department of Health Surveillance, SESACRE, Acre
Suely Melo	State Secretary of Health, Rio Branco, Acre
Oscar Martin Mesones Lapouble	Technical Consultant, National Program for Malaria Control, Brasília
Mayira Sojo Milano	RAVREDA Coordinator, PAHO/WHO, Brasília
Franklin Simoes Santana	Fundação de Medicina Tropical, Manaus
Ana Carolina Santelli	National Malaria Control Program, Brasília
Tayma Holanda	Gerente Estadual de Endemias. Acre.
Colombia	
Silvia Blair	University of Antioquia, Medellin
Lesly Bustamante	Hospital Cooperative of Antioquia (PAHO/WHO Collaborating Center for Drugs)
David Calle	School of Public Health, Antioquia University
Pablo Chaparro	Responsible for Public Health Surveillance, Malaria, National Institute

Fredy Cordoba	of Health of Colombia
Jose Pablo Escobar	Chief, Malaria Program, Choco, Quidbo
Armando Galeano	Health Surveillance and Disease Prevention and Control. PAHO/WHO,
Jorge Gonzales	Bogota
Guillermo Guibovich	Malaria Unit, Antioquia, Medellin
Socrates Herrera	Executive Unit, el Valle Unviversity, Cali
Juan Gabriel Jimenez	International Advisor on Disease Control, PAHO/WHO Country
Ana Cristina Nogueira	Representative Office, Colombia
Adriana Pabon	International Centers of Excellence for Malaria Research
Julio Padilla	University of Antioquia, Medellin
Marta Quiñones	PAHO/WHO Country Representative
Nancy Saravia	University of Antioquia, Medellin
Cesar Segura	Coordinator, National Prevention and Control Program for Malaria and
Edison Soto	Other Vector-Borne Diseases
	Entomologist, Health Unit, Cali
	General Coordinator, CIDEIM, Cali
	University of Antioquia, Medellin
	Project Manager, Global Fund financed Malaria Project
Ecuador	
Efrain Beltran	National Malaria Eradication Service (SNEM)
Gustavo Bretas	Health Surveillance and Disease Prevention and Control, PAHO/WHO,
Enrique Castro Suarez	Guayaquil
Fatima Franco	National Malaria Eradication Service (SNEM)
Javier Guerrero	Under Secretary of Health for the Coastal Area, Guayaquil
Mauricio Muñoz	National Malaria Eradication Service (SNEM)
Mercy Silva	National Malaria Eradication Service (SNEM)
Julio Valencia	National Malaria Eradication Service (SNEM)
Raul Veloz	Director, National Malaria Eradication Service (SNEM)
Honduras	
Tamara Mancero	Health Surveillance and Disease Prevention and Control, PAHO/WHO,
	Tegucigalpa (phone interview)
Peru	
Jaime Chang	Infectious Diseases Initiative, United States Agency for International
	Development, Lima (phone interview)
United States of America	
Maria Paz Ade	Malaria Regional Program, PAHO/WHO, Washington, DC
Keith Carter	Malaria Regional Program, PAHO/WHO , Washington, DC
Alexandre Macedo	Malaria Advisor, United States Centers for Disease Control and
	Prevention, Atlanta, Georgia, USA

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