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Pan American Health Organization's Proposed Contribution to the United States Agency for International Development (USAID) / Latin America and Caribbean Bureau's Amazon Malaria Initiative (AMI):

Project Proposal and Workplans for Years 2 & 3



(March 2003)

**Communicable Disease Unit
Division of Disease Prevention and Control**

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I. Background

1. Available Data

In the Region of the Americas, the most common parasites in malaria infection are *Plasmodium vivax* and *Plasmodium falciparum*. The later produces the highest lethality and has been increasing in the Americas in the last decade.

Based on 2001 data, the total occurred cases of *Plasmodium falciparum* in the Region of the Americas was 277,773, of which 95 % were recorded in the Amazonian countries (Bolivia, Colombia, Ecuador, Guyana, French Guyana, Peru, Suriname, and Venezuela), where activities to determine the resistance of this parasite to the anti-malarial drugs are being carried out. Furthermore, 84% of the 219 dead reported in the region occurred in the countries sharing the Amazon jungle.

Efficacy studies conducted in Peru during 2001 reported *Plasmodium falciparum* resistance to chloroquine (the first-line treatment) and to Sulfadoxine pyramethamina (a second-line antimalarial drug) in different country areas. These results led them to change the treatment schemes. Moreover, in Bolivia they have conducted similar studies, with mefloquine (monotherapy) versus mefloquine plus artesunate and mefloquine alone. Based on whose results, also new treatment schemes were adopted.

2. Prior Activities

In 1998, the Pan American Health Organization (PAHO), Regional Office of the World Health Organization (WHO) convened a group of experts in Brazil to review a protocol for monitoring the efficacy of anti malarial drugs. The group developed a standardized method for evaluating the therapeutic efficacy of malarial drugs used in the management of cases of *P. falciparum* in the Americas.

In addition, in the same meeting, a draft guidelines for assessment of the therapeutic efficacy of Chloroquine for *P.vivax* malaria were developed, revised by a PAHO convened group in 2000 and reviewed in 2001 at a WHO meeting on monitoring resistance to antimalarial drugs. With those developments, it is expected that guidelines for monitoring *P.vivax* will be soon available.

As of December 1998, Peru had begun using the WHO/PAHO protocol and received support from the Centers for Disease Control (CDC) and the US Navy Medical Research Unit (NAMRID) based in Peru. Subsequently, NAMRID and CDC supported studies in Bolivia and then in Suriname in 2001. Additionally, along with collaboration from the Peruvian National Health Institute, technical support was provided for studies financed by the Tropical Disease Research (TDR)/PAHO in Ecuador.

Within the framework of WHO's "Roll Back Malaria" initiative, PAHO has been supporting the Amazon countries in establishing a surveillance network for monitoring anti-malarial drugs resistance in the Amazon (Spanish acronym, RAVREDA). The idea was to use the WHO/PAHO adapted document as the common protocol, facilitating comparison of results between regions and countries.


In October 2001, as part of the US Agency for International Development's (USAID) Latin America and Caribbean Bureau's (LAC) infectious diseases grant to PAHO, PAHO initiated a program of activities to support the USAID funded Amazon Malaria Initiative (AMI). The PAHO program was designed to support the AMI objective of "Malaria control programs in target countries in the Amazon Basin subregion substantially incorporate selected best practices," and to contribute to the USAID Latin America and Caribbean Regional Strategic Objective "More effective delivery of selected health services and policy interventions." The project also contributes to the worldwide goal of Roll Back Malaria Initiative to significantly reduce the global burden of malaria through interventions adapted to local needs.

PAHO/Washington provides technical cooperation, coordinates activities, and through PAHO country offices, oversees implementation of country level activities in six of the eight Amazon Basin target countries (Brazil, Colombia, Ecuador, Guyana, Suriname and Venezuela.). Support to Peru and Bolivia is provided through USAID field mission programs in those countries, and coordinated with PAHO. CDC provides technical assistance to support implementation of regional and country level activities. This program description describes proposed activities to be implemented by PAHO to support AMI during years 2 and 3 (October 2002 - September 2004).

II. Accomplishments and Progress

Funds provided by USAID to date have greatly contributed to the development and strengthening of a regional network a regional network for surveillance of antimalarial drug resistance. National surveillance networks were established in each target country to assess the efficacy of antimalarial drugs. In addition, studies of efficacy of malarial drugs for *P. falciparum* were initiated and studies of *P. vivax* drug resistance were contemplated in few countries.

The AMI includes three intermediate results. The first intermediate result (IR) is "reliable and standardized malaria drug efficacy information available."

During 2001-2002, major activities related in IR 1 at *regional level* were the development of a priority agenda, and the design of monitoring and evaluation instruments for regional and national workplans. A technical meeting with participation of representatives of all participating countries, USAID, CDC and PAHO was held and partnership roles and responsibilities agreed upon. All participating countries agreed to use the PAHO/WHO protocol for efficacy evaluation of antimalarial drugs. In an effort to facilitate planning and implementation of efficacy studies, a generic protocol was prepared and agreed upon by implementing partners and target countries. The generic protocol is to be field-tested. Information on the developments within the network will be disseminated through the PAHO website. 

With the exception of Guyana, most countries either have technical competence or have recently undertaken in vivo studies. As a result, regional technical support was provided to Guyana to assist in initiating project activities. A registry of the sentinel sites selected by all the participating countries was generated. Collection of technical information of the project, like geographical setting of the sentinel sites and anti-malarial drugs to be tested, as well as the First Technical Coordinating Committee Report has begun, and will be posted on PAHO's web site. Maps identifying sites where studies have been undertaken and those for proposed surveillance sites have been developed. The establishment of priority areas for operational research was completed, and the call for proposals for small grants is underway.

At the *country level* activities focused on the establishment and support of a National Coordinating Technical Committee to operate and maintain a surveillance network of malaria in each country. Selection and rendering sentinel sites operational to initiate the collection of the data for the evaluation *in vivo* of the efficacy of the malarial drugs was also completed for those planned for the first year. During 2001/2002 sentinel sites were provided with equipment and supplies (Brazil, Colombia, Ecuador, Suriname, Venezuela) and training of human resources for the execution of the standardized protocols (Brazil, Ecuador, Suriname, Venezuela) and malaria microscopy and parasite density determination (Ecuador, Suriname). The generic PAHO/WHO protocol was reviewed and approved, and data collection is underway (Ecuador, Brazil). Data collection started (Suriname). Table 1 shows the drugs selected for testing, the sites already selected in each country and the duration period for studies proposed.

The second Intermediate Result (IR) is "tools and approaches developed, adapted, tested, and/or disseminated." PAHO specific activities focused on the evaluation of rapid tests for malaria diagnosis. For this purpose, sites were identified and in Suriname and Brazil, and studies were initiated. Implementation of rapid tests may be appropriate especially where health facilities do not exist and/or establishment of laboratory facilities is not considered feasible.

The third IR of the project is "partnerships to improve malaria control in the subregion enhanced" and aims to facilitate the dialogue and joint efforts among the target countries and their institutions. In this context the first Technical Coordination Meeting was held to present the first year work plans for all project partners. In addition, sentinel sites or possible areas were proposed to conduct both national and border studies for the prevention and control of anti-malarial resistance. Furthermore, preliminary commitments were established among expert institutions identified in South America and the national representatives of project target countries in relation to the requirements and needs for training and technical assistance of participating countries.

III. Proposal for Years 2 and 3 of the AMI Project

This proposal describes the activities and related budget for the AMI project to be implemented over a two-year period and to be completed by September 30, 2004. The proposed budget for USAID funding is US \$1,644,000 and US \$1,065,000 for fiscal years 2002 and 2003 respectively, for a total of \$2,709,000.

The activities proposed are based on progress achieved to date, the original five-year plan for the regional surveillance network prepared by the countries, and recommendations provided during the First Project Technical Coordinating Committee held in Santa Cruz, Bolivia, in March 2001. These activities were further elaborated in an informal meeting of PAHO, CDC, and USAID that took place in Lima on April 8-10, 2002—taking advantage of the presence of project representative partners at the International Seminar of Malaria Prevention and Control, sponsored by the Ministry of Health of Peru and VIGIA Project.

During the second and third years of the AMI work initiated in the first year will continue with the aim of concluding drug resistance studies and providing an evidence base to support processes of ratification/reform of national malaria treatment policies.

PAHO will continue to coordinate and monitor the implementation of the project as a whole, while providing technical cooperation to the target countries. During these two years the project

will focus on completing malaria drug efficacy studies, assisting in data analysis and evaluation of alternative treatments, and on revising malaria treatment policy (for non-complicated *p. falciparum*). As new treatment policies are adopted, PAHO will assist countries to plan and implement the new treatment policies, and to implement effectiveness studies to monitor the implementation of new treatment regimens. Operations research, training, and South to South activities will also be undertaken. Below are the proposed activities, by intermediate result.

IR1: Reliable and Standardized Malaria Drug-Resistance Information Available

The activities programmed to obtain this intermediate result will be targeted to development and/or strengthening of surveillance systems and to finalize the studies of resistance to anti-malarial drugs.

- *Technical cooperation to establish and monitor surveillance sites*

The selection and implementation sentinel sites will be completed in order to carry out the studies of efficacy of the anti-malarials. Moreover, and for the purpose of maintaining the quality in the performance of the studies, monitoring of the sentinel sites both from the regional level and national will be conducted.

- *Technical cooperation to develop/adapt protocols (at country level).*
- *Technical cooperation to develop the capacity of human resources in surveillance sentinel sites.*

The implementation of policies in the use of anti-malarial drugs depends on the capacity of the health services in the endemic areas, which means that the capacity for surveillance, diagnosis and treatment will be strengthened.

- *Technical cooperation to establish/strengthen the National Coordinating Committees (NCC)*

The NCC is an interdisciplinary group of representatives of the malaria surveillance network as well as MOH programs and other institutions involved in malaria prevention and control. Its mission is to promote sustainability of the network, provide general supervision of the studies and advocacy to policy makers to orient national policy formulation to manage safe and effective anti-malarial drug treatment based on study findings. The NCC will be strengthened in the countries. PAHO/Washington will coordinate with USAID missions and PAHO local office in Bolivia and Peru to rendering operational these committees including PAHO participation.

- *Technical cooperation to carry out regional quality controls (RQC) for in vivo studies (microscopic diagnosis and drug quality)*

The establishment of subregional laboratories has been proposed to support quality control of the laboratories, such as: Peru for Bolivia and Ecuador; Colombia for Venezuela, and Brazil for Guyana and Suriname.

- *Technical cooperation on data analysis, and to reach consensus on evaluated treatment alternatives or new treatment guidelines.*

Based on the results of the efficacy studies, the countries will propose treatment regimens, and whenever possible, the use of similar regimens in areas of common epidemiological interest will be agreed upon under PAHO's coordination, including monitoring and evaluation.

- *Technical cooperation to implement efficacy studies.*

After having identified the treatment regimens from efficacy studies, effectiveness studies will be conducted to assess side effects and adverse drug reactions, patient compliance, and drug availability, with PAHO's coordination, including monitoring and evaluation.

- *Technical cooperation for dissemination of information through the PAHO website.*
PAHO will assist in the dissemination of data on the efficacy of anti-malarial drugs in the Region, as well as provide access to technical material through its Web page.

IR2: Tools or Approaches Developed and/or Adapted, Tested and Disseminated

- *Technical cooperation to carry out field tests of rapid diagnosis (RDT)*
Community health workers will be trained in the use of rapid tests in areas with no access or poor access to health services. The WHO protocol will be used in RDT evaluation.
- *Technical cooperation to carry out a subregional training workshop on EPI Info*
PAHO will support organization of workshop and country participants.
- *Convene regional expert group to build consensus about revised in-vivo efficacy protocol, including the WHO up dated protocol (Geneva, December 2001).*
- *Convene regional expert group to build consensus about effectiveness protocols.*
- *Provide technical cooperation in developing revised treatment guidelines, including monitoring and evaluation.*
- *Technical cooperation in the preparation and dissemination of new treatment guidelines.*
- *Technical cooperation to implement operational researches areas defined in Santa Cruz meeting.*
Review, select and provide funding for proposals.

IR3. Partnerships to Improve Malaria Control Enhanced

- *Plan and organize the AMI Annual Meeting (in order to strengthen the planning and coordination of FY02 and FY03 activities).*
- *Convene the first Technical Advisory Group (TAG) Meeting.*
Outside experts will be convened to review the strategy and the process of the project, as

well as the research findings with a view to examining the course in the project and issue recommendation.

- *Participation and technical cooperation in the subregional training on data analysis.*
PAHO will support organization of the workshop with participation of PAHO focal local point and technical support (trainers), and country participants.
- *Participation and technical cooperation on a subregional training workshop on anti-malaria drug-policy reform processes.*
PAHO will support organization of the workshop with participation of PAHO focal local point and technical support (trainers), and country participants.
- *Technical cooperation on South-South activities (assistance and training).*
- *Technical cooperation to centers of excellence supporting the processes and promoting South-South cooperation.*
- *Technical cooperation on a subregional training in management of malaria at the district level.*

IV. Monitoring and Evaluation

PAHO will continue to use the jointly agreed upon indicators and targets to measure progress and impact of the program. Initiative level indicators will be collected and reported in the annual report.

SO-Level Indicator: Number of target countries that develop or revise and implement evidence-based malaria treatment

IR 1: Target countries that complete anti-malarial drug resistance studies based on WHO/PAHO protocol.

IR 2:

- Tools or approaches developed and/or adapted, tested and disseminated.
- Number of country target countries that use tools disseminated by the initiative.

IR 3: Number of South to South training or technical exchange activities.

Process indicators and milestones will be updated and revised as necessary, and reported on every six month (See Table 2).

V. Management of the Project

The coordination of AMI will be carried out through a Steering Committee with representatives of the financing agency (USAID), of PAHO, the CDC, and new partners RPM Plus (Rational Pharmaceutical Management Plus Program) and USPDQI (United States Pharmacopeia Convention Drug Quality and Information). The Committee aims to facilitate coordination and

information sharing between AMI partners, and serves as a mechanism for discussion of technical issues.

The National Coordination Committees will coordinate, guide and support AMI activities at the country level, with inclusion of the focal points of PAHO, including the countries where the project is executed by USAID missions (Bolivia and Peru).

Under the direction of Dr. Renato Gusmao, Coordinator of the Communicable Disease Program the following PAHO staff from Regional Office will take part in this project:

- Dr. Gustavo Bretas, *Roll Back Malaria* Advisor for Amazon Countries (30%)
- Dr. Keith Carter, Regional Advisor in Malaria, Project Coordinator (30%)
- Dr. Roberto Montoya, Project Technical Coordinator (100%) (Post funded by USAID project funds)
- Ms. Raquel Requejo, Project Manager Consultant (50%)
- Ms. Roxane Salvatierra-González, Public Health Officer (10%)
- Dr. Zaida Yadón, Regional Advisor, TDR (10%)

At country level, PAHO staff from Regional Office in Brazil, Colombia, Ecuador, Guyana, Suriname, and Venezuela will provide technical cooperation supporting the national project coordinators and Coordination National Committee in executing project activities. In Bolivia and Peru coordination of efforts will be provided by the USAID offices, with collaboration of PAHO staff.

The PAHO staff from the Regional Office involves in the project is:

- Dr. Enrique Gil, Bolivia
- Dr., Carlos Catao Loiola Prates, Brazil
- Dr. Celsa Sampson, Colombia
- Dr. Angel Valencia, Ecuador
- Dr. Bernadette Theodore-Gandi Guyana
- - Dr. Rubén Figueroa, Peru
- - Dr. Marthelise Eersel, Suriname
- Dr. Mario Valcárcel, Venezuela

I. Budget

The proposed second and third year budget for PAHO's proposal for USAID funding is US\$ 1,644,000 and US\$ 1,065,000 respectively for a total budget of \$2,709,000.¹

PAHO will provide \$390,000 total (FY 2002, \$240,000 and FY 2003, \$150,000) in direct contribution to malaria activities, in addition to approximately \$531,000 in staff salary support (\$265,500 for each year). The FY 2002 and FY 2003 budget provided by USAID and PAHO combined amounts to \$2,149,500 and \$1,480,500 respectively, for a total budget of \$3,630,000.

¹ Expenditures support for programs included.

TABLE 1 - RAVREDA/AMI PROJECT - PAHO MATRIX OF INFORMATION FOR TECHNICAL SUPPORT

Items	Bolivia	Brazil	Colombia	Ecuador	Guyana	Peru	Suriname	Venezuela
Drug interested in studying	Mefloquine + Artesunate	Quinine	Amodiaquine	Chloroquine	Sulfadixine/pyrimithamine	Chloroquina Sulfadoxine/Pyrimethamine	Mefloquine vs. Mefloquine + Artesunate	Chloroquina
		Doxycycline	Sulfadixine/pyrimithamine	Sulfadixine/pyrimithamine (SP)		Quinine+clindamycin (short course)	Doxycycline + Artesunate	Quinine Combination derived from Artemisinin
		Primaquine	Quinine sulphate			SP+Artesunate (Adverse reactions)	Artesunate + Lapdap (?)	Artemether + lumefantrine
		Chloroquine	Mefloquine			Mefloquine+Artesunate (adverse reactions)		Mefloquine + artesunate
						Chloroquine-Primaquine (short course) (P.vivax)		
Sentinel sites location, number, and initiation date and duration period for studies	Cobija, Guayaramerin, Puerto Rico, Riberalta	Amapá (2)	Turbo (Antioquia)	Portoviejo (Manabí)	Barima-Waini (1*)	North Cost Area (Tumbes-Piura)	Paramaribo	Atures (Amazonas)
		Amazonas (4) (2*) (Manaus)	Bagre (Antioquia)	Babahoyo (Los Ríos)	Cuyuni - Mazaruni	North Rainforest Area (Loreto)	Njun Jacob Kindre	Manapiare (Amazonas)
		Maranhao (3)	Guapi (Cauca)	Milagro (Guayas)	Potaru - Siparuni	North Rainforest Area (San Martin)	Dritabiki	Sifontes (Bolívar)
		Mato Grosso (1) (1*) (Cuiba)	Tadó (Chocó)	Santo Domingo (Pichincha)	Upper Takutu - Upper Essequibo			
		Pará (3) (1*) (Belem)		Esmeraldas (Esmeraldas)		Cental Rainforest Area (vivax)	Cajigal (Sucre)	
		Rondonia (5) (1*) (Porto Velho)		Machala (El Oro)				
		Roraima (3)						
		Total (21) Year 01 (*)				<i>Year 01 (*)</i>		

Table 2 - Process Indicators

AMI/RAVREDA

Intermediate Result	Process Indicator	Indicator Definition	Indicator Calculation	Data Source	Methodology for data collection	Frequency	Responsible for data collection	Responsible for analysis and reporting
IR 1: Reliable and standardized malaria drug efficacy information available.	Percent of sentinel sites where data collection has been initiated.	Data collection is initiated when the information of follow up on recruited patients is registered in the data-collection sheet.	# of sentinel sites where data collection has been initiated divided by total # of sentinel sites selected.	Supervisory visits.	Countries will complete standardized reporting form every 6 months.	<ul style="list-style-type: none"> ▪ March ▪ September 	National Coordination Committee	National Coordinator and PAHO focal point.
	Percent of functioning sentinel sites that comply with quality control procedures as defined by country protocol.	Functioning sentinel sites are those where health personnel have been trained and where all necessary supplies and equipment are in place to implement the protocol. Quality control procedures are defined in each country protocol.	# functional sentinel sites in compliance with quality control protocol divided by total # of sites that are functioning.	Supervisory visits.	Countries will complete standardized reporting form every 6 months.	<ul style="list-style-type: none"> ▪ March ▪ September 	National Coordination Committee	National Coordinator and PAHO focal point.
IR 2: Tools and approaches developed, adapted, tested and/or disseminated.	Percent of planned tasks completed.	Tasks are steps specified in a country workplan that are related to developing or adapting, testing and/or disseminating a tool or approach.	# of completed tasks divided by # of planned tasks	Supervisory visits.	Countries will complete standardized reporting form every 6 months.	<ul style="list-style-type: none"> ▪ March ▪ September 	National Coordination Committee	National Coordinator and PAHO focal point.
IR 3: Partnerships to improve malaria control in the sub-region enhanced.	Percent of planned South - to- South activities that were completed	A South -to- South training or technical exchange activity is one in which two or more target countries participate.	# of South to South activities completed divided by South-South # activities planned.	Supervisory visits.	Workplans, activity reports and workshop reports.	<ul style="list-style-type: none"> ▪ March ▪ September 	National Coordination Committee	National Coordinator and PAHO focal point.

RPM Plus

Latin America and the Caribbean Amazon Malaria Initiative (AMI) (October 2002–September 2003)

Background

Malaria is one of the major infectious diseases that continue to present a serious threat in the Latin America and Caribbean region. The Amazon Malaria Initiative (AMI) has been launched by USAID LAC/RSD to address the impact of ineffective control and treatment of malaria in the different countries of the Amazon Basin. The Amazon Basin region (Bolivia, Brazil, Colombia, Ecuador, Guyana, French Guiana, Peru, Surinam and Venezuela) began to experience a reemergence of malaria in the early 1990s, including the appearance of *Plasmodium falciparum* and resistance to inexpensive, first-line antimalarial drugs. *P. falciparum* resistance to chloroquine is common and treatment failure rates of 20% have been reported in some areas of the Amazon. Furthermore, sulfadoxine pyramethamine (a second-line antimalarial drug) resistance has been reported in Colombia, Peru, and Venezuela.

A major contributor to the development of antimicrobial resistance is the unnecessary use of antimalarials of their use in inappropriate doses. Physicians, pharmacists and drug vendors contribute to the unnecessary use of these drugs, and patients experienced with the benefits of antimicrobials tend to self medicate when they can not access formal health care services. Availability of antimalarial drugs varies from country to country.

RPM Plus has been invited to join the AMI during FY 2002. USAID's LAC Regional Bureau has provided RPM Plus US \$60,000 for activities within the AMI. This reflects the USAID's commitment to address the regional needs in the area of improving drug management for malaria in the LAC Region.

RPM Plus Technical Objectives and Rationale

The long-term strategy of RPM Plus is to strengthen the ability of policy makers, health care providers and institutions in the region to improve drug management. At the same time, RPM Plus plans to work with its partners, international health care organizations, and national and local health officials to develop policies and strategies to improve the treatment of infectious diseases. Through the USAID funded LAC Amazon Malaria Initiative, RPM Plus will be working with the Pan American Health Organization (PAHO), CDC, USPDQI Program, USAID/Peru, USAID/Bolivia and other local mission officers to effectively develop and implement strategies to improve malaria drug management in the region. These activities will also contribute to the accomplishment of the Regional Bureau for Latin America and Caribbean's Strategic Objective: "*More Effective Delivery of Selected Health Services and Policy Interventions.*"

Technical Objective 1:

Strengthen Health Systems for the Appropriate Drug Management of Malaria in the LAC Region

The role of RPM Plus will be to ensure that drug management for malaria is properly addressed to enhance effectiveness of the initiative activities. RPM Plus will participate on the AMI Steering Committee meetings. The data collection instrument developed with USAID BGH funds to assess malaria drug use at the community level will be tailored to the needs of the initiative partners and translated into Spanish to be used in the region. The tool will be field tested through funds provided by other partners for country activities. RPM Plus will participate in the training of country personnel to use the tool as well as to analyze the data collected.

Depending on availability of funds, RPM Plus will also adapt and translate into Spanish a module on drug management for malaria. This module may be incorporated to other training tools that initiative partners' have already developed.

RPM Plus activities in this area will contribute to the SO-level statement of AMI: "Malaria control programs in the Amazon Basin sub-region substantially incorporate selected best practices". RPM Plus participation will contribute to the achievement of the following intermediate objectives:

- IR-2 Tools and approaches developed, adapted, tested and/or disseminated.
- IR-3 Partnerships to improve malaria control in the sub-region enhanced.

Planned Activities

IR-2 Tools and Approaches Developed, Adapted, Tested and/or Disseminated

1. Adaptation and Translation of the Community-Level Drug Management for Malaria Tool

RPM Plus with funds from BGH is preparing materials for a training course on drug management for malaria. With funds from LAC/RSD RPM Plus will adapt and translate this module to be used in the LAC region. The materials will be ready for individual countries to use during training activities, and for future AMI training workshops at the sub-regional level.

In collaboration with CDC and the local AMI team the data collection instrument developed with USAID BGH funds to assess malaria drug use at the community level will be tailored to the need of the initiative partners and translated to be used in the region.

RPM Plus will provide training to local personnel in the country where the activity will take place. Coordination has been established with the Peru AMI team to conduct this activity.

RPM Plus will work with country counterparts to analyze the data and modify the tool according to results of the field test.

2. Adaptation and Translation of a Module on Drug Management for Malaria

RPM Plus with funds from BGH will prepare a module addressing the main aspects of drug management for malaria programs. With funds from LAC/RSD RPM Plus will adapt and translate this module to be used in the LAC region.

IR-3 Partnerships to Improve Malaria Control in the Subregion Enhanced

3. Coordination of Activities with AMI Partners

This activity includes technical activity coordination, workplan development, budget monitoring, progress monitoring, reporting, meetings, and communications with partners and collaborators.

RPM Plus will participate on technical meetings with other members of the initiative. It is expected that the AMI Steering Committee will meet at least once during the current FY. Funds will also be allocated to attend a Technical Coordination Meeting with national managers from participant countries.

USP Drug-Quality and Information Program (USP DQI)

Potential Collaboration with Partner Institutions Working under the Amazon Malaria Initiative (AMI) to Address Problems with Anti-Malarial Drug Quality

(November 2002)

Long-Term Goal

To strengthen antimalarial drug-quality assurance in the Amazon region in order to increase treatment efficacy, reduce antimalarial drug resistance, and maximize the use of health care resources for malaria.

Background

The National Malaria Programs (NMPs) of eight countries in the Amazon region have identified surveillance sites in malaria high-risk areas that will do diagnostic testing, provide treatment, and conduct in vivo drug sensitivity studies based on the WHO/PAHO efficacy study protocol. These sites will not only provide national level data for treatment policy decision making, but through the use of a standardized protocol, provide reliable and comparable data for the monitoring of sub-regional trends in antimalarial drug resistance.

USP DQI, a cooperative agreement between USAID Bureau for Global Health (BGH) and the U.S. Pharmacopeia, is working in Africa and Asia to help assure the quality of antimalarial drugs through assessment of national quality control systems, strengthening drug quality control laboratories, conducting baseline assessments of the quality of specific products and training sentinel surveillance site staff to do rapid testing for drug identity. USAID's Regional Bureau for Latin America has provided initial FY 2002 funding for USP DQI to begin work in antimalarial drug quality control in the Amazon region in FY 2003 under the Amazon Malaria Initiative (AMI). Target countries of AMI are Brazil, Bolivia, Colombia, Ecuador, Guyana, Peru, Suriname and Venezuela.

In addition to its USAID-supported activities, USP is conducting an external quality control of national labs in sixteen Latin American countries in collaboration with PAHO's Essential Drugs and Technology Program and will be including additional countries not yet covered and the Caribbean countries during the coming year. The goals of this study are to optimize and standardize the methodologies of drug analysis among countries and to ensure reliability of analytical results produced by the official control labs

A two-year planning matrix has already been developed by USAID, PAHO and CDC and surveillance sites have been selected by the eight participating countries. Some data collection on resistance has already started. All countries have agreed to adopt the PAHO protocol for noncomplex *falciparum* malaria and are now identifying the drugs to use. CDC

has developed a cost-effectiveness tool for rapid diagnostics and has been working in Peru since the recent malaria epidemic.

Proposed USPDQI Assistance

USP DQI met with USAID/LAC/RSD-PHN technical advisor Susan Bacheller, as well as Dr. Keith Carter and Ms. Raquel Requejo, PAHO, to discuss potential areas of cooperation and collaboration within AMI. Due to limited resources available, USP DQI will work in a maximum of two countries in the region during the first year. The selection of the two countries will be made in collaboration with PAHO, USAID, and the NMPs and will occur after the NMPs have finalized their program plans within AMI. Within each country, USP DQI will target two to three sites for malaria drug quality monitoring during the first year.

Technical assistance will focus on strengthening capacity of the sites to collect drug samples, conduct basic tests for quality, identity and strength, and record and submit data to the NMP. Products that fail the screening tests conducted at the surveillance sites will be sent to a regional or national reference laboratory for more thorough quality testing. Drug quality data collected at the sites can be fed back to provincial and central levels of the NMPs, drug regulatory systems, and drug distribution systems. Appropriate national agencies can take corrective actions when substandard and/or counterfeit products are identified.

After an assessment of drug quality assurance capabilities in the area where sentinel sites are located, USPDQI will develop training programs tailored to local needs to provide ongoing monitoring of antimalarial drug quality. Training for sentinel sites will include the following:

- How to test drugs using easy, low technology methods, e.g. TLC and colorimetric methods.
- Appropriate record-keeping/documentation practices.
- How to build a database of drug-quality reports.

Training for potential reference laboratories might include the following:

- Training in more sophisticated drug testing methods according to international standards, e.g., dissolution, HPLC, UV, as well as TLC.
- Good laboratory practices, e.g. maintenance of equipment, proper calibration, how to keep logbooks, etc.
- Reporting systems, i.e. back to the sentinel sites and to the NMPs.

A possible multi-year strategy for routine drug-quality monitoring might look like this:

1. Establish collection points at the final selected surveillance sites in the two countries based upon staffing and facilities.
2. Train site staff to sample and analyze drug content using TLC for the drugs used as first line treatment in the site area following standard protocols and procedures.
3. Collect a three-day regimen of any product suspected of clinical failure for submission to the designated reference laboratory for quality assessment. The reference lab may be a district, national or Regional facility.

4. Collect samples equivalent to a three-day regimen of any new products seen in the market place. Ship for formulation quality assessments to a reference laboratory.
5. A three-day regimen of all products which appear by screening analysis (TLC) to be substandard or which contain a previously unobserved component should be sent for formulation assessment to one of the selected reference laboratories.

Proposed for Year One

USP DQI proposes to initially begin in two sites selected by the AMI partner organizations in each of the selected countries. USP DQI will assess capacity at the site, i.e. human resources, lab equipment, communications equipment, etc. and work with the NMP to identify specific people to be trained. It is anticipated that staff at four sites will be trained this fiscal year. Training modules will be based upon working currently ongoing in Africa and Asia.

The country(s) must have the following:

- Adequate human resources at the surveillance area who can be trained in drug sampling, TLC, and proper documentation of test results or other topical areas when identified as needed by the specific area.
- Access to a reference laboratory that can do advanced drug testing including HPLC, ultraviolet, infra red, and dissolution at minimum.
- Availability in country of necessary supplies, e.g. reagents, glassware.
- Reasonable access to the surveillance sites via air.
- Willing collaboration by the local institution doing drug-resistance monitoring.
- Approval of national malaria control program and drug regulatory authority.
- An environment conducive to broad dissemination of drug-quality data.

Annex III

Regional, RPM and National Workplans

(accessible at <http://www.paho.org/english/hcp/hct/mal/paho-ami-2.htm>)