

The Amazon Network for the Surveillance of Antimalarial Drug Resistance (RAVREDA) and the Amazon Malaria Initiative (AMI) are part of the joint efforts of the Amazon countries and institutions (PAHO/WHO, USAID, CDC, USP, MSH) for Roll Back Malaria (RBM) in the Americas



RAVREDA-AMI Newsletter

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The RAVREDA-AMI Newsletter is a quarterly news and information publication of RAVREDA-AMI where the latest activities and progress of the Amazon Network for the Surveillance of the Antimalarial Drug Resistance are reported and shared.

RAVREDA Regional News

During the second quarter of the year, RAVREDA-AMI held five regional activities on subjects for which it was necessary to define lines of work and study protocols: rapid diagnostic tests, adherence to antimalarials, stratification in malaria, use of *in vitro* tests for monitoring resistance, and techniques for the surveillance of insecticide resistance in malaria vectors. Each one of these activities concluded with a specific work agenda to guide RAVREDA-AMI's approach to these subjects and activities for the coming years. The Internet portal provides access to documents with the summary and conclusions from each meeting.

Meeting to Design Studies to Evaluate Antimalarial Adherence

During 18-20 April 2005, a technical group met in Caracas to define the methodological aspects for evaluating antimalarial adherence. The intent was to develop a strategy aimed at promoting the adoption of standards and antimalarial prescribing and dispensing behaviors that lead to good patient adherence to treatment. Using this approach, three subjects were proposed for study: i) measuring the adherence problem, ii) analyzing the determinants of adherence, in order to guide improvements in care and in drug dispensing, and iii) studying compliance with prescription and dispensing guidelines and standards. The core of the proposed algorithm are the studies to measure adherence; the basic details of the protocol were worked out, and it is proposed that these be following in studies conducted in the region.

Workshop on Stratification in Malaria Using Geographic Information Systems

A workshop on stratification in malaria and the use of GIS was held in Santacruz, Bolivia on 16-19 May 2005, with participants from Colombia, Venezuela,

Bolivia, Brazil, Guyana, and Ecuador. The objective of the workshop was to define an approach to stratification for the different levels of complexity of the countries' Ministry structures to guide the planning, monitoring, and rational implementation of malaria control. A proposal and methodological guidelines were prepared so the participants of every country could do a stratification exercise as a starting point for this line of work within the control programs.

Meeting about Operations Research on the Implementation of Rapid Diagnostic Tests

Although studies on rapid diagnostic tests in RAVREDA-AMI have already been conducted, there was no well-defined line of work to guide the contribution that the Network can make to control programs in this field. For this reason a meeting was held with the people who have coordinated studies on this subject in the countries as part of RAVREDA-AMI, with the support of Dr. John Barnwell of the CDC. The meeting was held in Guayaquil, Ecuador, on 23-25 May, with the objective of defining lines of operations research and a plan for a joint effort on this subject. The conclusions of the Meeting are presented in a document that starts by considering the process of implementing rapid tests (RT) as a cycle and then for each part of this cycle determines the needs for operations research and methodological proposals. In addition to operations research to guide the implementation of RT in the field, some subjects that were not initially on the RAVREDA-AMI agenda emerged as priorities, such as quality control in procurement processes and field evaluation of tests already available on the market but unknown in the region.

Workshop on the use of *in vitro* Testing to Monitor Susceptibility to Antimalarial Drugs

With the coordination of PAHO–WHO (Roll Back Malaria Department) and the parasitology laboratory of the Evandro Chagas Institute in Belém, Brazil, a workshop was held on 28 May and 3 June on the use of new methods for evaluating *in vitro* susceptibility to antimalarial drugs. The instructors participating were doctors Harald Noedl (*University of Vienna–USAMC-AFRIMS Bangkok*), David Bacon (*Naval Medical Research Detachment Center, Lima, Peru*), and Jacques Le Bras (*University Paris Descartes*), and Pascal Ringwald (*WHO*). The participants on behalf of the countries were chosen by the Ministries of Health of five of the eight Amazon countries (Brazil, Colombia, Venezuela, Guyana, and Peru). Laboratory practice was done, and sessions for analysis and discussion were held about the two ELISA methods (pLDH and HRP2) and on the method using SYBR Green. The good concordance shown during the practice and the simplicity of the methods favor the viability of setting up a system for monitoring temporal and spatial variations in susceptibility to antimalarial drugs, which would complement effectiveness studies as an early warning system. It was agreed to implement a first phase to evaluate laboratory capability to rigorously follow a standard protocol and the details of a future phase for implementation were defined.

Workshop on Monitoring Insecticide Resistance in Malaria Vectors

In keeping with the program developed at the Lima meeting in February 2005, where it was agreed to focus on the subject of vector control in RAVREDA—AMI, a workshop was held in Iquitos, Peru to define protocols and a work plan on the subject of insecticide resistance surveillance (IRS). Experts from the CDC and NNCRD participated along with professionals from the reference centers in the countries. Laboratory practice was done on the bottle techniques and the WHO method with impregnated paper and discussions were held on the details of the protocol and interpretation of results. At the end, they worked on drafting a standard protocol and a model national work plan for IRS. It was agreed that all the Amazon countries would implement the bottle test as an initial screen because of its greater sensitivity and the impregnated paper method for confirmation when reduced susceptibility to insecticides is detected. Some aspects on taxonomy and the use of GIS were also discussed.

Country News

◆ Bolivia

Administrative Aspects

In the second quarter of the year, there were changes in the coordination of RAVREDA-AMI. Dr. Dennis Navarro joined as the medical specialist and Dr. Arletta Añez as national coordinator.

Participation in Regional Events

On 21 and 22 June, they participated in the meeting on the use of rapid tests for malaria diagnosis held in Guayaquil, Ecuador. Preliminary results were presented at this activity from the cost effectiveness study on the use of rapid tests by volunteers in the Amazon region of Bolivia.

Study of the Cost Effectiveness of the use of Rapid Tests by Volunteers in the Amazon Region of Bolivia

Once field work was finalized, the blood samples were processed to determine parasite density and support the sensitivity and specificity analysis. The study should be concluded by October. At the same time, a search is being carried out for asymptomatic carriers of *P. vivax* and *P. falciparum* malaria in the localities of Riberalta and Guayaramerín for the purpose of determining the prevalence of inapparent infection following the Brazil nut harvest. It should be pointed out that the majority of the migrant population that does this work comes from these cities. Technical personnel for malaria were trained in the use of OptiMAL tests. There was participation in the III Evaluation of Actions and Commitments to Brazil-Nut Workers' Health Care, where fulfillment of the actions scheduled for the period during the 2004–2005 harvest was evaluated and a next meeting was scheduled to plan strategies for the 2005–2006 Brazil-nut harvest.

Entomological Surveillance

Staff training continued at the Yacuiba entomology laboratory on techniques related to entomological surveillance activities that are going to be implemented.

Study on Malaria Vector Insecticide Sensitivity/Resistance

Insecticide assays were done with the laboratory reference strains to establish controls for the sensitivity analyses. The Mataral and Chaco strains were evaluated, using 600 mosquitoes. The

insecticides evaluated are Deltamethrin 0.05%, 0.025%, 0.01%, and 0.005%, and permethrin 0.75%. In the preliminary results, the reference control strain has shown 100% mortality with all the concentrations evaluated.

◆ Brazil

Conclusion of Effectiveness Studies for the Official Regimens

At the end of May, the RAVREDA sentinel sites in Brazil concluded the effectiveness evaluations of the antimalarials in use in the country. During June, they worked on preparation of a double entry database. The total number of patients enrolled in the effectiveness studies was 242 patients treated with mefloquine monotherapy, 166 patients treated with quinine + doxycycline, and 910 patients with *P. vivax* malaria treated with chloroquine.

Meeting of the Technical Board

On 11 and 12 June 2005 a meeting was held in Brasilia of a technical board convened by the Ministry of Health to review the therapeutic regimens in use in Brazil for the treatment of uncomplicated *P. falciparum* malaria. Results were presented of the evaluations of therapeutic response to the quinine + doxycycline combination done in the RAVREDA sentinel sites in the states of Pará and Amapá. The studies reveal a therapeutic failure rate of 10% in Pará and 18% in Amapá. With these results and considering other history of therapeutic failure to this combination, the increase in the percentage of *P. falciparum* cases in some states, and the problems with adherence to quinine, it was decided to recommend a change from this regimen to a combination therapy using artemisinin derivatives (MQ+ASU or Coartem®). The group also defined a working agenda for effectiveness evaluations of the new alternatives, review of the official guidelines, and a controlled intervention with the fixed combination of MQ+ASU.

Study of Rapid Tests Begins in Rondonia, Mato Grosso, and Pará

In the states of Mato Grosso, Rondonia, and Pará, a study was begun on the performance of rapid tests in temperature and moisture conditions normal for localities in the Amazon region. The study has an expected duration of 10 months.

Evaluation of Antimalarial Quality

From April to June, quality analyses were done of the drugs used in the RAVREDA effectiveness studies and a protocol was implemented to evaluate drug stability under normal storage conditions in Amazon region health posts.

External Performance Evaluation of Diagnosis

Also during this second quarter, the shipment of sets of thick blood film slides began for the external performance evaluation of malaria laboratories in the state of Pará. Among the state's diagnostic sites, 113 laboratories were invited to participate and they are initially working with the 18 that accepted. This pilot experience in Brazil corresponds to the methodology proposed at the 2004 Caracas meeting.

◆ Colombia

Antimalarial Effectiveness Evaluation

With the support of the CIDEIM, data collection for the study of the *in vivo* effectiveness of CQ was finished and work was done on collecting information from the effectiveness studies of AQ and AQ+SP in the Buenaventura, Valle sentinel site. It was concluded that CQ continues to be effective for the treatment of *P. vivax* malaria in Buenaventura, since there was only 1 therapeutic failure among the 42 analyzable patients. Stocking of the Tumaco sentinel surveillance site was completed. The National Institute of Health supported Guyana in the control of microscopy quality for *in vivo* effectiveness studies.

Adherence to Drugs

Analysis and dissemination of the results of studies on adherence to treatments for *P. falciparum* and *P. vivax* malaria were carried out in two municipalities of the Department of Córdoba and in the municipality of Guapi in the department of Cauca. The study in Córdoba included analysis on access to antimalarials and the sale of drugs not included in the official regimens; problems were recorded with the prescription, dispensing, and use of antimalarials. In the municipality of Guapi, with support from the CIDEIM and Valle University, the adherence of all the actors involved in malaria treatment was studied. This study contributes to the methodology used in evaluating adherence through the use of a combination of quantitative and qualitative methods. Noteworthy among the findings are: i) that the health workers responsible for prescribing the treatment do not always apply the official regimen and on some

occasions continue to prescribe chloroquine instead of amodiaquine; ii) the availability of the drugs and the perceptions of the drug's effectiveness seems to directly affect nonadherence by the prescriber; iii) there is lack of coordination within and among the health institutions concerning the supply of drugs and the information given to the patient on the requirements and steps that should be followed both for diagnosis and treatment.

Analysis of Malaria Mortality in Pacific Coast Municipalities

During April, data analysis of institutional mortality from malaria in Tumaco, Nariño, and Quibdo, Choco was concluded. In Tumaco, death certificate records (from DANE) and hospital records coincided.

Dissemination of Results and Training in the Detection of Warning Signs of Complicated Malaria

After training the new personnel at the Tumaco sentinel site, the Ministry of Health in Nariño, with support from the CIDEIM, have been carrying out workshops since June on "detection of early signs of complicated malaria" for the medical staff, nurses, nursing auxiliaries, microscopists and pharmacy managers. During June, 5 workshops were held and a total of 131 people trained.

Malaria Stratification and Surveillance

An electronic database was created for information on malaria morbidity from the endemic municipalities of the department of Nariño. To date, 70,590 records corresponding to malaria cases from 2001, 2002, and 2003 have been entered. The central level was supported by funding for malaria control stratification activities with MIS support.

In the Guapi sentinel site, an evaluation of the malaria surveillance system found underreporting of cases and problems with entry and analysis. Strategies were proposed for strengthening the surveillance system that would subsequently permit the implementation of passive surveillance of antimalarial drug resistance at this sentinel site.

Regulating Changes in Policy and Document Preparation

Advances have been made in the preparation of the first draft of the antimalarial drug policy document, which is being reviewed.

***In vitro* Monitoring of Temporal and Spatial Variations in Susceptibility to Antimalarial Drugs**

The National Institute of Health, the CIDEIM, and the laboratory group from the Evandro Chagas Institute in Belém (Brazil) met in April in the city of Cali, to share experiences and review laboratory procedures for *in vitro* monitoring of susceptibility to antimalarial drugs using the new ELISA tests. Basic equipment and consumables were also acquired for the implementation of ELISA tests for monitoring resistance in an endemic locality in Colombia.

Entomology Activities

Progress was made in funding and selecting the four priority sites for implementing the proposed evidence-based vector control model in Lima. Shortly, the emphasis at these locations will be on monitoring malaria vector insecticide susceptibility and resistance.

National Meetings Held with RAVREDA-AMI Support

With the involvement of the Ministry of Social Protection and officials from several departmental and municipal Health Secretariats, a workshop was held in April on malaria prevention and control programs on the Colombian Pacific Coast, where important commitments were made to strengthen control measures in this region of the country. During May, the Ministry of Social Protection convened and held a successful national meeting in Bogota of chemical control experts to review instructions on the use and purchasing decisions for insecticides for the control of malaria and other vector-borne diseases, for the purpose of making more cost-effective, rational use of these products.

◆ Ecuador

Evaluation of the Therapeutic Effectiveness of Antimalarials

In June, a study to evaluate the therapeutic effectiveness of Coartem® was started at the RAVREDA sentinel sites in the cities of Esmeraldas, Milagro, and Santo Domingo. Coartem® is the second-line treatment for uncomplicated *P. falciparum* malaria in Ecuador. Due to the reduction of *P. falciparum* malaria cases and the need to reduce the time for implementing the studies, this evaluation is being done with a sole caseload among the three sites. To date, in these three Pacific sentinel sites together, approximately 18 patients have been enrolled and no failures have been recorded.

Implementation of the new First-Line Therapeutic Regimen for Treatment of Uncomplicated *P. falciparum* Malaria

In coordination with the Provincial Health Bureaus, training workshops have been held in the endemic provinces along the country's coast for health workers in public and private institutions on the use of the new regimens for the therapeutic management of malaria. To date, the distribution of Artesunate has been carried using a donation from Peru of 50,000 tablets (50mg). At the end of this quarter, the Ministry of Public Health (MPH) was in the process of procurement.

Operations Research on Rapid Diagnostic Tests

With regard to the study conducted in Ecuador on the performance of OptiMAL-IT® tests by local health workers in remote areas, during the last three months information from these places was entered into a database and it was agreed that a new coordinator would be designated for this line of work in Ecuador.

Malaria Information System

The software designed for the registry and management of information linked to the SIVE-ALERT system of the MPH is being evaluated. Field tests are being carried out at present and a training workshop is being planned with personnel from the provincial and local level who will handle this computer application.

Evaluation of Drug Quality Through the use of Minilabs by Provincial Teams

From April to June, the first round of antimalarial quality analysis using Minilabs was carried out in the provinces of Esmeraldas, El Oro, and Pichincha. This activity, with technical support from the United States Pharmacopeia (USP), is being carried out according to the timetable, with the involvement in each one of the provinces of technical personnel from the Provincial Health Bureau, the National Institute of Hygiene (INH), and the NMES. Samples of primaquine, chloroquine, Artesunate, quinine, sulfadoxine—pyrimethamine, and mefloquine collected in health posts, drug warehouses, and pharmacies were evaluated through thin-layer chromatography. A total of 52 samples were evaluated, one part of these, in accordance with the protocol being used, was also analyzed at the INH national reference laboratory.

Evaluation of the Quality of Diagnostic and Treatment Services

Progress was made on an assessment of “Factors associated with the supply, demand, access, and delivery of services for malaria diagnosis and treatment by Public and Private Health Services in endemic communities in urban and rural areas in Ecuador.” Activities carried out in two provinces in recent months include workshops with interviewers and with the services involved, the validation of instruments, and collection of the required information.

Quality Control for Malaria Diagnosis

Following up on the activities proposed in the document from the April 2004 Caracas meeting, in recent months work has been done toward preparing slide sets for conducting the External Performance Evaluation (EPE). Committees were formed in the provinces of Esmeraldas and El Oro for the baseline information survey on census and laboratory and human resources conditions. The preparation of a guide and procedures manual is pending. The plan is to work first on implementation of the EPE and a new methodology for indirect evaluation in the two aforementioned provinces before continuing with the other endemic provinces.

Implementation of a Model for Evidence-Based Vector Control

Regarding the follow-up to the methodology proposed in Lima to promote the use of entomology to guide interventions, the advances in this period in Ecuador consist of a training for entomology auxiliaries in nine NMES operational areas on basic aspects of morphology, taxonomy, ecology, vector control measures, captures, and susceptibility tests. Ecuador also participated in June at the meeting in Quito on evaluating insecticide resistance.

Malaria in Pregnancy

In the province of Esmeraldas the RAVREDA-AMI group has been doing work on malaria in pregnancy to follow up on activities that the NMES group in this province was already engaged in. In the last three months, instruments were introduced that had already been designed and evaluated in pilot studies in MPH maternal and child healthcare programs in patients receiving prenatal care. During this period, the thick blood film test has been introduced as routine for all prenatal visits in three cantons in the Province of Esmeraldas. One preliminary finding is the recording of 47 cases of malaria from January to June in

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asymptomatic pregnant women who attend the prenatal clinics at three hospitals in these cantons.

◆ Guyana

Coordination of RAVREDA–AMI

In the last few months, the RAVREDA-AMI committee and the National Malaria Committee in Guyana were reactivated. They had interrupted their usual activities due to the national emergency caused by flooding in January and February 2005. This committee, which is led by the Minister of Health, has played a fundamental role in guiding important advances on malaria control in the last year.

Monitoring the Therapeutic Effectiveness of Antimalarials

In June, the effectiveness study for monotherapy with MQ and the MQ+ASU combination was finished. Although Guyana already defined its new therapeutic regimen for treatment of uncomplicated *P. falciparum* malaria (Coartem®), it was important to know the effectiveness of mefloquine and of the other combination most used in the region. The study was conducted in Madhia, creating a new sentinel site for RAVREDA-AMI. For 28 days, 172 patients (86 in each group) were followed, with few dropouts. Two therapeutic failures in the MQ group were recorded. Also during recent months, progress was made in Colombia and Peru on the review of slides for control of the quality of microscopy in the Coartem® effectiveness study done in 2004 and the slides from the first 62 patients of the study on mefloquine versus MQ+ASU.

Antimalarial Drug Quality Management

Antimalarials were collected from Region 8 and sent for quality control in the laboratories of the USP. Also, during the last quarter, work was done on the design of the external drug quality control laboratory, located in the department for Drug and Food Control of the Ministry of Health of Guyana.

Expanding Coverage for Diagnosis

In the framework of the decentralization of malaria control that the Ministry of Health in Guyana is carrying out, in recent months work was done on the design of a national Plan for training in malaria microscopy, with the support of RAVREDA-AMI. The proposed activities correspond to the process of horizontalizing interventions and the strategic lines promoted by the RBM initiative.

Access and use of Antimalarials in the Mines

Also during the last quarter, the preparation of a protocol was concluded to evaluate the access and use of antimalarials in the mining population. The study was designed in coordination with the Ministry of Health and the Commission on Geology and Mines with the Gold and Diamond Association of Guyana. Field activities were scheduled to begin in July 2005.

Implementation of the Policy on the Supply and Distribution of Antimalarials

Progress was made in recent months in implementing the use of Coartem® in Region 8. Also as part of the process of implementing the new therapeutic regimen, RAVREDA - AMI worked on the new strategy for implementing malaria activities in general health services and on organizing the distribution of the drug to the regional offices and malaria control teams. Also on this subject, progress was made in coordinating with the local MSH team on future support for assessing the situation of processes for procurements, supplies, and the implementation of improvements in the delivery system.

Morbidity Data

As a routine activity in the last year, adjustments were made in the process of inputting data into the malaria information system databases, and the visit of a consultant was organized to support the implementation of a system that permits the spatial analysis of the malaria situation using GIS tools and appropriate stratification at the national level.

◆ Peru

Strengthening Entomological Surveillance and Vector Control in Peru

The conclusions and recommendations of the technical meeting on Entomology for Malaria Control and Prevention held in Lima from 21 to 24 February 2005 will serve as input for a consultancy to conduct a situation assessment of surveillance and vector control activities in 4 Regional Health Bureaus and prepare a technical proposal for the vector surveillance and control system in Peru. From March to June, the terms of reference were prepared for this consultancy and the paperwork started for the notice of vacancy and start up.

Design of the Proposal to Monitor Vector Insecticide Susceptibility and Resistance in Peru

From 13 to 17 June 2005, a meeting was held in Iquitos on methodologies for monitoring vector insecticide susceptibility and resistance, with the involvement of representatives from five RAVREDA-AMI member countries (Brazil, Ecuador, Suriname, Colombia, and Peru), PAHO and the CDC. They discussed the methodologies and procedures necessary for establishing an insecticide resistance surveillance system in the countries and worked on a general plan for its implementation. The agreements and recommendations from this meeting will serve as input for the technical proposal for this System, which is part of the surveillance system and vector control consultancy.

Effectiveness of Three Different Primaquine Regimens for the Prevention of Relapses From *P. vivax* Malaria in the Amazon Region of Peru

During the last three months, efforts have been made for procuring the necessary inputs and equipping the health facilities that will participate in the study. Delays occurred in initiating the study, and it is expected to start in August.

◆ Suriname

Evaluation of the Effectiveness of Artecom®

In June, a study was begun in the RAVREDA sentinel site in Paramaribo on the therapeutic effectiveness of Artecom®. This combination of dihydroartemisinin + piperazine + trimethoprim is not part of the official regimens in Suriname, but is an alternative that is being marketed in the country's endemic areas. The study also includes a group to evaluate Coartem®.

Molecular Markers in Monitoring Resistance

During the last quarter, implementation of molecular biology protocols concluded in the University of Suriname laboratory. A training was done on techniques to monitor the presence of molecular markers of resistance and on genotyping techniques for differentiating recurrence and reinfection.

Entomological Characterization–Baseline

A year of entomological survey activities ended in 4 localities on the Maroijne River. Information was recorded on anopheline habits and behavior and infection in mosquitoes (ELISA).

Diagnostic Quality Management

A protocol was prepared for implementing a quality control system for microscopic malaria diagnosis. All the materials were written in Dutch and include the component on the External Performance Evaluation, as well as methodology for quality control of rapid tests.

Quality Management of Malarial Drugs

Samples of antimalarials that are being marketed in gold mining areas were collected and sent for quality analysis. In keeping with the agreement to carry out this activity in cooperation with the USP, the samples were sent to the USP laboratory via PAHO.

RAVREDA Newsletter in Suriname

During the last quarter, editing and distribution began of a local newsletter on RAVREDA–AMI in Suriname. The bulletin is in Dutch and should come out monthly. To date, two issues have been prepared (May and June).

Interventions in Gold Mining Areas

During the last months, visits were made to gold miners in the areas of Selakreek and Benezorp, which is predominantly a population of African descent, with the objective of designing an intervention plan to be implemented in conjunction with the Global Fund project.

Evaluation of the Availability and use of Antimalarials in Suriname

In June, an evaluation was finished on the availability and use of antimalarials in the Suriname health services. The study was carried out by the Medical Mission in coordination with the methodology developed by MSH.

Procurement Processes and Equipment in RAVREDA

During the last few months, the Malaria Board was provided with equipment to support the management of surveillance activities, operations research, and control that are being worked on as part of RAVREDA-AMI. Similarly, procurement of rapid tests moved ahead for the implementation of a study on *P. vivax*.

◆ Venezuela

During the last quarter, changes were made in the national coordination of RAVREDA/AMI in the Ministry of Health and Social Development.

Evaluation of the Effectiveness of 2 Days of Mefloquine + Artesunate in Mining and/or Indigenous Populations

Patient enrollment continued in the study to evaluate treatment with two days of MQ+ASU. At the end of the second quarter of the year, 30 patients have been included at the Atures sentinel site and no more patients have been included at the Km. 8 sentinel site in the state of Bolivar. In Tumeremo, 27 patients have been included with a rate of patients lost to follow-up by day 28 greater than 80%. It should be pointed out that there is a low number of *P. falciparum* cases in the endemic areas.

Implementation of Changes in Antimalarial Policy

Activities continue for implementing the new regimens with priority given to the states with greater endemicity: Amazonas, Bolivar, and Sucre. Together with the Regional Representative Office for Science and Technology of Guyana, implementation activities were carried out in 22 localities in the southern part of the country distributed in the state of Bolivar, with special interest on the areas bordering Brazil and Guyana. A plan was done for implementation activities by state, beginning in the most remote areas that have problems of access to health services in the states of Bolivar and Amazonas.

Systematic Case Monitoring

Systematic monitoring was done of the response to treatment in patients treated with MQ+ASU at sentinel posts of the states of Bolivar and Amazonas, with ACR (Adequate Clinical Response) in the majority of patients that have completed follow-up until day 28.

Evaluation of Chloroquine Effectiveness in the Treatment of *P. vivax* Malaria

The admissions of patients of this study continues at a very slow pace. To date, 29 and 35 patient have been included in Bolivar and Amazonas states, respectively. Only 6 therapeutic failures have been observed in the Bolivar state with chloroquine. Steps are being taken to ship blood samples to Peru to determine levels of chloroquine and desethylchloroquine.

Quality Management in Malaria Diagnosis

With the new managerial changes in the Ministry of Health, the need was proposed to facilitate taking the

necessary steps for quality management training following the recommendations of the 2004 Caracas technical meeting. The activity is planned for August 2005. A census of the positions for malaria diagnosticians was begun in the 4 states considered to be priority: Sucre, Bolivar, Amazonas, and Delta Amacuro.

Malaria Stratification

Following the work plans for Stratification of Malaria worked on in Santacruz, Bolivia, in July 2005, a census was begun of localities considered “probable malaria infection sites” with information from the epidemiological surveillance system from 2002 to present. The hope is to strengthen the group with other partners in endemic diseases: Chagas’ disease, dengue, and leishmaniasis, to consolidate a national database.

Monitoring Adverse Reactions to Combination Therapy

In the sentinel sites in Atures (Amazonas) and Tumeremo (Bolivar) there has been ongoing evaluation of adverse reactions to treatment in all patients who have received combination therapy with artemisinin derivatives. As of the end of June 2005, there was information on nearly 1,000 patients. Adverse effects basically occur by day 7 and data entry is starting for their analysis.

Dissemination of Results and Scientific Output by RAVREDA-AMI Venezuela

RAVREDA Venezuela participated in four national scientific events and submitted papers to the VII Session of Doenças Tropicais do Baixo Amazonas to be held in Santarém, Brazil in July. Similarly, abstracts were sent to the annual meeting of the American Society of Tropical Medicine and Hygiene to be held in Washington in December 2005, as well as a talk plus abstracts for the I International Congress of Therapeutics, to be held in Caracas in October 2005. Furthermore, Dr. Leopoldo Villegas was given the Award for Science, Technology and Innovation, in the area of applied research, by the Ministry of Science, Technology and Innovation of Venezuela. A ministerial order defined a national line of research in malaria by priority municipalities and a committee of advisers in operations research for this ministry.

Activities Calendar

Upcoming regional activities on the Project calendar:

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| 9-10 July | Meeting on the use of molecular markers in monitoring resistance to antimalarials in the Amazon region. São Paulo, Brazil |
| 19-22 July | Workshop on tools to evaluate antimalarial management. Bogota, Colombia |
| 25-27 July | Meeting on malaria in mobile populations (Brazil, Suriname, Venezuela, Guyana, and Bolivia). Santarém, Brazil |
| 29 August–2 September | Techniques for monitoring mosquito insecticide resistance (Suriname, Guyana, Venezuela, and Bolivia). Paramaribo, Suriname |
| 26–30 September | Workshop on the use of Minilabs for antimalarial quality control. Tumeremo, Venezuela |

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