RAVREDA/AMI Newsletter

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RAVREDA Regional News

Workshop on the use of tools to evaluate the management of antimalarials
As follow-up to the workshop held in Lima, Peru in 2004 and in coordination with RPM MSH, a second workshop was held in July to discuss the progress made and to review details of implementing the manual *Pharmaceutical Management for Malaria–PMM Assessment Tool*. This manual presents a methodology for evaluating various aspects of antimalarial management, including their availability and patterns of use. Participating were professionals from the Ministries of Health of the eight Amazon countries. The methodology designed by MSH was reviewed, and the instruments were analyzed. As a field exercise, the group was divided up to allow for visits to several health facilities and apply the instruments defined in the protocol. The last day included a review of factors related to analyzing the results and indicators. The participants prepared a work agenda (including the selection of tools and indicators most appropriate to the situation in each country) as part of a proposal to be included in the RAVREDA 2005–2006 plans. The document detailing the meeting and conclusions can be found on the RAVREDA-AMI website.

Meeting of experts in the molecular biology of malaria
On 9 and 10 July 2005, in São Paulo, a technical group met to discuss the use of molecular markers in the monitoring of antimalarial drug resistance in the Amazon region. It was proposed that instead of working on a plan of activities based on the RAVREDA-AMI project, a broader proposal, involving cooperation among the different actors involved in this field in the region, would be formulated. In this context, RAVREDA—with its strengths as a regional surveillance network and a venue for technical cooperation among countries—would participate in lines of work deemed most salient to public health. The discussion began with the work proposal from the meeting held in Mérida in 2004, on which basis five subject areas were redefined, involving molecular biology issues of particular interest to RAVREDA, given their potential for short-term application in malaria surveillance.

A document detailing the meeting and the conclusions can be found on the RAVREDA-AMI website.

II Workshop on monitoring the malaria vector resistance to insecticides
From 29 August to 2 September, a workshop was held in Paramaribo, Suriname on methodologies for the surveillance of malaria vector resistance to insecticides. This was done in coordination with the CDC, Atlanta, with the participation of technical personnel from Suriname, Guyana, and Venezuela—countries that did not participate in the similar meeting held in Iquitos in June 2005. This activity will bring together the three countries, which will take part in the plans agreed upon at the meeting in Iquitos, where a concrete activities agenda was drawn up for initiating standardized monitoring of anopheline resistance to insecticides.

Workshop on the use of minilabs for antimalarial quality control in the field
In the last week of September, a workshop on the use of German Pharma Health Fund (GPHF) mobile laboratories for quality control of antimalarials was held in Tumeremo, Venezuela. Technical personnel from Brazil, Colombia, Ecuador, Guyana, Suriname, and Venezuela participated. The activity was coordinated by a team from the United States Pharmacopeia (USP) and the RAVREDA-AMI committee from Venezuela. (A training session was held for this purpose at the beginning of the year in Ecuador, with the further participation of technical personnel from Bolivia.) The people trained in the use of the GPHF minilabs in Tumeremo will replicate the experience in their countries, forming field teams to conduct regular monitoring of the quality of drugs available in endemic areas. It is hoped that this will yield results for a first round of evaluations by March 2006, which can then be presented at the V Annual Meeting of RAVREDA-AMI.

Meeting of the RAVREDA-AMI Coordinating Committee
On 14 and 15 September, the VII meeting of the RAVREDA-AMI Coordinating Committee was held in Washington, D.C. Network advances over the past year and work plans for the 2005–2006 period were reviewed. Emphasis was placed on carrying out the proposed work agendas for each 2005 subject area during the upcoming period. Mention was made of the need to improve coordination of the supply and demand for...
technical cooperation among countries and institutions that support the network—USP, MSH, and CDC—as well as the need to promote the use of network products by monitoring programs and initiatives in which they can be implemented, such as projects financed by the Global Fund.

News from the Countries

◆ Bolivia

Administrative Aspects
On 15 August, the Bolivian Minister of Health, Dr. Álvaro Muñoz Reyes, came to the City of Cobija to inaugurate the RAVREDA-AMI laboratories equipped with facilities for diagnosing and conducting Parasitology and Entomology research. Partial equipment deliveries also occurred. The RAVREDA-AMI Laboratory is expected to serve as a reference laboratory for the Amazon region in Bolivia, given the importance of its geographic location. On 14 and 15 September, at the VII Meeting of the RAVREDA-AMI coordinating committee in Washington, D.C., the RAVREDA-AMI Bolivia work plan was presented.

Study of the Cost Effectiveness of the Use of Rapid Tests by Volunteers in the Amazon region of Bolivia
Finally, the blood samples obtained during the field work were read, and the data is currently being entered in the respective database. The study is expected to be finished by the end of October. At the same time, the reading of blood samples in connection with the study on Identification of Asymptomatic Carriers of *P. vivax/falciparum* was begun, using Rapid Tests in the localities of Guayaramerín and Riberalta, Beni. The already-concluded field work was done among nonfebrile patients living in neighborhoods with a high incidence of malaria, where the majority of people working in the chestnut harvest this year reside. This study represents one-third of a series of studies carried out before, during, and after residents of the area were mobilized for the chestnut harvest.

*In vivo* monitoring of the efficacy of chloroquine in the treatment of *P. vivax*
The protocol was prepared for this study, to be conducted in the localities of Riberalta and Guayaramerín, in the Department of Beni, and in the locality of Yacuiba, in the department of Tarija, for the purpose of evaluating the efficacy of chloroquine in the current National Malaria Program treatment regimen, with the further aim of determining chloroquine levels in blood. To this end, a technical assessment of the health network laboratories where the study is to be held was conducted, in order to determine the characteristics of each malaria diagnosis center. Contacts necessary for the implementation of the study are currently being established, involving the training phase for personnel who will be participating in the research, as well as necessary arrangements for beginning the work in November of this year.

Study of Pharmaceutical Management for Malaria Bolivia
On 19-22 July, representatives of RAVREDA-AMI Bolivia participated in the “Workshop Course in the Application of Tools for Analysis of the Pharmaceutical Management of Malaria” which was held in Bogotá, Colombia. This event gave rise to the preparation of the corresponding protocol for conducting the “Study of Pharmaceutical Management for Malaria Bolivia.” The protocol is currently being reviewed and approved, and arrangements are being made to begin training field personnel.

Training Workshop in Microscopic Diagnosis of Malaria, Treatment, and Maintenance of Microscopes
In Cobija, with the collaboration of the Instituto de Laboratorios en Salud (INLASA), a workshop was held on malaria diagnosis in the Department of Pando, in anticipation of the imminent migration of inhabitants for the chestnut harvest—the most economically important extractive activity in Bolivia. This workshop was directed at physicians, nurses, technical staff dealing with malaria, and volunteers. The topic of microscope maintenance was covered due to the region’s geographic remoteness, so as to provide for the ability to perform adequate maintenance of equipment. This same workshop is expected to be conducted in the localities of Riberalta and Guayaramerín, given that the majority of the population working in the chestnut harvest is associated with these two localities.

Strengthening AMI’s entomological component and activities
The entomology laboratory of the Instituto de Laboratorios en Salud (INLASA) was organized and divided into four sections: biochemistry and molecular biology, taxonomy, bioassays and insectariums, where research projects are carried out in each of the respective areas. The insectarium was established to produce sufficient biological material (*Anopheles pseudopunctipennis*) for bioassays. Six technical staff in medical entomology were trained in the areas of taxonomy, bioassays, and insectariums.

Advances in recent months have already led to initial results on the monitoring of anopheline resistance to insecticides. The sensitivity of all evaluated strains of *Anopheles pseudopunctipennis* to the pyrethroids used (deltamethrin and permethrin) was recorded, as well as potential resistance of *Anopheles darlingi* to deltamethrin in the Amazon region of Bolivia. These surveys make it possible to assess the response of insect populations to the insecticides used in vector control. Moreover, in the municipality of Yacuiba, in southern Bolivia, an inventory of anopheline fauna has begun, with identification of the following species: *An. pseudopunctipennis*, *An. benarrochi*, *An. argyritarsis*, *An. triannulatus*, and *An. rondoni*.

Participation in other regional events
On 24-27 July, Bolivia participated in a presentation on the topic, “Malaria in the Chestnut Worker Population of the Bolivian Amazon region,” during the First Meeting on
Migrant Populations of the Amazon Region and the VII Session on Tropical Diseases of the Lower Amazonas, held in the city of Santaré, Brazil. At this meeting, the current status of malaria among the migrant populations of the different countries of the Amazon region was analyzed.

Evaluation of the therapeutic effectiveness of antimalarials
During the last three months, progress was made in systematizing the information from the efficacy studies that concluded in May. All data were input, using double entry of data, which were then validated by cross-checking the two sets of entries. In subsequent months, the information will be analyzed statistically. In July patients began to be enrolled in the study on the therapeutic effectiveness of Coartem® in the municipality of Coari, in the state of Amazonas, while expanding these efforts to the municipality of Porto Velho, Rondonia, in late August. The protocols used in other RAVREDA countries were reviewed and adapted to evaluate these combinations. In the states of Mato Grosso and Amapá, studies on the therapeutic effectiveness of the combination of mefloquine and artesunate were initiated.

Evaluation of adherence to P. vivax-malaria treatment
During the months of August and September, a study of 96 patients was conducted in the state of Pará on adherence to official P. vivax-malaria treatment (7-day CQ + PQ regimen). The data are currently being processed for analysis. The same protocol is being implemented in a study initiated in September in the state of Mato Grosso.

Measurement of drug levels in blood
Blood samples of patients who presented therapeutic failure in the efficacy studies conducted by RAVREDA were sent to the Pharmacy Laboratory of the Universidade Federal del Pará, where analyses of blood levels for the relevant drugs have been conducted out in recent months. These results will help guide the analysis of the studies conducted regarding the effectiveness of CQ in P. vivax malaria.

Evaluation of the stability of rapid tests in the temperature and humidity conditions prevalent in the Amazon region
The study initiated in the preceding quarter in the states of Mato Grosso, Rondonia, and Pará was also begun during the most recent quarter in the states of Amazonas and Amapá.

Evaluation of the quality of antimalarials
In cooperation with the drug quality laboratory of the Federal University of Minas Gerais, quality analyses of drugs to be used in studies on the effectiveness of combinations using artemisinin derivatives were conducted.

Effects of administering fixed dosages of the ASU+MQ combination on malaria transmission in communities of the Amazon Basin
Preparation of a protocol for use in high-risk municipalities in the states of Amazonas and Pará, and evaluation of the effect of using a fixed-dosage formulation of the MQ+ASU combination as a first-line noncomplex P. falciparum malaria treatment. This intervention is part of the gradual introduction of the use of ACT to create a more effective policy with a greater impact on P. falciparum malaria transmission. At present, the protocol is being evaluated by the National Commission on Ethics in Research with Humans, since the fixed combination is not yet registered in the country.

Malaria stratification
Following the conclusions of the Santa Cruz meeting on malaria stratification, the General Coordinating Office of the Ministry of Health’s Malaria Program has been conducting a stratification exercise using the different variables routinely registered for SIVEP–Malaria.

Evaluation of anopheline resistance to insecticides
Baselines for susceptibility of Anopheles darlingi to cypermethrin were conducted in the states of Amapá, Rondonia and Maranhão, with mosquitoes from areas in which insecticides were not used.

Expanded meeting of the RAVREDA advisory committee
On 11 and 12 July an expanded meeting of the RAVREDA-AMI national advisory committee was held in Bogotá to undertake a review and comprehensive analysis of the principal research activities and malaria surveillance and control in the country during the last year, and to identify critical problems and define responsibilities, priorities, and an activities agenda, with emphasis on the RAVREDA-AMI project plan for the October 2005–September 2006 period.

Pilot study on the availability and use of antimalarial drugs in noncomplex malaria treatment in three high-risk departments
Based on the guidelines and commitments defined in the regional workshop held in Bogotá with MSH between 19 and 22 July, a working team was formed with officials from the Vice-Ministry of Health and CIDEIM, presenting the advances in the following areas: (i) preparation of the research protocol and discussion with MSH; (ii) preparation and review of instruments; (iii) review of budgets; (iv) formation of field teams; (v) preparation of a manual for data collectors; and (vi) planning of workshops to train data collectors. The work timetable anticipates that data collection will conclude in mid-October 2005.

Evaluation of introducing the combined use of Artemisinin derivatives in treating P. falciparum malaria in high-risk departments
The Ministry of Social Protection, in coordination with the Departmental Secretariats of Health and with support from
RAVREDA-AMI Newsletter, No 4, July-September 2005

RAVREDA-AMI is planning to conduct an intervention study on implementing the use of ASU+SP in the Departments of the Pacific Coast; ASU+MQ in the Department of Antioquia; and Coartem® in the Department of Córdoba. Plans have been made to develop an integrated protocol for evaluation of in vivo efficacy — effectiveness in sentinel sites within the departments where the new intervention is to occur. This measure is part of a strategic plan by MPS to develop high-impact interventions in critical municipalities.

Joint supervisory visits to the sentinel sites for monitoring the effectiveness of antimalarials

With the participation of officials from the Vice-Ministry of Health, National Institute of Health, CIDEIM, and PAHO/WHO, arrangements were made for a supervisory visit to the sentinel sites of Buenaventura (in the del Valle department) and Tumaco (in the Nariño department), where CIDEIM, in coordination with the Departmental Ministries of Health, us concluding studies on the effectiveness of chloroquine in the treatment of P. vivax malaria; and amodiaquine plus sulfa-pyrimethamine and amodiaquine alone for the treatment of noncomplex P. falciparum malaria, based on standard PAHO/WHO protocols.

Changes in the reference document on national policy on antimalarials, and preparation of the plan to implement it

During this period, progress was made toward revising the preliminary version of the document on antimalaria-drug policy, duly linked to the general policy on medications, while efforts were begun to circulate this policy among concerned social actors, along with information about the preparation of the plan for its implementation.

Entomology and vector control activities

With the support of an entomologist who joined the RAVREDA-AMI team in Colombia, efforts to review the national literature on malaria vectors have been undertaken, and progress toward developing a national plan for monitoring the susceptibility and resistance of these vectors to insecticides has been made, pursuant to the plan of activities agreed upon at the Lima meeting.

Linking RAVREDA-AMI activities with other malaria control projects

In order to rationalize the use of resources and achieve greater sustainability in regard to research, surveillance, and control activities, the results of RAVREDA-AMI activities are being shared in an attempt to provide a linkage with the national program and other initiatives, such as the Global Fund for the Andean Countries project and the Adaptation to Climate Change in Health project, thereby seeking to improve efforts to prevent and control malaria and dengue.

**Ecuador**

Evaluation of the therapeutic effectiveness of antimalarials

Between July and September, patients continued to be included in the study to evaluate the therapeutic effectiveness of Coartem® for patients infected with *P. falciparum* in key RAVREDA sites in the cities of Esmeraldas, Milagro, and Santo Domingo. To date, approximately 39 patients in these three key localities in the Inter-Andean subtropical coastal region, who have had a positive clinical response to Coartem®, were studied.

Implementation of the new first-line therapeutic regimen for noncomplex *P. falciparum* malaria treatment

For the implementation of the new therapeutic regimens, workshops are continuing to be held for public- and private-sector medical staff and for NMES microscopists, expanding the activities to the subtropical areas of the Sierra and Eastern provinces region. Delays in the procurement of Artesunate have limited the use of new first-line schemes throughout the country.

Evaluation of drug quality by provincial teams through the use of minilabs

In July, a meeting was held in Guayaquil to evaluate the first-round quality analysis of antimalarials using minilabs, with the participation of officials from the provinces of Esmeraldas, El Oro, and Pichincha, as well as from the Quality Control Laboratory and the National Institute of Hygiene’s (INH) Registry of Medications. The results of the portable TLC analysis were presented, along with the confirmatory dissolution and quantification tests. Collection of samples from the second analytical round is in progress, as envisaged in the evaluation protocol.

Evaluation of the quality of diagnostic and treatment services

Based on the study “Factors associated with health services’ supply, demand, access, and delivery of malaria diagnostic and treatment services” under way in endemic urban and rural communities, data collection is continuing, with the data currently being entered into the Epi-Info database for analysis.

Quality control of malaria diagnosis

Advances in the census of laboratories that perform malaria diagnosis. Holding of a workshop on the standardization of thick blood film reading and techniques in the province of Esmeraldas, with the participation of technical personnel from MPH, Social Security, the Armed Forces, and private institutions accredited to carry out microscopic diagnosis of *plasmodium*, using the manual of procedures developed by NMES as a reference. Similar activities are taking place in the province of El Oro.
Use of geographic information systems for malaria stratification and control

With support from the Asistencia Social Integral (ASI) foundation, the parameters for implementing these tools have been defined. Updating of the theme maps provided by CLIRSEN has begun, based on the work in the provinces of Esmeraldas and Manabí. It is proposed that variables involving socioeconomic, land use, predominant culture, and other issues be employed in addition to the classical variables for malaria. The use of free GIS systems such as Phill-Carto or Geodata for implementing this process—following the recommendations provided in Santa Cruz, Bolivia on GIS systems—remains to be determined.

Guyana

Monitoring the therapeutic effectiveness of antimalarials

With the support of national reference laboratories in Colombia and Peru, the reading of external quality control slides from the study on the effectiveness of Coartem® and on the MQ+ASU combination versus MQ was concluded. On receipt of the respective reports, the data will be analyzed.

Expanding diagnostic coverage

As part of the plan to improve malaria diagnosis in Guyana, 10 health workers (with no previous training in malaria) from highly endemic areas were trained in malaria management and microscopy at the Fracesco Vitanza Research Center (CICVF) in Tumeremo, Venezuela. Another training session in microscopy, overseen by Truus Derks, was carried out for health workers with previous training in malaria, in order to update and improve their knowledge.

Access to, and use of, antimalarials in mining areas

A study was launched on access to malaria diagnosis and treatment in the mines, in coordination with the Ministry of Health, the Commission of Geology and Mines, and the Guyana Gold and Diamond Association. The work began with data collection in regions 1, 7, and 8. It is anticipated that work will proceed to the analysis of this type of information in order to identify gaps in knowledge and develop an action plan for malaria control in miner populations in Guyana.

Implementation of antimalarial supply and distribution policy

In coordination with MSH and the Ministry of Health, progress was made toward defining possible lines of work for the 2005-2006 period. MSH carried out a preliminary assessment designed to improve the management of malarial drugs based on the needs encountered in Guyana.

Antimalarial quality control

An initial workshop on High-Performance Liquid Chromatography (HPLC) was held in Guyana, in which the conditions for installation of laboratory quality control equipment were verified. Staff in charge of the national reference library participated.

Peru

Initiative for intermittent irrigation in rice paddies for malaria control along the northern coast of Peru

In view of the potential positive results of employing a intermittent irrigation as the appropriate way to manage water in a desert area, such as the Northern Coast, where water is scarce; protect the soil from salinization; and reduce malaria vectors, the Ministry of Health, Ministry of Agriculture, Lambayeque Region and other regional social actors involved in rice farming (farmers, universities, NGOs, etc), with financial and technical support from the WATCHMAN project (Ministry of Health/USAID), as part of the Amazon Malaria Initiative, agreed to begin implementing an intermittent irrigation technique along the Northern Coast. Thus, on 19 September, the initiative was launched and the official commitments were signed by representatives of each of the participating institutions: the Regional Government of Lambayeque, the Regional Agriculture Office, the Chancay Lambayeque Irrigation Users’ Board, the Joint Effort to Combat Poverty, the Vista Florida Experimental Station/National Agrarian Extension and Experimental Research Institute, the Regional Health Bureau, the Lambayeque Regional Health Office, and the WATCHMAN project.

Strengthening entomological surveillance and vector control in Peru

In September, the convening of a consultation to perform a situational analysis of surveillance and vector control activities in four Regional Health Bureaus, and a technical proposal for the Entomological Surveillance and Vector Control System in Peru were initiated.

Suriname

Training in Geographic Information Systems

In the most recent quarter, a training session was held on the use of geographic information systems (GIS) in the city of Paramaribo. The training was geared to staff from the Epidemiology Department in the Public Health Coordination Office of the Ministry of Health.

Evaluation of the therapeutic efficacy of Artecom® and Coartem®

Enrollment of patients in the study on the efficacy of antimalarials, begun in June at the RAVREDA sentinel site of Paramaribo, is continuing. The therapeutic efficacy of Artecom® is being evaluated, comparing it with another group of patients who are receiving Coartem®. To date, approximately 50 patients have been enrolled.

Evaluation of the quality of antimalarials

Participants from Suriname participated in a training program, conducted in Tumeremo, Venezuela, during the final week of September, on the use of minilabs for antimalarial quality
control. Two GPHF minilabs were already placed in the endemic areas where the rounds of antimalarial evaluations are to be carried out.

Workshop on techniques for monitoring the resistance of malaria vectors to insecticides

From 29 August to 2 September, with the support of the CDC in Atlanta, the RAVREDA group in Suriname coordinated the holding of a second workshop on the use of techniques to monitor the anopheline resistance to insecticides. This effort will bring Venezuela, Suriname, and Guyana into the effort to implement the work agenda in this area, as defined at the meeting in Iquitos in June 2005.

**Venezuela**

Evaluation of the effectiveness of 2-day administration of mefloquine plus artesunate in mining and/or indigenous populations

By the end of September, 80 patients—41 in Bolivar and 39 in Amazonas—had been enrolled. Admission of patients has been very slow in view of the low incidence of cases of *P. falciparum* that meet the selection criteria. The study is expected to conclude during the next transmission period of December 2005 to January 2006.

Implementation of changes in the policy on antimalarials

On three occasions, implementation of the policy has been affected by managerial changes at the Pharmaceutical Products Supply Headquarters (SUMED/SEFAR) of the Ministry of Health. There is an 8-month backlog of orders for antimalarials to treat *P. falciparum* infections in the country. At a joint follow-up meeting with the new SUMED/SEFAR officials, procedures for emergency purchases of antimalarials were expedited for critical areas with *P. falciparum* malaria.

Systematic case monitoring (SCM)

The systematic monitoring of cases has continued in the sentinel sites of Tumeremo and Atüres. By 30 September, a total of 944 patients had been included—795 in Tumeremo and 149 in Atüres. 919 patients have received combined therapy with artemisinin derivatives for *P. falciparum* and/or mixed infections, showing a 100% efficacy rate. In the SCM of *P. vivax* and *P. malariae* infections, 3 and 22 patients, respectively, have been enrolled.

Evaluation of the efficacy of chloroquine in treating *P. vivax* malaria

A total of 84 patients—53 in Atüres and 31 in Tumeremo—have been enrolled. In the state of Bolivar, enrolling patients continues to be problematic, due to the high dropout rate. This is expected to conclude by the next transmission period. The shipment of blood samples from cases with therapeutic failure of chloroquine is being coordinated to provide for drug-level analysis.

Quality management in malaria diagnosis

Quality-management training activities, following the guidelines from the Caracas meeting, could not be carried out, due to changes in management and restructuring at the central malaria quality control laboratory. The activity is expected to conclude in November. The state of Sucre completed the survey of 99% of their diagnostic posts, only 70% of which are georeferenced. In Amazonas and Bolivar, there is an up-to-date list of malaria diagnosis and treatment centers. However, georeferencing has required more time, given the logistical constraints involved.

Malaria stratification

The Environmental Health Bureau, through the Malaria Coordinating Office, has already completed the updating of population censuses with growth projections. The probable localities representing origins of malaria infection have been identified in the last 5 years, with a database created for this purpose. By November, it is expected that there will be up-to-date maps indicating API and numbers of cases.

RAVREDA-AMI Venezuela dissemination of results and scientific output

Participation of RAVREDA Venezuela in the “VII jornada de Doenças Tropicais do Baixo Amazonas” held in the city of Santarem, Brazil in July, where 7 papers were presented, receiving first- and second-place awards for best scientific work. Three posters were accepted for the 54th annual meeting of the American Society of Tropical Medicine and Hygiene, to be held in Washington, D.C., on 11-16 December. Also accepted were 5 charts of RAVREDA-AMI results, to be presented at the Jornadas Anuales del Centro Amazónico de Investigación y Control de Enfermedades Tropicales, in the state of Amazonas on 12-15 October 2005. The RAVREDA team was also invited to participate in the Jornadas Arnoldo Gabaldón, to be held 3-6 December at the Dr. Arnoldo Gabaldón Maracay Instituto de Altos Estudios de Salud Pública.

**Venezuela-Guyana South-South Cooperation**

The Tumeremo Field Research Center received the first 10 participants for the First International Course on Malaria Diagnosis, aimed at health workers from different regions of Guyana. This intensive 6-week course included in-service training in composing slides, conducting thick and extended blood film procedures, malaria diagnosis (Fp, Pv, Pm and mixed infections), malaria case management, malaria management in pregnancy, and special case management. A total of 288 academic hours were completed. The Venezuelan Ministry of Health provided 2 instructors and a translator.

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