The idea of the RAVREDA/AMI newsletter has been proposed at several meetings as an important tool to improve communication among the members of the network. The preparation of the first issue was prolonged due to discussions on the newsletter’s structure and operation, but the need for improving the exchange of information has become more persistent. RAVREDA/AMI has been a very important agent for the promotion of some of the elements of the Roll Back Malaria initiative and its efforts to consolidate and improve communication. The network has a dissemination space in the PAHO web page and an internet portal has recently been created in order to facilitate the exchange of documents, protocols, and research instruments, to promote discussion groups and to disseminate information on the activities. With this maiden issue of the RAVREDA/AMI Newsletter we try to promote the initiative of consolidating a news medium among the members of the network. We currently present it without greater concern on its structure and operation with the conviction that it was more important to begin to disseminate the news and in the progress to receive suggestions on how to do it better. We thank the coordinators of the project in the countries and focal points of PAHO, USAID, MSH to have provided the information on this first release.

RAVREDA Regional News

Work Plan 2004 – 2005
The work plans of RAVREDA/AMI for the September 2004 - October 2005 period were reviewed by the project’s coordinating committee and finally approved for its execution. Some modifications were discussed with the countries, directed in general to guarantee the inclusion of activities for implementation of the changes in policy and coordinate better the introduction of the lines of work in entomology. It was also recommended to prioritize the effectiveness studies in those countries where there are still no conclusive information from critical regions.

RAVREDA-AMI Portal
Those who recently entered our page in mayeticvillage noted that improvements for the operation of the RAVREDA/AMI internet portal were recently introduced. (www.mayeticvillage.com/RAVREDA). The inter-face no longer contains product banners (notifications) and was adapted to RAVREDA as user. We now have a greater capacity for storage and sharing of attachments and other options that will improve communication among the members of the network. It is possible to use Chat within the page. The interested parties need a password. It makes it possible also to have statistical use and backup.

RAVREDA-AMI Symposium at the 53rd Annual Meeting of the American Society of Tropical Medicine
The symposium "RAVREDA/AMI: An Amazon Regional Approach for Antimalarial Therapeutic Efficacy Surveillance and Drug Policy Formulation" was a very important endeavor for the dissemination of the advances of the surveillance network. It was in addition an opportunity to share the experience with participants of the Central American countries with endemic transmission of malaria and where there already are concerns on the importance of monitoring the resistance to the antimalarials. The meeting with the members of the network of the different countries, likewise, made possible the discussion of adjustments to the work plans for 2005

External Evaluation of Diagnostic Performance of Reference Laboratories
In November, countries of the region were sent panels of slides of thick blood film for an external quality evaluation of the diagnosis of malaria in the national reference laboratories. The evaluation program is being coordinated by the Communicable Diseases Unit and the Drugs and Technology Unit of PAHO/WHO with the support of the Hospital Pitie Salpetriere (Paris) and is linked to the advances made in RAVREDA/AMI on the improvement of quality assurance systems (Guide developed in the meeting of Caracas, July 2004).
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Workshop on Bioethics and Good Clinical Practices
From the 4th to the 7th of October, a workshop on bioethics and good clinical practices was held in Cartagena, Colombia. The workshop was lead by the Latin American Forum of Ethics Committees in Health Research (FLACEIS) and the CDC, in coordination with the Communicable Diseases Unit of PAHO and participated by a total of 18 professionals from Bolivia, Brazil, Colombia, Ecuador, Guyana and Venezuela. The participants analyzed and shared the current situation in the countries, and recommended the continuation of the training of the ‘investigators’ in aspects related to bioethics and good clinical practices, and promoting the creation of an ethics committee in all the countries that still do not have this resource.

Workshop on Management of Antimalarials
With the coordination of the Rational Pharmaceutical Management Plus Program (RPM Bonus) of the Management Sciences for Health (MSH), a workshop on Management of Antimalarials was held in Lima, Peru from October 4 to 8. A total of 50 delegates from Bolivia, Brazil, Colombia, Ecuador, Guyana, Peru, and Venezuela participated in the activity (see page. 7-news of Peru).

Workshop on the Quality of Antimalarials
A workshop on the quality of antimalarials was held from October 12 to 15 at the National Laboratory for Quality Control of Drugs and Toxicology, in La Paz, Bolivia. Providing support for the activity were Dr. José María Parisi, Drug Quality Assurance Consultant of PAHO/WHO Washington; Dr. Nilka de Solis of the Institute of Specialized Analysis of the University of Panama; and Dr. Juan Ortiz Bernaola, of the National Center for Quality Control of the National Institute of Health of Lima, Peru. 14 staff members of Paraguay, Ecuador, and Bolivia participated. During the event the analytical techniques for ‘Artesunate’ and ‘Mefloquine’ tablets were standardized (identification, dissolution and quantification).

Country News

◆ Bolivia

Prevention and Control of Malaria among Chestnut Collectors
Between October 13 and 16 in Riberalta, Beni, an evaluation was made of the first plan and preparation by consensus of the second plan of action for the prevention and treatment of malaria among the population of chestnut collectors in the Amazon subregion. The activity was done with the participation of the Ministry of Health, PAHO/WHO, municipal authorities, NGOs, entrepreneurs, and community organizations of chestnut collectors.

Round Table on "Malarial Drugs and the Problems Related to the Management of the Supply, Quality Control, Utilization, and Sanitary Regulation"
Consistent to the framework of the regional workshop on the quality of antimalarials this important event was held in October 19 with the participation of different offices of the Ministry of Health and Sports and representatives of PAHO/WHO Bolivia and Washington.

Completion of the Study on the Effectiveness of CQ in the Treatment of P. vivax Infections
In November, important progress has been made in the specialized laboratory tests and in the preparation of the article on the study conducted in the SC of Yacuiba, Tarija, and Riberalta, Beni.

Patient Adherence to the Treatment of P. vivax Malaria
As of December the research team was processing the data corresponding to the study conducted in the SC of Guayaramerin–Riberalta.

Susceptibility and Resistance to Insecticides of Malaria Vectors
In December, the last entomological sampling was conducted in the priority sites of research as defined at the national level for the initial baseline survey.

Effectiveness of Rapid Tests Used In the Diagnosis and Treatment of Malaria by Health Volunteers among Chestnut Collector Populations
The corresponding study on the OptiMAL rapid test started in November with 20 health volunteers and the participation of staff members at the municipal level.

Adherence of Technical Staff Members to Technical Malaria Treatment Standards
With the research team from SC of Riberalta, revisions were made in December on this research protocol approved by the TDR, in order for it to begin in February 2005.

With 20 of the principal actors of the project participating in the event, the national workshop was held from November 29 to 30. Remaining pending are adjustments to the document for its official presentation during the first quarter of 2005.

Third Meeting of the National Coordinating Committee of RAVREDA/AMI,
Proceedings of the aforementioned event, which was held in November 30 and participated in by 30 specially invited members of the national committee, are now available.

New Manual on the Standards for Malaria Prevention and Control Techniques
With the participation of a team of national experts and of PAHO/WHO, the review and revision of existing
standards are to be completed by the end of December. These include standards on management, epidemiological and entomological surveillance, diagnosis and treatment, control, health promotion and prevention of malaria. The document will be published and disseminated during the first quarter of 2005.

Brazil

Evaluations of Antimalarial Effectiveness
In the months of October and November, administrative difficulties in the execution of antimalarial effectiveness evaluations in the states of Amazonas and Pará have been settled. Adding these sentinel locations to the studies that were already in progress, it is confirmed that the evaluations of the effectiveness of Mefloquine, ‘Quinine’, and ‘Chloroquine’ are currently being conducted in the sentinel sites of the states of Amazonas, Amapá, Rondonia, Maranhão, Mato Grosso and Pará, specifically as follows:

- Mefloquine’: Porto Velho, São Luis, Macapá, Manaus and Careiro.
- ‘Quinine’ + ‘doxycycline’: Belém and Macapá;
- ‘Chloroquine’ (P. vivax): Porto Velho, Belém, São Luis, Macapá, Manaus, Careiro and Cuiabá

Another noteworthy development in the progress of the activities over the last few months is the greater participation of the State Health Secretary of the Amazonas in the undertakings of the surveillance network.

Plan to Initiate Evaluations on ‘Artemisinin’ Derivative Combinations in 2005
At the RAVREDA committee meetings in October 2004, it was agreed upon that as soon as the evaluations of the official therapeutic regimens are concluded, the evaluation of the effectiveness of the Artemisinin derivative combinations will commence. ‘Artesunate’ and ‘Mefloquine’ were already acquired and the shipment of Coartem® is currently in progress. The administrative mechanisms for the first studies in the sentinel sites of Rondonia and Mato Grosso have likewise been approved.

Evaluation of the Quality of Antimalarials Used in Health Units
In the month of December consensus has been reached on the administrative aspects of the evaluation of the quality and stability of antimalarials distributed by the Ministry of Health for malaria treatment in the endemic regions. The evaluation that is scheduled to begin in February 2005 will include the analysis of samples collected in six health posts of the Amazon region, three state warehouses and of the national drug plants. Aspects related to the storage and manipulation of the drugs will be also evaluated.

Validation of In Vitro Test Methodology Proposed in Bogotá
Following the plan of activities proposed at the Bogotá meeting on the use of in vitro tests in RAVREDA, the laboratories of the Evandro Chagas Institute and of the Foundation of Tropical Medicine of the Amazon made evaluations of the susceptibility to ‘Quinine’ and to ‘Mefloquine’ comparing two methods (WHO and HRP2) and also comparing the results in fresh isolates versus frozen strains. In these tests, other aspects of the standardized methodology in Bogotá were also implemented (preparation of plates, use of gas mixture in the incubation and use of Albumax as supplement in the preparation of the parasites). The results will be presented in the next regional activity for standardization of these tests in RAVREDA.

Congress of the Brazilian Society of Tropical Medicine
In March 2005, a week before the Annual Meeting of RAVREDA/AMI, the XIII Congress of the Brazilian Society of Tropical Medicine will take place in Florianopolis, Brazil. The Ministry of Health will organize with PAHO a symposium on malaria where they will have two round table discussions on resistance to and policies on malarial drugs. The results of the studies of effectiveness conducted in Brazil and new therapeutic alternatives will be presented and discussed with the members of RAVREDA and the Ministry of Health.

Colombia

Recommendations of Experts on Changes in Therapeutic Schemes
From September 28-30, 2004, a meeting was convened by the Ministry of Social Protection in Bogota to analyze the results of the evaluations of effectiveness carried out in RAVREDA in Colombia and to submit recommendations on the necessary changes in the therapeutic schemes. Among the recommendations presented was to change the first-line of treatment used in the Amazon region and Orinoquía for uncomplicated P. falciparum malaria. The recommended regimen is the combination of Mefloquine’ + ‘Artesunate’. The same regimen was recommended as second line for the rest of the country, where the use of Amodiaquine + SP will still continue as first line. Arguments used in favor of changing this first line include the need for protecting the SP, the possibility of having greater impact on the control of the transmission using derivatives of the ‘Artemisinin’ and the findings of significant levels of therapeutic ineffectiveness with the sole use of Amodiaquine. Against the findings of high therapeutic effectiveness of the combination regimen was the low cost of the current scheme. Consensus was reached to suspend the use of monotherapy with ‘Mefloquine’ as third line.

Evaluation of the Therapeutic Effectiveness of the ‘Artesunate’ + SP Combination
In 2004, the evaluation of the AS+SP combination began in the sentinel sites of Turbo and El Bagre, through the coordination of the Malaria Group of the University of Antioquia and the support of the Health Secretary of Antioquia. The findings were presented at the policy
meeting. Attention was focused on the least proportion of gametocyte carriers in regard to the evaluations of the official scheme (AQ+SP) made in the same sentinel sites (SC) of RAVREDA/AMI.

Support for the Process of Formulation and Implementation of the Policy on Antimalarials Since December, technical support was contracted to facilitate the processes of formulation and implementation of the changes recommended in the antimalarial policy. The objective is to support the preparation of the policy document and to promote the processes for the regulation and implementation of the new schemes.

Replication of the Lima Workshop on Procurement and Supply of Antimalarials During the end of November, the participants of Colombia in the workshop on the management of antimalarials, carried out with 6 staff members of the Ministry of the Social Protection a sharing of the knowledge and practices carried out in Lima. This subject is of the greatest importance considering the information presented at the national meeting of experts on problems in the access to the antimalarials and official schemes.

Reactivation of the SC Team of Tumaco for Evaluations of Effectiveness Since the beginning of the second year of operation, the sentinel site of Tumaco had reported operational difficulties regarding the assignment of human resources by the health services. The difficulties were recently resolved, but the problem of the sustainability of the surveillance network and the need for defining the role of the different levels of the health services surfaced. This subject can be addressed through the regulation of the evaluation component of the policy document.

Validation of the in vitro Test Methodology Proposed in Bogotá As agreed upon in the meeting at Bogotá, the equipment of the CIDEM linked to RAVREDA/AMI evaluated the performance of the HRP2 methodology for in vitro susceptibility tests comparing them with the WHO method for AQ and CQ. The performance of the tests was compared in cultivated isolates. The results will be presented at the second meeting on in vitro tests in RAVREDA in 2005.

**Ecuador**

Ministerial Agreement No 0001286
On December 1st, 2004, Ecuador’s Minister of Public Health, Dr. Teófilo Lama Pico, signed the Ministerial Agreement No 0001286 which establishes a new treatment regimen for uncomplicated P. falciparum malaria. In the agreement, the following therapeutic regimens are established and are to be disseminated by the National Service of Arthropod Vector-borne Disease Control (NMES) and the Coast-Insular Regional Health Department and Provincial Health Bureaus.:

- **First line**: ‘Artesunate’ (4mg/kg on 3 days) + ‘Sulfadoxine’–`pyrimethamine’ (25 mg/kg/dose single)
- **Second line**: Artemeter 20 mg + Lumefantrina 150 mg (Coartem®)

Monitoring the Quality of Antimalarials
The GPHF-Minilab® kits for the evaluation of the quality of antimalarials in Ecuador are already in the field. The minilab kits were acquired by the United States Pharmacopeia (USP) to set up a monitoring system for the quality of the antimalarials that circulate in and are used in the malaria program of Ecuador. With the kits already available, the training for antimalarial quality control by the health services and the malaria program at provincial level is already scheduled and will be participated in by the USP, the National Institute of Hygiene, the NMES, and PAHO.

Adherence in the Treatment of Malaria by *P. vivax*
Recently, two evaluations of the adherence to the treatment of malaria by *P. vivax* have been concluded in areas of concern in Esmeralda and Milagro. The findings call attention on a high proportion of deficiencies in adherence to the 14-day Primaquine regimen and the need for establishing the use of written instructions as routine in the care of patients with malaria.

Evaluations of Effectiveness in the Amazon Region
In recent months, the training of personnel for the evaluation studies on the effectiveness in the treatment of malaria by *P. falciparum* has been carried out. Microscopists and the possible places of study have been identified but the very low incidence of malaria has prevented the progress of the studies. In this regard it is important to discuss within the framework of RAVREDA possible regional strategies to monitor the resistance in situations where there are very low number of cases: the multi-center effectiveness studies, complemented with the use of in vitro tests and for the particular case of Ecuador the use of molecular markers to evaluate the resistance to SP.

Evaluation of Rapid Tests in the Field
An evaluation of the OptiMAL IT is in progress, in localities of the Amazon region and in the province of Esmeralda. To date, no reports of considerable difficulties in the use of the tests have been reported by the local health workers. The stability in field conditions is good. The end results will be available in February.

**Guyana**

Implementation of Policy Changes
After the launching of Coartem® as the first-line of treatment for uncomplicated *P. falciparum* malaria in September 2004, the implementation of the new regimen
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by regions has begun. The incremental implementation plan started with regions 4 and 9.

Evaluation of the Effectiveness of Coartem®
The study started in May and finished in October 2004. 73 patients were evaluated with an excellent adherence to the study and a 100% adequate response to the treatment.

Evaluation of the Effectiveness of ‘Mefloquine’ and Mefloquine+ Artesunate
A study on the effectiveness of ‘mefloquine’ and the combination of ‘mefloquine’ + ‘artesunate’ recently started in region 8 (Madhia). The inclusion of patients in the study has been very fast and the study is going adequately with the same equipment used for the Coartem® study in Georgetown. To date there are 62 patients enrolled in the study. The results of this evaluation are of great interest particularly for the history of high proportion of treatment failure from `mefloquine` confirmed in Port Kaituma in the 2003.

Preparation of National Standards and Guide/Manual for the Management of Malaria in Guyana
During the last two months, progress has been made in the preparation of the technical document that will serve as basis for the preparation and redefinition of standards and updating of national guides in malaria. Since December the training guides are being updated according to new standards.

National Malaria Day
In this 6th of November, the Minister of Health launched the first day of Malaria in Guyana in Lethem, region 9 with the objective of increasing public awareness on this health problem. Following this initiative it will be proposed to have a malaria day in the Americas.

Control of Malarial Drug Quality
In December 2004, an evaluation of the possibility of strengthening the National Laboratory for the Control of Drugs and Food in Guyana was made. Guyana produces malarial and retroviral drugs, the quality control of which, however, needs to be strengthened. Dr. José Parisi of PAHO’s External Control of Reference Laboratory, is technical coordinator for developing this capacity for external control of malarial drugs.

Peru

Meeting on the Management of Drugs and Essential Supplies for Malaria Control Programs in the Amazon Basin
This activity was carried out in the city of Lima from October 4 to 8, with the participation of USP/RPM, representatives of PAHO and of the countries of the RAVREDA/AMI, with a the objective of strengthening the decision-making capacity in the planning, definition of specifications, selection, and supply of drugs and essential supplies for the malaria control programs in the Amazon basin. Experiences were shared among the countries in: the selection of therapeutic lines for malaria in the countries, procurement and quality control of drugs, storage and distribution, use of drugs and supervision and monitoring.

Monitoring of Adverse Reactions to the MQ-AS Combination Therapy in the Peruvian Amazon Region
November marked a year of monitoring the adverse reactions to the MQ-AS combination therapy, which is carried out in 23 health facilities of Loreto. Surveillance has been the responsibility of the workers in the health facilities, with the participation of the Regional Bureau of Drugs of Loreto’s Regional Health Bureau, and the Direcccion General de Medicamentos Insumos y Drogas. During the process of implementation of this surveillance, the foundations were laid for the design and operation of the “Surveillance System for Adverse Reactions to Strategic Drugs in Public Health.”

Evaluation of the Implementation of Combination Therapy along the Northern Coast and Along the Peruvian Amazon Region
The field work for this evaluation culminated in June, and the preliminary report on this evaluation was socialized with the Peruvian Ministry of Health, after having been presented in the Congress of the Society of Tropical Medicine–Miami in November. Among the most salient preliminary findings noted: the preference of the patients and health workers for the SP-AS and MQ-AS over only the SP or only the ‘Quinine’; the high rates of RAMs (mild-moderate) in patients that received MQ-AS without significant effect on the adherence to the treatment and the problems in the availability of drugs in the health facilities.

Monitoring of the Resistance of P. falciparum to the Antimalarials in the Peruvian Amazon Region Using Molecular Markers
Completed in the last quarter of the year was the installation of the “Monitoring of the Resistance of P. falciparum to the Antimalarials in the Peruvian Amazon Region, Using Molecular Markers” in the 8 Amazon basins of Loreto. This surveillance will make it possible to know the distribution of strains of P. falciparum resistant to CQ, MQ, and SP, and predict the resistance to the antimalarials in the western area of the Peruvian Amazon Region.

Suriname

Reduction in Morbidity from Malaria: Impact of the Introduction of ACT Use?
Malaria by P. falciparum in Suriname has declined to just a little more than 50% of the figures of 2003. In 2004 Suriname, with support of RAVREDA/AMI, has introduced ACT (Coartem) as first line of treatment. The preliminary analyses indicate that the role of Coartem in the decline is important. The numbers of P. vivax have not
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undergone such an important reduction and cases in areas where the introduction of Coartem was late diminished only after its introduction.

Advances in Entomological Evaluations
Suriname is finishing a behavioral study of the principal vector within country, A. darlingi, as a preliminary stage to the assessment of impact of the use of LLN that will be introduced this year.

Venezuela

Implementation of Change in Antimalarial Policy
The implementation is in progress for the use of MQ+AS as first line treatment for uncomplicated P. falciparum malaria. A Ministerial Circular Letter was released to affect the change in the policy. The process of implementation, however, has been relatively slow in recent months due to changes in authorities in the states. The latest activity was held on December 8th in the state of Bolivar.

Evaluation of Therapeutic Effectiveness of MQ + AS versus Coartem®
The evaluation of the effectiveness of MQ +AS3 versus Coartem® in Amazonas has been concluded. 120 patients were studied with the last monitoring completed in December 27, 2004. The data are being integrated into the database. The same study in Tumeremo (State of Bolivar) has had problems with the monitoring, as more than 50% of patients were lost to follow-up due to the intense mining activity.

Therapeutic Effectiveness of the Two-Day Treatment with MQ + ACE
An evaluation has began on the therapeutic effectiveness of the two-day MQ+AS regimen as an alternative that can be used in areas of mining where it is difficult to guarantee adherence to the 3-day regimen. A systematic case monitoring is being carried out and currently includes 152 patients.

Evaluation of Therapeutic Effectiveness of ´Chloroquine´ in the Treatment of Malaria Caused by P. vivax
Studies were carried out in Venezuela by RA VREDA on the effectiveness of ´Chloroquine´ in the treatment of malaria caused by P. vivax, which evaluates the effectiveness of the official regimen of simultaneously using Chloroquine and Primaquine. There was a protocol recently implemented, recommended at the meeting in Iquitos, that evaluates only ´Chloroquine´ which leaves initiation of ´Primaquine´ intake only after the day 28. Some therapeutic failures have been reported from which blood samples have been taken for measurement of ´Chloroquine´ levels.

Analysis

Plans on the Implementation of Changes in Antimalarial Drug Policy
Beginning the year 2005 a situation of great importance is expected to happen in the Amazon region regarding policies on antimalarials: five Amazon countries will be, this year, in the process of implementing new therapeutic regimens for the treatment of uncomplicated P. falciparum malaria. By the end of 2003 in Suriname, there already was a consensus on the introduction of the use of Coartem®. In Venezuela, from the middle of 2004, the need for implementing the use of the combination of `Mefloquine´ + ´Artesunate´ has been discussed and is already being authorized for implementation. In September 2004, Coartem® was officially launched in Guyana and more recently, Ecuador’s Ministry of Health established the ´Artesunate´ + SP regimen as first line. Finally, in September 2004, at a meeting of national experts in Colombia, the use of the combination ´Mefloquine´ + ´Artesunate´ was recommended as first line for the Amazon region and second line for the rest of the country, while the effectiveness of the combination Amodiaquine + SP is being monitored carefully.

These effective therapeutic alternatives were already implemented totally or partially in these countries and in four of them have now been made as official schemes. The impact that these policy changes can have in the control programs depends on the access, the quality and the adequate use of the drugs. The implementation of the policy includes activities related to the procurement, distribution and access to drugs of good quality, and to their adequate prescription and use. The process requires the participation of several actors: from the authorities responsible for drug control, the health authorities of states or provinces, up to the service providers and health workers at the local level.

A management that convenes the participation of the different levels and that prioritizes and guides orderly the implementation process requires the formulation of a plan. The "Implementation Plan" is part of the "auxiliary" documents of the policy and basically includes a major content of Information, Education and Communication (IEC) and of measures to guarantee the access to drugs of good quality. The Plan should include the activities, actors, and necessary resources for the adequate implementation of the therapeutic regimens, and those that point out the importance of working in RAVREDA/AMI at the country level, in 2005, in the formulation and execution of the "Implementation Plan" that is presented in a concrete document that should be used to orient the management on health services.
Schedule of Activities

Presented below are the immediate regional activities in the RAVREDA/AMI Calendar:

**Feb 21 - 24**  In Lima, Peru, the first meeting will be held on entomology in malaria control. The lines of work and activities to be developed in this subject will be agreed upon with the countries involved in RAVREDA/AMI.

**Mar 14 - 15**  From March 14 to 15 2005, RAVREDA/AMI will hold its IV Annual Meeting in Cartagena, Colombia.

**Mar 16 - 17**  From March 16 to 17, 2005, after the IV Annual Meeting, Cartagena will host the VI Meeting of the Coordinating Committee.

**Apr 18 - 19**  For the month of April, a technical group meeting is scheduled for the review of adherence study protocols and the preparation of recommendations for the execution of these studies in RAVREDA/AMI.

**Apr**  The II Meeting of standardization of in vitro tests in RAVREDA/AMI is being planned for the month of April. The arrangements are being made with the host country for the event. The experiences of the countries will be evaluated since the meeting in Bogotá and training will be carried out on the use of the new tests based on ELISA.

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