SESSION 5: Quality of the ANTIMALARIALS

Strengthening of the medicines quality control laboratories
in the region of the Americas
and the support of AMI/RAVREDA

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PRESENTATION SCOPE

I - *Activities of PAHO with the OMCL*

A. Pan-American network of Official Medicine Control Laboratories (OMCL)
B. External Quality Control Program (EQCP)
C. WHO Prequalification Program for National Laboratories

II - *The support of AMI/RAVREDA to the Strengthening of the medicines quality control laboratories*
To assure the quality of pharmaceuticals in the Region of the Americas, it is necessary to have:

- Adequate facilities
- Equipment and supplies
- Human Resources well trained
- Quality Assurance System implemented
Pan American Network of OMCL

- **Started in 2000 with the 2\textsuperscript{nd} Pan American Conference of Drug Regulatory Harmonization**

- **25 Official Medicine Control Laboratories from 23 countries (represented MERCOSUR, ANDEAN COMMUNITY, SICA, CARICOM, NAFTA)**

- **Secretariat (PAHO) Jose M. Parisi**

<table>
<thead>
<tr>
<th>23 countries in the Network</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. ARGENTINA</td>
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<td>2. BOLIVIA</td>
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<td>3. BRASIL (2)</td>
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<td>4. CHILE</td>
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<td>5. COLOMBIA</td>
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<td>6. COSTA RICA (2)</td>
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<td>7. CUBA (2)</td>
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<td>8. ECUADOR</td>
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<td>9. EL SALVADOR</td>
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<td>10. GUATEMALA</td>
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<td>11. GUYANA</td>
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<td>12. HONDURAS</td>
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<td>13. JAMAICA</td>
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<td>14. MÉXICO</td>
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<td>15. NICARAGUA</td>
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<td>16. PANAMÁ</td>
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<td>17. PARAGUAY</td>
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<td>18. PERÚ</td>
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<td>19. DOMINICAN REPUBLIC</td>
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<td>20. TRINIDAD &amp; TOBAGO</td>
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<tr>
<td>21. URUGUAY</td>
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<td>22. VENEZUELA</td>
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<td>23. SURINAME</td>
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</table>
Pan American Network of OMCL

MISSION

Strengthen the performance of the Official Medicines Control Laboratories (OMCL) in the countries of the Region of the Americas through implementation of Good Laboratory Practice

OBJECTIVES

- Improve the performance of the quality control laboratories
- Promote implementation of GLP self evaluation guidelines
- Harmonization of methodologies to facilitate the acceptance recognition of obtained results among countries
- Increase the communication and exchange of information between the OMCL, local pharmaceutical manufacturers, and the academia
EXTERNAL QUALITY CONTROL PROGRAM (EQCP)

Technical activity carried out by PAHO in collaboration with the USP (United States Pharmacopeia) and the participation of the OMCL network

OBJECTIVES

- To evaluate the quality of medicines used in priority programs (TB, Malaria, HIV, Neglected diseases)
- To optimize testing capacity and analytical reporting
- To identify the areas that demand technical cooperation
- To develop the concept of reference QC laboratories throughout the region

DEVELOPMENT

- Phase 1: Diagnostic study of the OMCL
- Phase 2: Performing test
- Phase 3: Training of human resources
PHASE 1: Diagnostic study of the OMCL

The main results indicated:

- 100% have HPLC and equipment for dissolution tests
- 50% have adequate facilities to implement GLP
- 24% have sufficient staff
- 24% have operational manuals as requested by ISO 17025
- 20% have a self-financed system
PHASE 2  (Performing test)

The EQCP measures the performance of the OMCL sending to them blind samples and corresponding standards for analysis, indications of the methodology to use and the form to report their results.

Results are evaluated by the United States Pharmacopeia (USP) classifying the laboratories in three groups:

Group 1: Laboratories that have performed an Excellent Job in all the tests

Group 2: Laboratories that have performed a Good Job. In this group, labs can miss some of the tests, or may have minimal errors to be corrected with appropriate training of their staff

Group 3: Laboratories that have performed a very Poor Job
To date the EQCP include 9 stages:

1) Acetyl salicylic acid (Aspirin) Ibuprofen (2001)
2) Acetaminophen (2001-2002)
3) Streptomycin powder for injection (2002)
6) Isoniazide (2005-2006)
8) Oseltamivir (2009-2010)
9) Mebendazole (2011)
PHASE 3: Training of human resources

Training workshops and seminars are planned and implemented in countries that need more assistance to overcome their difficulties, according with the results at the performing evaluation (PHASE 2)

To date the following activities have been implemented:

- 21 countries received GLP training Workshops and implementation of PANDRH self inspection guidelines
- 17 countries received training in HPLC, Dissolution test, and Microbiologic methodologies
- 15 countries received Evaluation of the Quality Management System of the OMCL
PREQUALIFICATION OF QUALITY CONTROL LABORATORIES

Procedure for assessing the acceptability of quality control laboratories for use by United Nations agencies, for the analysis of pharmaceutical products meet the requirements recommended by WHO

This is done through a standardized quality assessment procedure to evaluate whether the quality control laboratories to be used for the analysis of pharmaceutical products meet the requirements recommended by WHO for such laboratories
WHO Prequalified OMCL for use by United Nations agencies
(2010/2011)

- BOLIVIA: CONCAMYT
- BELO HORIZONTE, BRASIL: FUNED
- PERU: CNCC
- URUGUAY: CCCM
OMCL are preparing for the WHO Prequalification and have received Evaluation of the Quality Management System by the other Prequalified in the region (Bolivia, Brazil, Peru, and Uruguay)

Jamaica
Chile
Guatemala
Honduras
Colombia
Brazil (INCQS)
Panama
Costa Rica (2)
Dominican Republic
The support of AMI/RAVREDA to the strengthening of the medicines quality control laboratories in the region of the Americas, has contributed to

- improve the OMCL performance in the Andean, Caribbean, and Central America countries, with the QC of antimalarial and other medicines for TB, HIV and neglected diseases
- harmonize the quality control methodology for artemesunate, mefloquine, artemether, lumefantrine, chloroquine, and primaquine
- train in QA/QC (quality assurance/quality control) and quality management system (QMS)
- give technical assistance in rehabilitation of the facilities and provision of new equipment, reagents, and reference standards
- give assistance for the WHO Prequalification Program
**Rehabilitation of facilities**

General Storage (racks for glass and reagents storage)
Drug Chemistry Laboratory (counter, workbenches)
Microbiology section (washing and sterilization sectors)

**Equipment and reagents purchased**

Dissolution test equipment
Karl Fisher titrator
HPLC (High Performance Liquid Chromatography)
Pump & vacuum systems
Analytical balance with anti vibration table
Refrigerator with freezer
Melting point apparatus
Emergency shower and eyewash equipment
USP-Reference standards
Reagents for Antimalarial drugs
quality control testing

**Provision of new equipment**

Analytical balance
Anti-vibration table
Refrigerator/freezer
Melting point apparatus
Karl Fisher titrator
HPLC system
Dissolution test equipment
Security shower
### Regional training workshops

<table>
<thead>
<tr>
<th>ACTIVITY</th>
<th>DATE</th>
<th>PLACE</th>
<th>COMENTS</th>
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<tbody>
<tr>
<td>Regional training workshops</td>
<td>Nov 2003</td>
<td>Ecuador</td>
<td>To improve the OMCL performance in the Andean countries</td>
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<tr>
<td>(9)</td>
<td>Oct 2004</td>
<td>Bolivia</td>
<td>Harmonization of a quality control methodology for ARTESUNATE and MEFLOQUINE, due to limited international compendia information</td>
</tr>
<tr>
<td></td>
<td>Dec 2005</td>
<td>Guyana</td>
<td>Training in anti-malarial 1st line drug quality control (Chloroquine and Primaquine)</td>
</tr>
<tr>
<td></td>
<td>Jun 2007</td>
<td>Guyana</td>
<td>To improve the Amazon and Caribbean OMCL performance and review the QC methodology for Coarten (Artemether + Lumefantrine)</td>
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<tr>
<td></td>
<td>May 2008</td>
<td>Colombia</td>
<td>Training in management supply systems</td>
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<tr>
<td></td>
<td>Nov 2008</td>
<td>Guatemala</td>
<td>Training in QA and management supply systems</td>
</tr>
<tr>
<td></td>
<td>Aug 2009</td>
<td>Lima, Peru</td>
<td>Strengthening in QA/QC of the OMCL</td>
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<tr>
<td></td>
<td>Nov 2011</td>
<td>Colombia</td>
<td>Three-level Approach for the Quality Control of Medicines in the supply chain, function of the OMCL and medicine quality monitoring</td>
</tr>
<tr>
<td></td>
<td>Apr 2012</td>
<td>Suriname</td>
<td>To improve the performance of the Amazon (BRA, GUY, SUR) and Caribbean (TRT, JAM, BLZ) OMCL in quality control methodologies for Coarten (Artemether + Lumefantrine)</td>
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<tr>
<td>ACTIVITY</td>
<td>DATE</td>
<td>PLACE</td>
<td>COMMENTS</td>
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<tr>
<td>Evaluation of the Quality Management System (QMS)</td>
<td>Mar 2003</td>
<td>Ecuador, Peru</td>
<td>To evaluate capacity in antimalarial QC testing</td>
</tr>
<tr>
<td>(10 audits)</td>
<td>Mar 2004</td>
<td>Suriname</td>
<td>To evaluate capacity in antimalarial QC testing</td>
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<tr>
<td></td>
<td>Dec 2004</td>
<td>Guyana</td>
<td>To evaluate capacity in antimalarial QC testing</td>
</tr>
<tr>
<td></td>
<td>Dec 2005</td>
<td>Guyana</td>
<td>To update the study of current conditions of the Food and Drug Department, FDD</td>
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<tr>
<td></td>
<td>Jul 2006</td>
<td>Brazil</td>
<td>To evaluate capacity in antimalarial QC testing, in Belo Horizonte, Para y Amapa</td>
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<tr>
<td></td>
<td>Jun 2008</td>
<td>Guyana</td>
<td>Technical support to the OMCL (FDD) relocated in the IAST building, University of Guyana</td>
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<td></td>
<td>May 2008</td>
<td>Colombia</td>
<td>Assist at the INVIMA in preparation for WHO Prequalification</td>
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<tr>
<td></td>
<td>Sep 2010</td>
<td>Guatemala</td>
<td>Follow up at the QMS audit performed by PQM at the OMCL (LNS)</td>
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<tr>
<td></td>
<td>Mar 2011</td>
<td>Panama</td>
<td>IEA, Panama University, to evaluate capacity in antimalarial QC testing</td>
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<tr>
<td></td>
<td>Nov 2011</td>
<td>Suriname, Trinidad-T</td>
<td>To update the study of current conditions at the BGVS (SUR) and the Chemistry FDD (TRT)</td>
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</tbody>
</table>
Finally,

A) The seven AMI-countries have their own OMCL (last one was SUR with the BGVS, 2011)

B) Three laboratories have been Prequalified by WHO as Reference laboratories for the UN agencies (BOL, BRA, PER)

C) Three countries implement their National network of QC Laboratories (BRA, COL, PER)

D) All the OMCL are participating in the annual international performing control with the EQCP
Future Perspectives

Training in QA/QC (quality assurance/quality control) and quality management system (QMS)
Amazon: ECU, GUY, SUR
Central America: GUT, HON, NIC

Giving assistance for the WHO Prequalification Program
DOR, COL, BRA (6)

Implementing National network of QC Laboratories
BRA, COL, PER

Improving the OMCL performance with the EQCP
all the network

Evaluation of the Quality Management System by the other Prequalified in the region
Jamaica, Chile, Panama, Costa Rica (2)