



OPS/DPC/CD/274/03
Original: Spanish

Recommendations of an Expert Committee:

**PERFORMANCE EVALUATION STANDARDS FOR THE
KIRBY-BAUER ANTIBIOGRAM
(AREAS OF INHIBITION OR INTERPRETATION)**

**(Santiago, Chile,
24-26 February 2003)**

The Expert Committee to define performance evaluation standards for the Kirby-Bauer antibiogram (areas of inhibition or interpretation) in Santiago, Chile, was made possible by the contribution from the Office of Sustainable Regional Development, Office for Latin America and the Caribbean, U.S. Agency for International Development, as agreed upon for subsidy No. LAC- // G-00-99-00008-99.

Table of Contents

Introduction	1
The Expert Committee's Objectives	2
Discussion Summary	2
Reports.....	4
General Considerations	4
Evaluation Methods.....	4
Evaluation.....	4
General Report to be Sent to the Participating Laboratories.....	5
Individual Report.....	5
Appendix 1: Summary of Activities 1996–2003	6
Appendix 2: List of Participants.....	7

INTRODUCTION

In 1995, due to the regional alert on the importance of emerging and reemerging diseases, which include resistance to antibiotics,¹ the Pan American Health Organization intensified its activities in this area. A network was developed for monitoring susceptibility to antibiotics for isolated *Salmonella* spp, *Shigella* spp and *Vibrio cholerae*. These three species are important etiologic agents of diarrheal diseases that may require antibiotic treatment. Their importance transcends individual medical aspects, since epidemics make them a public health problem. Furthermore, the importance of food contamination, sometimes at the source, due to the infection of farm animals, transforms an individual medical problem into an epidemiological problem with serious economic and social implications. The same thing occurs when these etiologic agents cause outbreaks in countries that obtain resources from tourism. This is the origin of a problem with a much broader economic and political impact than the impact of the original medical problem.

The surveillance network for etiologic agents of enteric diseases, sponsored by PAHO, commenced operations in 1996 with the participation of the national reference laboratories (NRLs) of Argentina, Brazil, Chile, Colombia, Costa Rica, Mexico, Peru, and Venezuela. Each of these laboratories became the head of a local network made up of the thousands of microbiology testing laboratories in the Region. In the end, isolation, identification, and determination of the sensitivity to antibiotics of the species subject to surveillance depend on the activities of those laboratories.

The participating countries concluded that, in order to obtain reliable results, it would be necessary to improve quality assurance for the internal practices of each laboratory and to establish a system to allow periodic evaluation of the performance of the national reference laboratory and the laboratory network in every country. Hence, the participating countries agreed that their contribution to the network would be contingent on the national laboratories exercising surveillance according to principles of quality assurance that guarantee the accuracy of the results obtained. Those results would ensure greater rationality in the empirical treatment of individual cases and potential control measures important to the community.

The National Laboratory for Enteric Pathogens (NLEP) in Canada agreed to serve as the organizing laboratory of the system, which laboratories in six Caribbean countries subsequently joined: Bahamas, Barbados, Jamaica, Saint Lucia, Trinidad and Tobago in 1998, and Cuba in 1999. With the support of the U.S. Agency for International Development, six more Latin American countries were also added to the network in 1999: Bolivia, Ecuador, El Salvador, Guatemala, Nicaragua, and Paraguay.

The countries participating in the network agreed to support their respective national reference laboratory. The NRL, in turn, is the head of the network that compiles national information identifying the species isolated and their sensitivity to antibiotics. Furthermore, the NRL oversees the application of quality assurance principles at each network laboratory through evaluation visits and is also responsible for evaluating each laboratory's performance. In this way, the information can be used to the extent that it is reliable.

Other community species were subsequently included in the network's surveillance: *Streptococcus pneumoniae* (invasive), *Haemophilus influenzae* (invasive) *Neisseria meningitidis*, *Escherichia coli* (urinary infection), and species isolated in hospital-acquired infections such as *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Acinetobacter* spp, *Enterococcus* spp (*E. faecalis*

¹ Regional Plan of Action to Combat New, Emerging and Reemerging Infectious Diseases in the Americas. OPS/HCP/HCT/95,060.

and *E. faecium*), *Klebsiella* spp and *Enterobacter* spp. The performance evaluation system for monitoring these bacteria is the responsibility of the National Institute of Infectious Diseases in Argentina. Appendix 1 gives a list of the principal activities carried out by the network that monitors resistance to antimicrobial drugs.

Evaluating surveillance activities in each country depends on expanding the geographical scope of the activities; increasing the number of participating laboratories (sentinel centers); increasing the number of isolates; improving the results of the international performance evaluation; the availability and dissemination of the information locally, nationally and regionally; and the percentage of agreement between the results of the network laboratories in each country and the national reference laboratory. (A summary of the activities to date by the countries participating in the surveillance network is provided below.)

Concerning the percentage of agreement between the results of the laboratories in each national network and the results from the corresponding national reference laboratory, the need to define and reach an agreement on the standards that will be applied in the performance evaluation became apparent. For this purpose an Expert Committee was formed to make recommendations to be presented at the annual meeting of the Latin American Network in May 2003. The Expert Committee met in Santiago, Chile, from 24 to 26 February 2003 and was made up of the participants that appear in Appendix 2.

THE EXPERT COMMITTEE'S OBJECTIVES

The purpose of the Committee's meeting was to define and document the standards that will be applied to the performance evaluation of laboratories participating in the Latin American Network for Monitoring Antimicrobial Resistance; to document the basic quality control standards for the laboratories that participate in the national surveillance networks and to draft recommendations for maintaining performance quality in all participating countries.

DISCUSSION SUMMARY

Based on the presentations of the different participants (Appendix 3, Agenda), a discussion ensued, with the following conclusions.

1. Laboratory performance evaluation seems to be a simple subject, but experience shows that it is tremendously complex. However, in spite of its complexity, there have been good experiences in Latin America, even though resources are limited. It is indeed essential to be willing to carry out the evaluation if laboratory performance is to be improved.
2. In general, the quality control programs are well accepted by the participating network laboratories in each country and are appreciated for the assistance they provide for the continuous improvement of laboratory performance.
3. The evaluation leads to ongoing improvement in the results over time. This has been seen in all national and international programs presented.
4. The coordinating laboratory should establish a regulatory framework for laboratory operations and other resources that accompany program operations in the national networks.
5. The objectives of network action are mainly to monitor resistance to antimicrobials and to obtain quality results that improve patient health care and promote the rational use of antimicrobials.

6. Evaluation programs should be educational and nonpunitive--that is, the greatest efforts should be directed towards training and improving skills, including knowledge of theory and feedback. The goal is to improve quality and to teach the laboratories to systematize internal quality control and make it a part of their routine. Quality control programs must include a determination of susceptibility and other aspects of bacteriology, such as identification of microorganisms, the preparation of reports, and the preservation of strains.
7. The assessment of results should be addressed with great caution in order to avoid punitive measures by the authorities against a laboratory--measures that might cause the laboratory to withdraw from the evaluation program.
8. It would seem that input sources are less important than internal quality controls.
9. The different international quality control programs should be consolidated into a single program to rationalize human resources and materials.

With regard to assessment of the results, the Committee concluded that:

1. Computer software should be available to take maximum advantage of the information obtained.
2. Evaluation should measure accuracy in the clinical use of the results.
3. There should be a strong educational component, although accreditation and quality assurance standards should be followed.
4. Microorganism identification in the laboratory should serve as an alert that emerging pathogens have appeared and should be linked to surveillance.
5. There should be a component for interaction with the laboratories through bulletins, updates, feedback, analysis of results and problems with their respective solutions (part of accreditation).
6. Evaluation results should be measured in terms of the interpretation of sensitivity (sensitive, intermediate and resistant) and halo size.
7. It should be ensured that the programs: continue to improve; have standardized methods; that the decision to use 2, 3 or 4 mm is made strain by strain; and that NCCLS standards are on hand.

Furthermore, for the purpose of establishing the Committee's task of issuing recommendations for the network, Committee members decided it was necessary to explicitly define the network's mission. Accordingly, it was agreed that the mission of the Latin American Network for Monitoring Antimicrobial Resistance would be *to obtain reliable, timely, and replicable microbiological data that will be used to improve patient care, and to strengthen surveillance programs by establishing sustainable quality assurance programs.*

The recommendations are summarized below, classified as general considerations, evaluation methods, evaluation *per se*, or the production of evaluation reports.

REPORTS

General Considerations

1. With regard to the purpose of the efficiency and quality control tests, the recommendation is to:
 - 1.1. Propose a standardized educational tool that guarantees data quality and compliance with NCCLS standards²
 - 1.2. Implement a process that permits continuous improvement in performance by the participating institutions
 - 1.3. Assess the maximum capacity of the laboratories and their potential deficiencies
 - 1.4. Identify system errors and establish corrective measures
2. Conduct surveys that show the methodology, equipment, and standards used by the participants
3. Conduct periodic evaluations or audits

Evaluation Methods

The following methods of evaluation were recommended:

1. Each evaluation survey should consist of at least three strains. It is highly desirable to include more than three strains a year so that the data are representative.
2. At least two surveys a year will be conducted.
3. The data collection form should include the following points, as a minimum:
 - 3.1. Identification: genus, species, method of identification, as a minimum;
 - 3.2. Sensitivity: type of medium; brand of medium; brand of disk; disk load; inhibition diameter; interpretation (S, I, R); comments (for example: BLEE+, inducible methylase).
 - 3.3. Antibiotics:
The response sheet should include key antibiotics selected by the coordinating laboratory, with additional space for entering the results of other antimicrobials that the participating laboratory uses.
4. The participating laboratories should carry out at least two internal quality controls per month, and the results should be reviewed periodically by the coordinating laboratory.

Evaluation

For results to be evaluated, the participating laboratories should respond within a month of the date that the survey is requested. .

Definition of indicators, by complexity:

- Submission of results
- Identification of the microorganism
- Susceptibility: interpretation of the sensitivity tests. The reference ranges will be obtained with data from the coordinating laboratory and data from other national laboratories that have a history of good performance in the country. The reference range will be calculated with 30 determinations as a minimum, 20 of which will have been made by the Coordinating Center and 10 by the selected laboratories.

² National Center for Clinical Laboratory Standards

- For ATCC strains, the ranges established by NCCLS will be used. For other strains, ± 2 standard deviations will be used, with a minimum of ± 3 mm of the average value (minimum range: 7 mm).
- In the case of strains with no inhibition halo, no range will be used.
- Interpretation of the diameter of the inhibition area (susceptible, intermediate or resistant): should agree with the interpretation by the NCCLS.

General Report to be Sent to the Participating Laboratories

This report will consist of the following items:

- Number of laboratories that received the survey, number of laboratories that responded, and the overall results from the entire network
- Reference results: separate identification and susceptibility for each isolate
- Summary of the characteristics of each isolate with bibliography. Reasons for the inclusion of each strain. National information
- Evaluation criteria, once a year
- Recommendations for improving the accuracy of test results
- Changes in participant and country indicators
 - % of agreement in identification
 - % of serious, very serious, and minor errors
 - % of agreement with the reference range
 - % of agreement in interpretation

Individual Report

This is a report that the national reference center prepares to be sent to each participating laboratory with feedback on the evaluation. It should include the following items:

- Score: identification, sensitivity
- Performance
- It is advisable for each coordinating laboratory to use national standard scoring.
- Comments
 - Corrective measures
 - Concerning interpretation errors, including consistency of halo sizes with the interpretation in the latest NCCLS guides, or errors related to incorrect identification of the strain sent

APPENDIX 1: SUMMARY OF ACTIVITIES 1996–2003

1. **1996-1999.** Regulating techniques for monitoring resistance to antibiotics in strains of *Salmonella*, *Shigella* and *Vibrio cholerae*, including quality assurance, in 19 countries
2. **2000-2002.** Standardizing techniques for monitoring resistance to antibiotics and quality assurance in relation to other community species and species isolated in hospital-acquired infections in six countries
3. **2000-2002.** Training in biosafety in the laboratory in nine countries
4. **2001.** Training in the management of WHONET in six countries
5. **2001.** Training in sample shipment in nine countries (IATA standards)
6. **1997-2002.** Quality assurance program, with performance evaluation, to identify microorganisms included in the surveillance and to determine susceptibility to antibiotics in all participating countries
7. **1997 and later.** Drafting an annual report on resistance to antibiotics in isolates of *Salmonella*, *Shigella* and *Vibrio cholerae* in 19 participating³ countries
8. **2000 and 2001.** Expanding the surveillance network in 12 countries to other community species: *Streptococcus pneumoniae* (invasive), *H. influenzae* (invasive) *Neisseria meningitidis* and *E. coli* (urinary infection), as well as species isolated in hospital-acquired infections such as *S. aureus*, *P. aeruginosa*, *Acinetobacter* spp, *Enterococcus* spp (*E. faecalis* and *E. faecium*), *Klebsiella* spp and *Enterobacter* spp (all species not in all countries)
9. **1997-2002.** Creating a database on antimicrobial resistance for use by the participating countries. This information is the baseline for analyzing antimicrobial resistance trends over time. The consolidated information for the year 2000, PAHO document HCP/HCT/201/02, is in press.
10. **2001-2002.** Developing a protocol to evaluate the cost of hospital-acquired infections. Based on this protocol, 14 studies were carried out in eight countries (Argentina, Chile, Bolivia, El Salvador, Ecuador, Guatemala, Paraguay, and Peru)
11. **2001.** Designing guidelines for evaluating the national monitoring system for emerging diseases, including resistance to antibiotics⁴
12. **1999-2002.** Producing materials to train laboratory professionals, and distributing literature to the NRLs and participating national laboratories
13. **2002.** For the purpose of promoting the rational use of antibiotics, the *Model Clinical Guide and Formulary for Treating Infectious Diseases* (Document PAHO/HCP/HCT/210/2002) was published and distributed.
14. Adaptation of the *Model Clinical Guide* to national conditions began in January 2003.
15. Adaptations have already been prepared in Bolivia, Ecuador, El Salvador and Guatemala, where the national guides are about to be printed and distributed.

³ Resistencia antimicrobiana de aislados de *Salmonella*, *Shigella*, y *Vibrio cholerae* en las Américas [Antimicrobial Resistance of *Salmonella*, *Shigella* and *Vibrio cholerae* Isolates in the Americas]. Supplement OPS./HCP/HCT/163/2000.

⁴ Workshop to develop guidelines for evaluating the surveillance system for emerging and reemerging diseases. HCP/HCT/193/01.

APPENDIX 2: LIST OF PARTICIPANTS

Dr. Marcelo Galas

Chief, Antimicrobial Drugs Department
National Institute of Infectious Diseases
ANLIS/Malbrán
Avenida Vélez Sarsfield 563
(1283) Buenos Aires, Argentina
E-mail: mgalas@anlis.gov.ar

Dr. Mario Fabián Martínez Mora

Central Laboratory Dpt of Microbiology
Ministry of Public Health
Asunción, Paraguay
Telephone: (595-21) 292-653
Fax: (595-21) 294-999
E-mail: mariomart@excite.com

Dra. Valeria Prado

Director, Microbiology Program
University of Chile
Medical School
Independencia 1027
Santiago, Chile
Fax: 56-2-7355855

Dra. Andrea Sakurada

Institute of Public Health of Chile
Clinical Trichobiology Section
Maratón 1000, Nuñoa
Santiago, Chile
Telephone (56-2)350-7405 / 350-7447
Fax (56-2) 350-7570 / 350-7582
Santiago, Chile
E-mail: asakurada@ispch.cl

Dr. Ingrid Heitmann

Chief, Expanded Vaccine Program
Ministry of Health
Mac Iver 541, Santiago Chile
Telephone 56-2-6300462
Fax 56-2-6300507
E-mail: iheitmann@minsal.cl

Dr. Lai-King Ng

Chief of the National Laboratory for Enteric
Pathogens
Health Canada
1015 Arlington Street
Winnipeg, Manitoba, Canadá R3E 3R2
Tel: (1) 204-789-2131
Fax: (1) 204-789-2140
E-mail: lai_king_ng@hc-sc.gc.ca

Lic. María Soledad Prat

Institute of Public Health of Chile
General Bacteriology Section
Maratón 1000, Nuñoa
Santiago, Chile
Telephone (56-2)350-7308 / 350-7424
Fax (56-2) 350-7570 / 350-7582
E-mail: sprat@ispch.cl

Dr. John Stelling

Brigham and Women's Hospital
Microbiology Laboratory
75 Francis Street
Boston, Massachusetts 02115
Tel: (617) 732-7388
Fax: (617) 277-1762
E-mail: jstelling@rics.bwh.harvard.edu

Dr. Fred C. Tenover

Associate Director for Laboratory Science
Division of Healthcare Quality Promotion
Centers for Disease Control and Prevention
1600 Clifton Rd Mailstop G-08
Atlanta, GA 30333
Phone: (404)-639-3375
Fax: (404)-639-1381
E-mail: fntl@cdc.gov

Dra. Jeannete Zurita

Chief, Microbiology Department
Vozandes Hospital
Quito, Ecuador
Tel: (593-2)262-142
E-mail: jzurita@hcjb.org.ec

SECRETARIAT

Dr. Christian Darras

PAHO/WHO representative in Chile
Pan American Bureau of Health
Avenida Providencia No. 1017
Piso 4 y 5
Santiago, Chile
Tel: (56-2)264-9300
Fax: (56-2) 264-9311
E-mail: darras@chi.ops-oms.org

Dr. Jean Marc Gabastou

Laboratory Consultant in Public Health
Essential Drugs and Technology Program
Division of Health Systems and Services
525 23rd Street, N.W.
Washington, DC 20007, U.S.A.
Tel: (202) 974-3485
Fax: (202) 974-3610
E-mail: gabastoj@paho.org

Mrs. Roxane Salvatierra-González

Specialist in Public Health
Infectious Disease Program
Division of Disease Prevention and Control
525 23rd Street, N.W.
Washington, DC 20007, U.S.A.
Tel: (202) 974-3883
Fax: (202) 974-3656
E-mail: gonzalzr@paho.org

Dr. Gabriel Schmuñis

Consultant
Infectious Disease Program
Division of *Disease Prevention and Control
525 23rd Street, N.W.
Washington, DC 20007, U.S.A.
Tel: (202) 974-3272
E-mail: schmunig@paho.org

SPECIAL GUESTS

Dr. Gustavo Chamorro Cortesi

Central Laboratory
Reference Bacteriology Department
Ministry of Public Health
Asunción, Paraguay
Tel/Fax: (595-21) 294-999
E-mail: chamorrogu@hotmail.com

Lic. Aurora Maldonado

Institute of Public Health of Chile
Neisserias Ref. Lab.
Maratón 1000, Nuñoa
Santiago, Chile
Telephone (56-2) 350-7428
Fax (56-2) 350-7570
E-mail: amaldona@ispch.cl

PAN AMERICAN HEALTH ORGANIZATION
Pan American Health Bureau, Regional Office of the
WORLD HEALTH ORGANIZATION
Area of Health Surveillance and Disease Management
Communicable Diseases Unit
525 Twenty-third St., N.W.
Washington, D.C. 20037, U.S.A.