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Generation, Presentation, and Application of Antimicrobial Susceptibility Test Data for Bacteria of Animal Origin

This report offers guidance on areas in which harmonization can be achieved in veterinary antimicrobial surveillance programs with the intent of facilitating comparison of data among surveillance programs.

A CLSI report for global application.

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Generation, Presentation, and Application of Antimicrobial Susceptibility Test Data for Bacteria of Animal Origin; A Report

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Shabbir Simjee, PhD
Robert E. Badal
William B. Brasso
David J. Farrell, PhD, D(ABMM), FCCM
Amy B. Frey, DO, MS
Patrick McDermott, PhD
Ron A. Miller, PhD
Lori T. Moon, MT(ASCP)
Florencia L. Pantozzi
Stefan Schwarz, DVM
Albert T. Sheldon, Jr., PhD
Thomas R. Shryock, PhD
Peter Silley, PhD
John Stelling, MD, MPH
Bernd Stephan, PhD
John D. Turnidge, MD
Jeffrey L. Watts, PhD, RM(NRCM)
Ching Ching Wu, DVM, PhD

Abstract

Clinical and Laboratory Standards Institute document VET05-R—*Generation, Presentation, and Application of Antimicrobial Susceptibility Test Data for Bacteria of Animal Origin; A Report* offers guidance on areas in which harmonization can be achieved in national veterinary antimicrobial surveillance programs, with the intent of facilitating comparisons of data among various national surveillance programs. CLSI veterinary antimicrobial susceptibility testing (VAST) methods are used to generate minimal inhibitory concentrations or zones of inhibition, and the laboratory interprets that information into a category of susceptible, intermediate, or resistant. The veterinarian uses this information to make an informed decision in the selection of an appropriate antimicrobial for animal treatment. However, various surveillance programs or projects use the data for many other purposes, including the drafting of risk assessments (subsequently used for risk management) or to determine the success of intervention policies. These programs include multiple national programs, several multinational programs, product-specific programs, and purpose-specific regional or local programs. Currently, there is a lack of standardized methodology describing how the data from these programs are presented in the reports and discussed with regard to the specific program objective. In keeping with the intent of CLSI document M39,[1] this document seeks to bring the CLSI VAST perspective to these programs and projects by means of a comprehensive report that can help form the basis for a global consensus.

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Foreword

Owing to the large number of national antimicrobial resistance (AMR) surveillance programs, harmonization among these various programs is becoming increasingly important. The aim of this report is to provide the perspective of the Subcommittee on Veterinary Antimicrobial Susceptibility Testing on the generation, presentation, and application of antimicrobial susceptibility testing (AST) data for bacteria of animal origin regarding these programs, and perhaps help form the basis for a global consensus.

This report provides guidance on aspects of AMR surveillance programs ranging from sample collection, AST methodology, data presentation, and data interpretation, including situations in which CLSI-approved veterinary-specific clinical breakpoints are not established. Efforts are made to highlight areas in which laboratories deviate from CLSI methodology and the subsequent misinterpretation of data that can occur. Comparisons are made among some of the more established veterinary AMR surveillance programs and among human AMR surveillance programs, along with indications of the usefulness of certain points of human AMR programs for veterinary programs. The anticipated users of this document are surveillance program managers, regulatory authorities, clinical laboratories, and academicians.

Key Words

Clinical breakpoints, coresistance, cross-resistance, epidemiological cutoff values, geometric mean, harmonization, MIC_{50}, MIC_{90}, multidrug resistance, surveillance

Generation, Presentation, and Application of Antimicrobial Susceptibility Test Data for Bacteria of Animal Origin; A Report

1 Scope

This report provides a review of current applications of susceptibility test data generated using CLSI methodology for bacteria of animal origin and recommendations for summarizing, presenting, and applying the data. More specifically, the report provides an overview of the CLSI veterinary antimicrobial susceptibility testing (VAST) approach to the use of reference methodology, quality control (QC), and establishment and use of clinical breakpoints and epidemiological cutoff values (ECVs). Recommendations for the presentation of minimal inhibitory concentrations (MICs) or zone inhibition data in frequency histograms and scatter plots are provided, in addition to recommendations for the use of ECVs and/or CLSI clinical breakpoints. A review of various applications of surveillance programs is provided, with clarification of descriptive summary statistics of MIC frequency histograms (eg, MIC_{50}, MIC_{90}, geometric mean), and recommended standardized approaches.

The report also provides a review of several select programs that monitor antimicrobial susceptibility in bacteria of animal origin (eg, Canadian Integrated Program for Antimicrobial Resistance Surveillance [CIPARS], Centre Européen d'Etudes pour la Santé Animale [CEESA], Danish Integrated Antimicrobial Resistance Monitoring and Research Programme [DANMAP], G*ERM*-Vet, Monitoring of Antimicrobial Resistance and Antibiotic Usage in Animals in the Netherlands [MARAN], US National Antimicrobial Resistance Monitoring System [NARMS]) with regard to methods and data presentation and interpretation. For comparison purposes, a similar review is provided for programs monitoring antimicrobial susceptibility in bacteria of human origin (eg, European Antimicrobial Resistance Surveillance Network [EARS-Net], SENTRY Antimicrobial Surveillance Program). This report is not intended to provide guidance for human antimicrobial surveillance programs.

Finally, consideration is given to the intended use of any antimicrobial resistance (AMR) surveillance program. The usual goal in collecting antimicrobial susceptibility data is to detect the early emergence of resistance for a given bacterial species/antimicrobial combination that may be used for the following purposes:

- Provide a basis for policy recommendations for animal and public health.
- Generate data that may guide the design of further studies.
- Provide information for prescribing practices and prudent-use recommendations.
- Determine the prevalence or trend in prevalence of reduced susceptibility (or resistance) to a certain antimicrobial in a defined population.
- Detect emergence of AMR (eg, particular phenotypes).
- Identify the need for potential intervention.
- Assess the impact of intervention(s).
- Identify the emergence of new mechanisms of resistance.

2 Introduction

Although there are many veterinary AMR surveillance programs throughout the world, the lack of harmonization in sampling, susceptibility testing methods, antimicrobial agents tested, interpretive criteria, and reporting often makes it difficult to compare data across programs.[2] One significant problem is the use of the term *resistant* to categorize bacteria whose susceptibility properties are determined using often incompatible laboratory parameters, namely, clinical breakpoints and ECVs. This confusion of terms often precludes a direct comparison of reported resistance patterns in different locales. This problem is further exacerbated by the use of different clinical breakpoints and ECVs in different countries. In addition, the term *resistant* often is used loosely to indicate *decreased susceptibility, a non–wild type, increased MICs,* or *acquired genetic markers,* or to designate a physiological change in the cell affecting antimicrobial metabolism. In addition, it is not uncommon for studies to report resistance patterns using invalid testing methods or illegitimate modifications of standardized methods. These factors confound data interpretation and comparison, and serve to highlight the need for consensus terminology and method harmonization when possible.

Franklin et al.[3] published a guideline on the harmonization of national AMR monitoring and surveillance programs in animals and animal-derived foods on behalf of the Office International des Epizooties (OIE). The objective of the guideline was to allow the generation of comparable data from national surveillance and monitoring systems in order to compare the situations in different regions or countries and to consolidate results at the national, regional, and international levels. The guideline emphasized that in order to achieve comparability of results; the following factors should be taken into account for the design of such programs:

- Animal species/categories (including age) to be sampled
- For food sampling, the relative merits of sampling at the abattoir and retail outlet should be considered. In addition to food of domestic origin, food of foreign origin may also be considered, possibly at the port of entry of the products.
- Sampling strategy to be employed, eg, active or passive collection of samples; random, stratified, or systematically collected samples; statistically based sampling; or opportunistic sampling
- Samples to be collected (feces, carcass, raw and/or processed food)
- Bacterial species to be isolated
- Antimicrobial agents to be used in susceptibility testing
- Standardized susceptibility testing
- QC and quality assurance (QA)
- Type of quantitative data to be reported
- Database design for appropriate data extraction
- Analysis and interpretation of data, which is especially important in regard to how resistance is defined
- Reporting (consideration of transparency of reporting and interests of stakeholders)

The Quality Management System Approach

Clinical and Laboratory Standards Institute (CLSI) subscribes to a quality management system approach in the development of standards and guidelines, which facilitates project management; defines a document structure via a template; and provides a process to identify needed documents. The quality management system approach applies a core set of "quality system essentials" (QSEs), basic to any organization, to all operations in any health care service's path of workflow (ie, operational aspects that define how a particular product or service is provided). The QSEs provide the framework for delivery of any type of product or service, serving as a manager's guide. The QSEs are as follows:

Organization	Personnel	Process Management	Nonconforming Event Management
Customer Focus	Purchasing and Inventory	Documents and Records	Assessments
Facilities and Safety	Equipment	Information Management	Continual Improvement

VET05-R addresses the QSE indicated by an "X." For a description of the other documents listed in the grid, please refer to the Related CLSI Reference Materials section on the following page.

Organization	Customer Focus	Facilities and Safety	Personnel	Purchasing and Inventory	Equipment	Process Management	Documents and Records	Information Management	Nonconforming Event Management	Assessments	Continual Improvement
		M29				X M31 M37 M39 M42 M42/M49-S1 M49					

Path of Workflow

A path of workflow is the description of the necessary processes to deliver the particular product or service that the organization or entity provides. A laboratory path of workflow consists of the sequential processes: preexamination, examination, and postexamination and their respective sequential subprocesses. All laboratories follow these processes to deliver the laboratory's services, namely quality laboratory information.

VET05-R does not address any of the clinical laboratory path of workflow steps indicated in the grid below. For a description of the documents listed in the grid, please refer to the Related CLSI Reference Materials section on the following page.

Preexamination				**Examination**			**Postexamination**	
Examination ordering	Sample collection	Sample transport	Sample receipt/processing	Examination	Results review and follow-up	Interpretation	Results reporting and archiving	Sample management
				M31	M31 M42 M42/M49-S1 M49 M100	M31 M42 M42/M49-S1 M49 M100	M31 M42 M42/M49-S1 M49 M100	

P: +1.610.688.0100 **Toll Free (US):** 877.447.1888 **F:** +1.610.688.0700

E: customerservice@clsi.org **www.clsi.org**

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