Rationale for Using CLSI Breakpoints

CLSI is a not-for-profit standards development organization (SDO) that brings together the global laboratory community for a common cause—fostering excellence in laboratory medicine. We do so by developing medical laboratory standards based on input from and consensus among health care professionals, government, and industry.

As a global organization, CLSI's members include 1,400+ organizations and 400+ individuals from over 60 countries. For over 50 years, CLSI's members, volunteers, and customers have made the organization a respected, transformative leader in the development and implementation of clinical laboratory testing standards.

On an annual basis, CLSI publishes M100, *Performance Standards for Antimicrobial Susceptibility Testing*, the content of which represents the most current information for drug selection, antimicrobial susceptibility test interpretation, and quality control (QC). The data provided in M100 are used extensively throughout the world by laboratorians, infectious diseases practitioners, and antimicrobial susceptibility testing (AST) device manufacturers whose software apply algorithms based on information derived from M100.

In addition, CLSI document M23, *Development of In Vitro Susceptibility Testing Criteria and Quality Control Parameters* supports introduction of and changes to interpretive criteria published in M100 by providing guidance for data submission to regulatory authorities by sponsors and details the criteria followed by the CLSI Subcommittee on Antimicrobial Susceptibility Testing to establish or revise QC ranges and susceptibility testing interpretive criteria.

In the United States, the American National Standards Institute (ANSI) is responsible for overseeing the creation, promulgation, and use of norms and guidelines that directly impact businesses in nearly every sector—including medical laboratory testing. In addition, per the ANSI Essential Requirements: Due process requirements for American National Standards, it accredits SDOs' procedures to ensure strict requirements are met for openness, balance, consensus, and due process.

CLSI was first accredited by ANSI in 1978 and has successfully maintained its accreditation since that time. As such, CLSI is the sole nationally or internationally accredited SDO developing and revising AST interpretive criteria worldwide.

CLSI is also globally recognized for its administration of the International Organization for Standardization (ISO) Technical Committee on Clinical Laboratory Testing and In Vitro Diagnostic Test Systems (ie, ISO/TC 212). ISO is the largest nongovernmental worldwide federation of national standards bodies. ISO/TC 212—through its Working Group 4 (WG 4) on Microbiology and Molecular Diagnostics—addresses issues related to AST. As the secretariat for ISO/TC 212/WG 4, CLSI is actively involved in ensuring global harmonization across standardization efforts.

Clinical and Laboratory Standards Institute
950 West Valley Road, Suite 2500, Wayne, PA 19087 USA | **www.clsi.org**
P: +1.610.688.0100 **Toll Free (US):** 877.447.1888 **F:** +1.610.688.0700

CLSI establishes and maintains well defined and monitored procedures to address potential conflicts of interest and ensure transparent decision making.

Due process requirements are an important attribute of CLSI's standards development program. These requirements are described below.

- **Open participation**. Participation in CLSI activities is open to all directly and/or materially affected persons and/or organizations.

- **Balance of interests.** CLSI maintains a forum for communication among health care professions, government, and industry as well as other entities concerned with the quality of medical laboratory services.

- **Lack of dominance.** No one constituency, organization, or person is permitted undue influence by the exclusion of fair and equitable consideration of other viewpoints.

- **Consideration of divergent views and objections.** Consideration of and response to all comments submitted by voting members of relevant committees and by public review commenters are considered and responses to comments are provided. When applicable, approved changes (based on responses to comments received) are incorporated into draft standards.

- **Notice of standards development activities.** Volunteer opportunities in standards development are announced on the CLSI website. Draft standards are made available for broad-based public review and comment (see CLSI website).

- **Consensus.** Consensus on a proposed standard is confirmed by the organization's consensus body—the Consensus Council.

- **Mechanism for appeal.** Any person or organization materially or adversely affected by the failure of a CLSI committee to resolve substantive and/or procedural issues or to provide due process during the CLSI Standards Development Process may appeal the decision.

- **Documented processes.** CLSI's Standards Development Policies and Processes document contains the approved policies and processes for developing CLSI consensus standards and other products.

Not only do the *Standards Development Policies and Processes* detail due process requirements for CLSI's standards development program, the policies contained within govern core CLSI principles and practices. Volunteers are required to complete and submit the Acceptance of CLSI Policies form. By signing the form, the individual agrees to abide by CLSI's Code of Ethics, select the constituency (ie, healthcare professions, government, industry he/she represents, disclose conflicts of interest, adhere to permissions requirements, and participate in accordance with established terms for standards development. Completed forms are maintained by CLSI and may be reviewed

upon request. In addition, a disclosure summary for the Subcommittee on Antimicrobial Susceptibility Testing is available on CLSI's website.

As outlined in the *Standards Development Policies and Processes*, CLSI conducts all meetings in an open forum and permits noncommittee participants to attend meetings. Face-to-face meetings of the Subcommittee on Antimicrobial Susceptibility Testing—and its working groups—are convened biannually, in January and June. All meeting materials—including summary minutes—are made freely available on the CLSI website.

Additionally, CLSI invites input on its documents throughout their "life cycle" as outlined below.

- **Development or revision.** As a document is developed or revised, input from all meeting participants is considered and decisions on the input provided are recorded in meeting summary minutes.

- **Proposed draft.** Once a document reaches the Proposed Draft stage, it is made available to a wide range of volunteers for review and comment. Also, at this stage, eligible members of the responsible committee vote on the document. All comments received during this stage are reviewed and responded to, and when applicable, the document is revised. All comments and responses submitted on draft and published documents are retained on file at CLSI and are available upon request.

- **Postpublication.** CLSI accepts comments on all published documents. Comments received after a document is published are retained on file and considered at the time of the document's revision.

CLSI's three AST interpretive criteria supplements for bacteria and fungi for human and veterinary use are freely available on its website. Other valuable resources related to the activities and decisions of CLSI's Subcommittee on Antimicrobial Susceptibility Testing are also available.

CLSI is uniquely qualified to serve as the go-to source of AST methods and interpretive criteria. Through the implementation of a well-defined, robust standards development program and participation of renowned experts, and by upholding demonstrable practices and principles, CLSI provides world class guidance in antimicrobial susceptibility testing that can be used with confidence to identify and update susceptibility test interpretive criteria.