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CLINICAL AND LABORATORY STANDARDS INSTITUTE®

CLSI Subcommittee on Antimicrobial Susceptibility Testing

CLSI AST News Update

Brought to you by the CLSI AST Outreach Working Group

What Is CLSI AST ORWG?

The CLSI AST **Outreach Working Group (ORWG)** is part of the CLSI Subcommittee on Antimicrobial Susceptibility Testing (AST) and was established in 2015. The formation of the working group originated in a desire to efficiently convey information regarding contemporary AST practices, recommendations, and resources to the clinical microbiology community.

Members:

Janet A. Hindler (Co-Chairholder), UCLA Health System, USA
Audrey N. Schuetz (Co-Chairholder), Mayo Clinic, USA
April Abbott, Deaconess Health System, USA
Stella Antonara, Nationwide Children's Hospital, USA
Marcelo F. Galas, National Institute of Infectious Disease, Argentina
Violeta J. Rekasius, Loyola University Medical Center, USA
Romney M. Humphries, UCLA Health System, USA
Nicole E. Scangarella-Oman, GlaxoSmithKline, USA
A. Beth Prouse, Peninsula Regional Medical Center, USA
Lars F. Westblade, Weill Cornell Medical College, USA

Inside This Issue:

Special Points of Interest:

- About CLSI AST ORWG
- CLSI AST Subcommittee and Meetings
- Availability of CLSI AST Subcommittee Materials
- Recently Published CLSI AST Documents
- Educational Materials for Carbapenem-Resistant *Enterobacteriaceae* (CRE)

Goals:

- Educate practicing clinical microbiologists and health care professionals about AST practices and recommendations.
- Provide resources to facilitate individuals in their understanding and implementation of CLSI AST recommendations.

What can you learn from CLSI AST News Updates?

Through periodic newsletters, the CLSI AST ORWG will direct you to educational materials to help you learn more about the CLSI Subcommittee on AST (CLSI AST SC) and the recommendations published in CLSI AST documents. Information will be provided through webinars, annotated presentations, self-study programs, case studies, articles, and more. A "hot topic" in antimicrobial resistance will be included in each issue of the newsletter. Educational materials will be provided by ORWG members and guest authors.

In this inaugural issue, we explain the role of the CLSI AST SC and the structure of CLSI AST SC meetings. We also provide a description of the types of information presented at these meetings and links to materials presented at past meetings. Through these newsletters, you will gain insight into the proceedings of the CLSI AST SC, which will help you determine if you might be interested in contributing to these activities.

What is the CLSI AST Subcommittee and where and when does it meet?

- The CLSI AST SC is a group of volunteers representing the government, industry, and the professions that researches contemporary issues in AST and, through a consensus mechanism, constructs the recommendations included in CLSI AST documents.
- The CLSI AST SC is comprised of microbiologists, infectious diseases physicians, pharmacists, public health specialists, and others. There is one appointed chairholder, a vice-chairholder, 12 appointed voting members, 12–20 appointed advisors, and an unlimited number of reviewers.
- Meetings are held twice a year (January and June), generally in cities near the East or West coasts (warm weather venue in January!)
- The meeting begins Saturday evening with a workshop (see CLSI AST SC Meeting Educational Workshops, later in this issue) and runs through Tuesday afternoon.
- The chairholder appoints working groups to address specific AST issues that need attention. Issues might be raised by an appointed member of the CLSI AST SC, a reviewer, or someone from outside CLSI.
- Working groups assemble at the face-to-face meetings and also meet by conference call multiple times between meetings.
- Final voting occurs at plenary sessions during which all topics are reviewed.
- CLSI AST SC meetings are open to interested individuals. Anyone can volunteer information to guide an issue under discussion.
- To learn more about upcoming or past meetings, please **click here.**

CLSI AST SC Meeting - January 11, 2016

How is content assembled for the face-to-face CLSI AST meetings?

The process of compiling CLSI AST SC meeting materials is:

- Approximately one month before each face-to-face meeting, those wishing to make recommendations or discuss an issue must request time to do so and submit supporting materials. Some of the materials are obtained from working group conference calls that take place between face-to-face meetings.
- An agenda book is constructed from the materials and shared with meeting participants two to three weeks before the meeting.
- Meeting participants review the materials before meeting attendance.
- During working group and plenary sessions, any needed changes to the AST documents are considered, along with material to support these changes, and a vote is taken. All decisions are made through the consensus mechanism.
- Chairholders of working groups submit a summary of material presented during the meeting.
- CLSI posts these summaries for public access **here.**
- Currently, meeting materials from January 2010 through June 2015 are accessible.

Interested in becoming a CLSI volunteer? Learn more here.

Upcoming Webinar

August 17th, 2016:

Verification of Commercial Microbial Identification and Antimicrobial Susceptibility Testing Systems

Janet A. Hindler, MCLS, MT(ASCP)
UCLA Health System, Los Angeles, CA

A. Beth Prouse, MS, MT(ASCP)
Peninsula Regional Medical Center

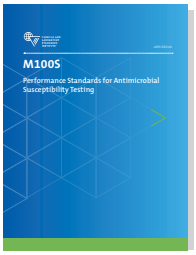
For more information on CLSI webinars, click here.

CLSI 2016 AST Update Webinar

In just 90 minutes, learn about all of the recent changes in the new M100 tables!

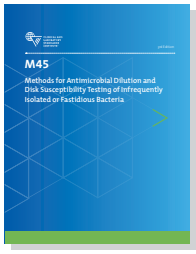
Click here to purchase the webinar.

Updated CLSI AST Documents Are Here!
So what's new?



M100S—Performance Standards for Antimicrobial Susceptibility Testing, 26th Edition

- **New breakpoints:**
  Ceftolozane-tazobactam for *Enterobacteriaceae* and *Pseudomonas aeruginosa*
  Oritavancin, tedizolid, and telavancin for staphylococci, enterococci, β-hemolytic streptococci, and viridans streptococci
- **Updated recommendations:**
  Staphylococcus pseudintermedius
  Cefazolin with *E. coli, Klebsiella pneumoniae,* and *Proteus mirabilis*
  Fluoroquinolones with *Salmonella* spp.
- **Expanded definitions:**
  Surrogate agent, equivalent agent, routine test, supplemental test, screening test
- **Updated intrinsic resistance tables**
- **New epidemiological cutoff values (ECVs):**
  Azithromycin for *Shigella flexneri* and *Shigella sonnei*



M45—Methods for Antimicrobial Dilution and Disk Susceptibility Testing of Infrequently Isolated or Fastidious Bacteria, 3rd Edition

- The M45 guideline underwent a major overhaul. Several new and updated recommendations were introduced throughout the document, derived from extensive literature review, *in vitro* testing, and the clinical expertise of the working group. Key updates include:
- **New organisms:**
  Aerococcus spp.
  Gemella spp.
  Lactococcus spp.
  Micrococcus spp.
  Rothia mucilaginosa
- **Updated recommendations:**
  Coryneform and *Bacillus*-related genera
  Campylobacter jejuni/coli disk diffusion method and addition of disk breakpoints for erythromycin, ciprofloxacin, and tetracycline
  HACEK group, including use of alternative test media

  Additionally, new or modified breakpoints and treatment comments were added for several antimicrobial agent/organism combinations based on contemporary data available.

NEW for 2016!

Now you can access the microbiology community's most trusted resource for effective antibiotic selection and usage in multiple ways!

For more information, **click here**.

M100 PLUS

Our Searchable XML-Based Version of M100

M100 PLUS provides full online access to M100, with added functionality and fast, easy data searching in a user-friendly electronic format.

M100 FREE

A Convenient Companion to the M100 Document

This complimentary, read-only version of the M100 document is available for fast online reference of key breakpoint data.

NEW!

M52—Verification of Commercial Microbial Identification and Antimicrobial Susceptibility Testing Systems, 1st Edition

The new M52 guideline provides recommendations for verification of US Food and Drug Administration–cleared identification and AST systems when adopting a new system or when making a change to an existing system. Some of the highlights include suggestions for:

- Designing the verification study and defining acceptance criteria
- Selecting isolates for testing (including numbers to test)
- Performing the verification
- Resolving discrepancies
- Preparing the verification report

Suggested postverification quality assurance activities are described, including:

- Review of unusual results
- Annual review of manufacturer's instruction for use
- Correlation of *in vitro* test results with clinical findings

CLSI AST SC Meeting Educational Workshops

To coincide with the January and June CLSI AST SC meetings, the ORWG coordinates an Educational Workshop, normally held on the Saturday evening before the start of the AST working group meetings. Past workshops included topics such as pharmacokinetic-pharmacodynamic (PK-PD) data, AST devices, biofilms, antibiotic stewardship, and antibiotic surveillance.

The June 2015 Workshop was entitled "Antibacterial Therapy – New Drugs and Approaches" and included presentations on newly approved antimicrobial agents, current antimicrobial agents in development, and the future of antimicrobial agents development.

The January 2016 Workshop focused on "Emerging Molecular and Novel Methods to Detect Antimicrobial Resistance" and highlighted currently available methods, implementation in clinical trials, methods under development, and the role of next generation sequencing for the detection of antimicrobial resistance. The topic selected for the June 2016 Workshop is "Unusual Suspects – Resistance Concerns and Susceptibility Testing Among Less Common, but Noteworthy, Bacteria." The ORWG welcomes suggestions for future educational workshops!

Slides presented at past sessions can be found **here.**

Future CLSI AST Subcommittee Meetings!

June 2–7, 2016 – San Diego, California, USA
January 11–17, 2017 – Tempe, Arizona, USA
June 22–27, 2017 – Philadelphia, Pennsylvania, USA

Links to Resources for Antimicrobial Agents and AST

Click here for a list of websites containing information that might help you better understand antimicrobial agents and AST. The links point you to descriptions of antimicrobial classifications, antimicrobial resistance mechanisms, recommendations for AST, development of IQCPs (Individualized Quality Control Plans) for AST, guidelines for antimicrobial therapy, and more.

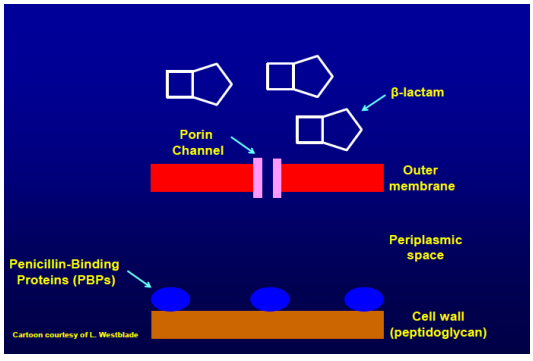
Carbapenem-Resistant *Enterobacteriaceae* (CRE) Educational Tools

Carbapenem-resistant *Enterobacteriaceae* (CRE) threaten health care systems throughout the world. The burden of disease in the United States due to CRE has been increasing, and the easy spread of these organisms within health care institutions presents many challenges to laboratorians, clinicians, pharmacists, and infection control practitioners.

The AST SC ORWG has developed an educational module to help you better understand contemporary CRE issues. Access this module at the link below.

- **Laboratory Detection of CRE**

In the coming weeks, we will release additional educational tools including a self-study program to help you further assess your understanding of CRE. Stay tuned!



A schematic of a gram-negative bacterial cell envelope with the target (PBPs) of carbapenems (β-lactams) highlighted

AST IQCP Materials Available

CLSI, together with the College of American Pathologists and ASM, developed materials to help you comply with the CMS program for implementation of an IQCP (Individualized Quality Control Plan). As of January 1, 2016, clinical laboratories were required to implement IQCP to define quality control (QC) performed in their laboratories or follow CLIA (Clinical Laboratory Improvement Amendments) default QC recommendations.

Materials including sample IQCP protocols and materials used during various presentations on IQCP can be found **here.** Additional materials are also available from:

- **Centers for Medicaid & Medicare Services (CMS)**
- **American Society for Microbiology (ASM)**

New Guidance for Laboratories That Perform Molecular Assays for Antimicrobial Resistance

The CLSI AST SC has developed tables to provide guidance for testing and reporting among laboratories that use molecular assays for detection of vancomycin resistance in *Enterococcus* spp. and methicillin resistance in *Staphylococcus aureus*. The tables and an introduction to this approach can be accessed **here.** Additional tables will be developed for other organisms and resistance mechanisms in the near future.

Resistance Hot Topic!

Transmissible colistin resistance

By Kurt Jerke, PhD, UCLA Postdoctoral Fellow

In recent years, there has been renewed use of the polymyxins (colistin and polymyxin B) to combat multidrug-resistant gram-negative bacteria. Resistance to the polymyxins is increasing among carbapenem-resistant *Enterobacteriaceae,* due to mutations acquired on the bacterial chromosome. Recently, a plasmid-borne colistin resistance gene, *mcr-1,* was described in an *Escherichia coli* isolated from an industrial pig farm in China.[1] This report documented the first known instance of transmissible colistin resistance. The *mcr-1* gene is similar to the gene encoding phosphoethanolamine transferases known to confer resistance to the polymyxins in other species, through lipid A target modification. Conjugation experiments demonstrated that colistin resistance (colistin minimal inhibitory concentration, 8 µg/mL) could be transferred from a resistant to a susceptible isolate of *E. coli* by the plasmid pHNSHP45, which harbors the *mcr-1* gene. Furthermore, this plasmid was found to be stable in the native and transconjuganted *E. coli* after 14 passages in the absence of colistin selection. This plasmid could also be transferred to *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* isolates with relative ease. Retrospective analysis of bacterial isolates in China identified *mcr-1*-positive *E. coli* in pig and other meat sources dating back to 2011, as well as in *E. coli* and *K. pneumoniae* isolated from human clinical specimens. It is therefore concerning that *mcr-1* could rapidly disseminate globally, rendering colistin ineffective for treatment of serious infections with multidrug-resistant *Enterobacteriaceae.* Indeed, since this initial report, the *mcr-1* gene has been identified in isolates from Cambodia, Canada, Denmark, England, France, and Germany.[2]

[1] Liu YY, Wang Y, Walsh TR, et al. Emergence of plasmid-mediated colistin resistance mechanism MCR-1 in animals and human beings in China: a microbiological and molecular biological study. *Lancet Infect Dis.* 2015;16(2):161-168.

[2] Schnirring L. More MCR-1 findings lead to calls to ban ag use of colistin. http://www.cidrap.umn.edu/news-perspective/2015/12/more-mcr-1-findings-lead-calls-ban-ag-use-colistin. Accessed May 3, 2016.

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