国際委員会　2016 Jun CLSI 報告

CLSI　4 Jun - 7 Jun 2016 AST meeting 報告
（2016 年 6 月 4 日～2016 年 6 月 7 日：カリフォルニア州サンディエゴ）
舘田　一博（東邦大学），大楠 清文（東京医科大学）

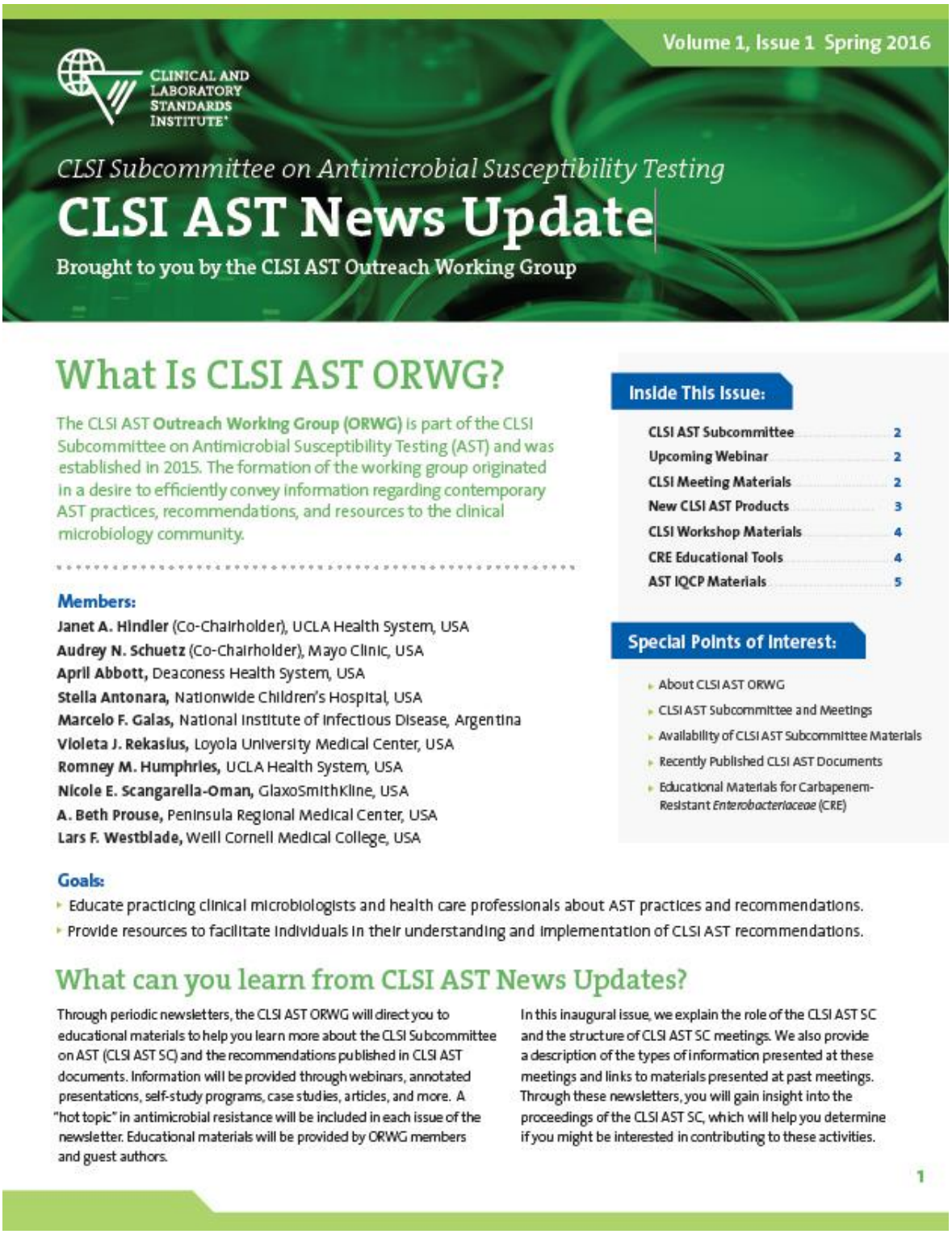
2016 年 6 月 4 日～6 月 7 日に開催された Clinical Laboratory Standards Institute （CLSI）の Antimicrobial Susceptibility Testing ミーティングに，日本臨床微生物学会から国際委員の舘田一博 委員長（東邦大学）と大楠清文 委員（東京医科大学）が参加した。3 日間にわたるプレゼンテーションおよびディスカッションが行われたのでその概要をワーキンググループ別に報告する。なお，今回の会議で決定された事項については 2017 年 1 月の AST ミーティングまでは最終ではなく，最終決定版はパブリックコメントを受けた上で 2017 年の 1 月に公表される予定である。

Outreach Ad Hoc ワーキンググループ

CLSI の広報活動として最新トピックスをニュースレターで発刊することが決定され、既に 2016 年年春号が公開されている。まずは、CLSI ホームページの以下のサイトに入る。
http://clsi.org/standards/micro/microbiology-files/

次に、左のバー「AST OUTREACH WORKING GROUP (ORWG) SRPING NEWSLETTER」をクリックすると以下のようなニュースレターが PDF 形式でダウンロード・閲覧できる。

http://clsi.org/wp-content/uploads/sites/14/2016/05/CLSI-AST-News-Update-Spring-2016.pdf



Volume 1, Issue 1 Spring 2016

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.

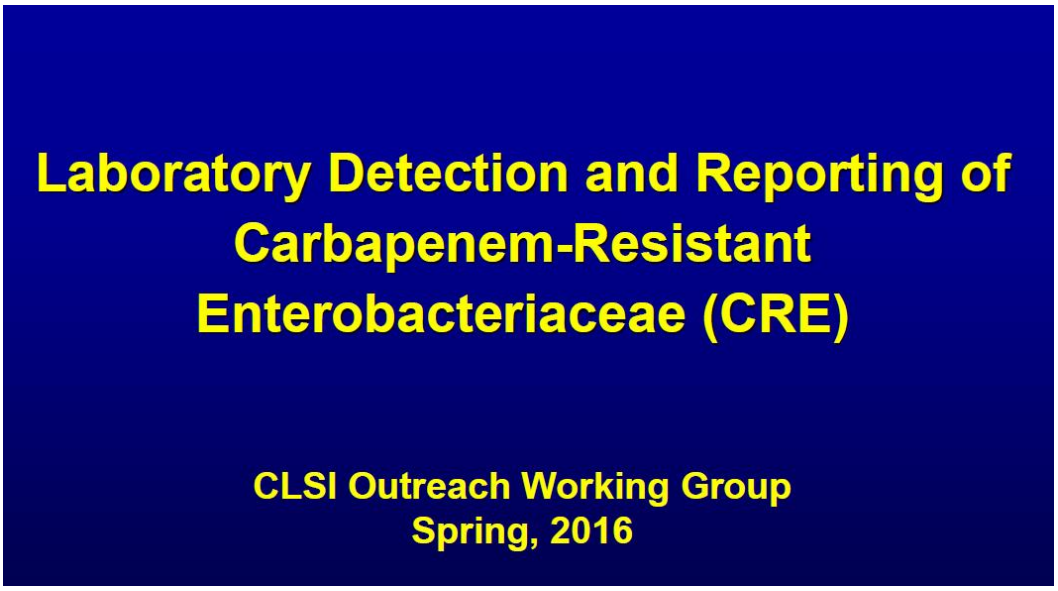
What can you learn from CLSI AST News Updates?

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.

このニュースレターには，教育的なツールとして過去にプレゼンテーションされたパワーポイントスライドがすべて PDF 形式でダウンロード可能である。

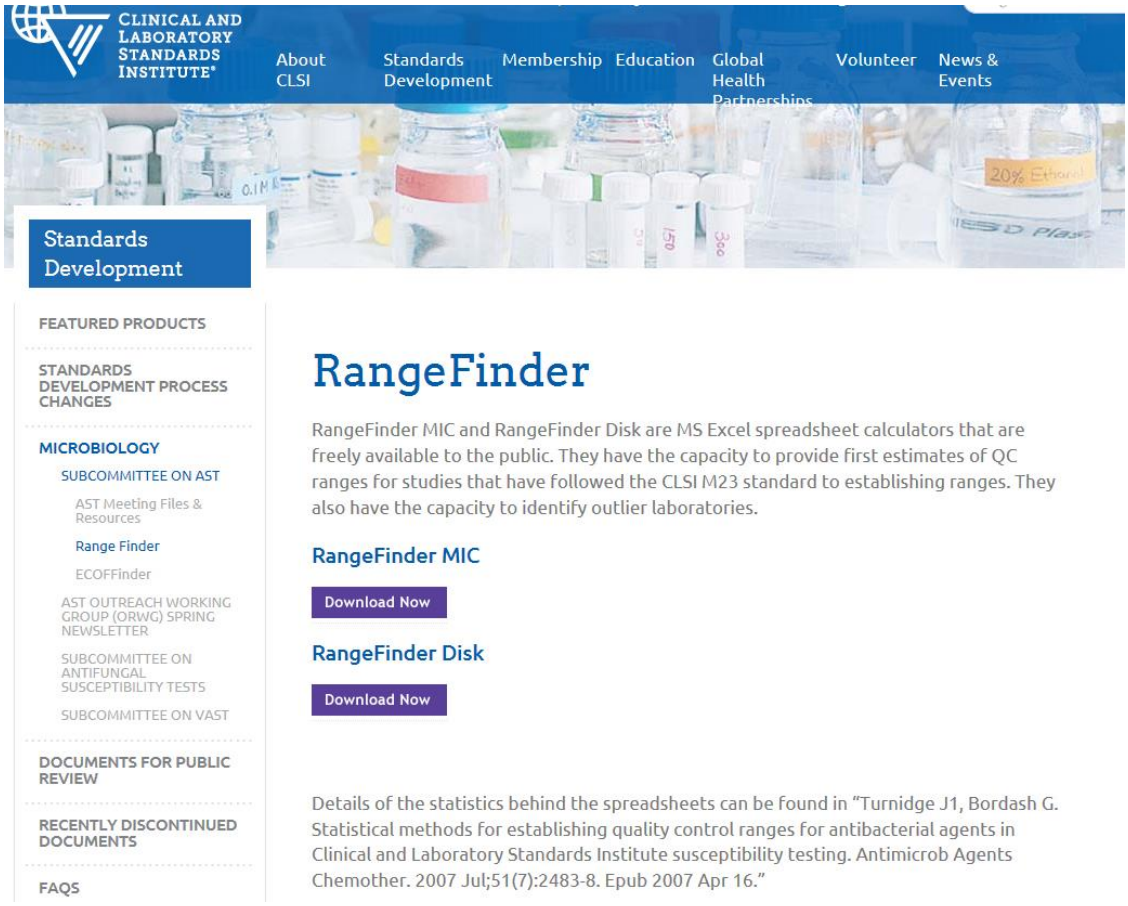
http://clsi.org/wp-content/uploads/sites/14/2013/11/ORWG-CRE-Laboratory-Role-5.30.16.pdf



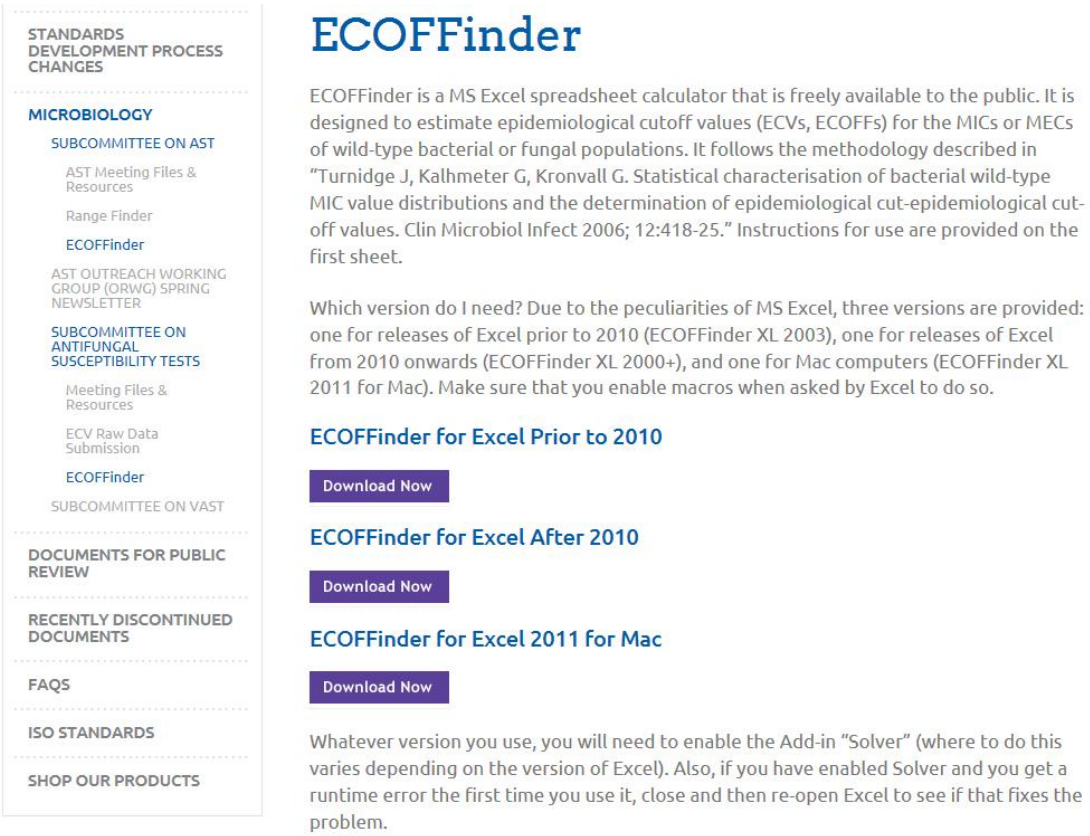
なお、CLSI 会議の前日に開催されているワークショップのプレゼンテーション・スライドも以下の画面（スクロール・ダウン）からすべて閲覧・ダウンロードできるので参照して頂きたい。

http://clsi.org/standards/micro/microbiology-files/

ところで，**QC レンジを計算するソフト**が以下のサイトからエクセルファイル形式でダウンロード可能である。http://clsi.org/standards/micro/rangefinder/



また，**ECOFF (Epidemiological cutoff values)を計算するソフト**が以下のサイトからエクセルファイル形式でダウンロードできる。http://clsi.org/standards/micro/ecoffinder/



ブレイクポイントワーキンググループ

- ***E. faecium* に対する Daptomycin のブレイクポイント（現在，≤ 4; susceptible only）の再評価が必要**であることが提案された。その根拠となった論文を以下にリンクする（**論文 No.1** ）。

Clin Infect Dis. 2016 Jun 15;62(12):1514-20. doi: 10.1093/cid/ciw173. Epub 2016 Apr 3.

Influence of Minimum Inhibitory Concentration in Clinical Outcomes of Enterococcus faecium Bacteremia Treated With Daptomycin: Is it Time to Change the Breakpoint?

Shukla BS[1], Shelburne S[2], Reyes K[3], Kamboj M[4], Lewis JD[5], Rincon SL[6], Reyes J[7], Carvajal LP[7], Panesso D[6], Sifri CD[5], Zervos MJ[8], Pamer EG[4], Tran TT[9], Adachi J[10], Munita JM[11], Hasbun R[9], Arias CA[6].

Author information

Abstract

BACKGROUND: Daptomycin has become a front-line antibiotic for multidrug-resistant Enterococcus faecium bloodstream infections (BSIs). We previously showed that E. faecium strains with daptomycin minimum inhibitory concentrations (MICs) in the higher end of susceptibility frequently harbor mutations associated with daptomycin resistance. We postulate that patients with E. faecium BSIs exhibiting daptomycin MICs of 3-4 µg/mL treated with daptomycin are more likely to have worse clinical outcomes than those exhibiting daptomycin MICs ≤2 µg/mL.

METHODS: We conducted a multicenter retrospective cohort study that included adult patients with E. faecium BSI for whom initial isolates, follow-up blood culture data, and daptomycin administration data were available. A central laboratory performed standardized daptomycin MIC testing for all isolates. The primary outcome was microbiologic failure, defined as clearance of bacteremia ≥4 days after the index blood culture. The secondary outcome was all-cause in-hospital mortality.

RESULTS: A total of 62 patients were included. Thirty-one patients were infected with isolates that exhibited daptomycin MICs of 3-4 µg/mL. Overall, 34 patients had microbiologic failure and 25 died during hospitalization. In a multivariate logistic regression model, daptomycin MICs of 3-4 µg/mL (odds ratio [OR], 4.7 [1.37-16.12]; P = .014) and immunosuppression (OR, 5.32 [1.20-23.54]; P = .028) were significantly associated with microbiologic failure. Initial daptomycin dose of ≥8 mg/kg was not significantly associated with evaluated outcomes.

CONCLUSIONS: Daptomycin MICs of 3-4 µg/mL in the initial E. faecium blood isolate predicted microbiological failure of daptomycin therapy, suggesting that modification in the daptomycin breakpoint for enterococci should be considered.

- *E. faecium*による敗血症の治療において，daptomycinのMIC値が3 – 4 µg/mL (E test) の株では2 µg/mL以下の株に比べて臨床的な予後が悪かったので，ブレイクポイントを下げるか，Intermediateを設定するか，ECOFF (Epidemiologic cut-off Values) の設定を行うか，SDDを設定するかなど，これらを検討するために**Ad Hocワーキンググループを立ち上げること**が承認された。

- **Table 1およびTable 2の*Staphylococci*の欄**からゲンタマイシンを除くアミノグルコシド系薬を**削除**することが承認された。
- *N. gonorrhoeae*のアジスロマイシンに対する**ECOFFを1 µg/mL**とすることが承認された。
- **M100 Table 2A-1**のフルオロキノロン系薬に関するコメント欄に以下のように記述することが承認された。**“*Salmonella* Typhi or *Salmonella* spp. isolated from extraintestinal source that demonstrates an ofloxacin, levofloxacin or ciprofloxacin MIC or ciprofloxacin zone diameter in the intermediate category may be associated with delayed response or clinical failure in fluoroquinolone-treated patients. In these cases suppress the MIC and report the isolate as fluoroquinolone resistant.”**
- コリスチンワーキンググループから腸内細菌科細菌の**ECV/ECOFFを2 µg/mL**に設定することが提案され，承認された。
- **Telavacinのディスク拡散法のブレイクポイントを削除**することが承認された。

- **USCAST；http://www.uscast.org/**が提案しているフルオロキノロン系薬に対するブレイクポイントが紹介された。CLSI, FDA, EUCAST, およびUSCSTのブレイクポイントを比較した表を以下に示す。なお，これらのブレイクポイントは以下のUSCASTのウエブサイトからも参照できる。**https://app.box.com/s/swc4pvnvh3hfvj3g7aqs3vvo2dd91em9**

Table 5　USCAST quinolone *in vitro* susceptibility test interpretive criteria

Organism/Antimicrobial	**MIC breakpoints in μg/mL by criteria organization Susceptible/Resistant**			
	CLSI[a]	**USA-FDA**	**EUCAST[b]**	**USCAST**
Enterobacteriaceae				
Ciprofloxacin	≤1 / ≥4	≤1 / ≥4[c]	≤0.5 / >1	≤0.25 / ≥1
Levofloxacin	≤2 / ≥8	≤2 / ≥8[d]	≤1 / >2	≤0.5 / ≥2
Moxifloxacin	-	≤2 / ≥8[e]	≤0.5 / >1	≤0.25 / ≥0.5 (valid for *E. coli*, *Klebsiella* spp., *Enterobacter* spp., *Citrobacter* spp., and *M. morganii*)
Norfloxacin (UTI)	≤4 / ≥16	≤4 / ≥16[f]	≤0.5 / >1	-
Ofloxacin	≤2 / ≥8	≤2 / ≥8[g]	≤0.5 / >1	-
Nalidixic acid (UTI)	≤16 / ≥32	≤16 / ≥32[h]	Screen only (a surrogate)	≤16 / ≥32 (Salmonella susceptibility screen)[i]
***Pseudomonas* spp.**				
Ciprofloxacin	≤1 / ≥4	≤1 / ≥4[c]	≤0.5 / >1	≤0.5 / ≥1 (high-dose)
Levofloxacin	≤2 / ≥8	≤2 / ≥8[d]	≤1 / >2	≤0.5 / ≥1 (high-dose)
Norfloxacin (UTI)	≤4 / ≥16	≤4 / ≥16f	-	-
Ofloxacin	≤2 / ≥8	≤2 / ≥8g	-	-
S. maltophilia				
Levofloxacin	≤2 / ≥8	-d	-	-
***Acinetobacter* spp.**				
Ciprofloxacin	≤1 / ≥4	-[c]	≤1 / >1	≤0.5 / ≥1 (high-dose)
Levofloxacin	≤2 / ≥8	-[d]	≤1 / >2	≤0.5 / ≥1 (high-dose)
Staphylococci				

Ciprofloxacin	≤1 / ≥4	≤1 / ≥4[c]	≤1 / >1	-
Levofloxacin	≤1 / ≥4	≤2 / ≥8[d]	≤1 / >2	≤0.5 / ≥2
Moxifloxacin	≤0.5 / ≥2	≤2 / ≥8[e]	≤0.5 / >1	≤0.25 / ≥0.5
Norfloxacin (UTI)	≤4 / ≥16	≤4 / ≥16[f]	-	-
Ofloxacin	≤1 / ≥4	≤2 / ≥8[g]	≤1 / >1	-
Enterococci				
Ciprofloxacin	≤1 / ≥4	≤1 / ≥4[c]	≤4 / ≤8 (UTI only)	≤4 / ≥8 (UTI only)
Levofloxacin	≤2 / ≥8	≤2 / ≥8[d]	≤4 / ≤8 (UTI only)	≤4 / ≥8 (UTI only)
Moxifloxacin	-	≤1 / ≥4e	-	-
Norfloxacin (UTI)	≤4 / ≥16	≤4 / ≥16f	-	-
S. pneumoniae				
Ciprofloxacin	-	≤1 / ≥4[c]	≤0.12 / >2	-
Levofloxacin	≤2 / ≥8	≤2 / ≥8[d]	≤2 / >2	≤2 / ≥4
Moxifloxacin	≤1 / ≥4	≤1 / ≥4[e]	≤0.5 / >0.5	≤0.5 / ≥1
Ofloxacin	≤2 / ≥8	≤2 / ≥8[g]	≤0.12 / >4	-
β-haemolytic streptococci				
Ciprofloxacin	-	≤1 / ≥4c	-	-
Levofloxacin	≤2 / ≥8	≤2 / ≥8d	≤1 / >2	≤2 / ≥4
Moxifloxacin	-	≤1 / ≥4e	≤0.5 / >1	≤0.5 / ≥1
Norfloxacin (UTI)	-	≤4 / ≥16f	-	-
Ofloxacin	≤2 / ≥8	≤2 / ≥8g	-	-
Viridans group streptococci				
Levofloxacin	≤2 / ≥8	-d	-	-
Moxifloxacin	-	≤1 / ≥4[e]	-	IE
Ofloxacin	≤2 / ≥8	-[g]	-	-
***Haemophilus* spp.**				
Ciprofloxacin	≤1 / -	≤1 / -[c]	≤0.5 / >0.5	≤0.06 / ≥0.12 (ECOFF)
Levofloxacin	≤2 / -	≤2 / -[d]	≤1 / >1	≤0.06 / ≥0.12 (ECOFF)
Moxifloxacin	≤1 / -	≤1 / -[e]	≤0.5 / >0.5	≤0.12 / ≥0.25 (ECOFF)
Ofloxacin	≤2 / -	≤2 / -[g]	≤0.5 / >0.5	-
Neisseria gonorrhoeae				
Ciprofloxacin	≤0.06 / ≥1	≤0.06 / ≥1[c]	≤0.03 / >0.06	≤0.03 / ≥0.12
Ofloxacin	≤0.25 / ≥2	≤0.25 / ≥2[g]	≤0.12 / >0.25	-
Neisseria meningitidis				
Ciprofloxacin (prophylaxis only)	≤0.03 / ≥0.12	-[c]	≤0.03 / >0.03	≤0.03 / ≥0.06

Levofloxacin	≤0.03 / ≥0.12	-d	-	-
Anaerobes				
Moxifloxacin	≤2 / ≥8	≤2 / ≥8e	-	-

a. CLSI M100-S25 (2015) interpretive criteria.

b. EUCAST breakpoint tables. Version 5.0, 2015. http://www.eucast.org [4].

c. Ciprofloxacin (CIPRO®) product package insert February 2015 [5].

d. Levofloxacin (LEVAQUIN®) product package insert May 2014 [6].

e. Moxifloxacin (AVELOX®) product package insert May 2015 [7].

f. Norfloxacin (NOROXIN®) product package insert August 2013 [9].

g. Ofloxacin (FLOXIN®) product package insert May 2011 [10].

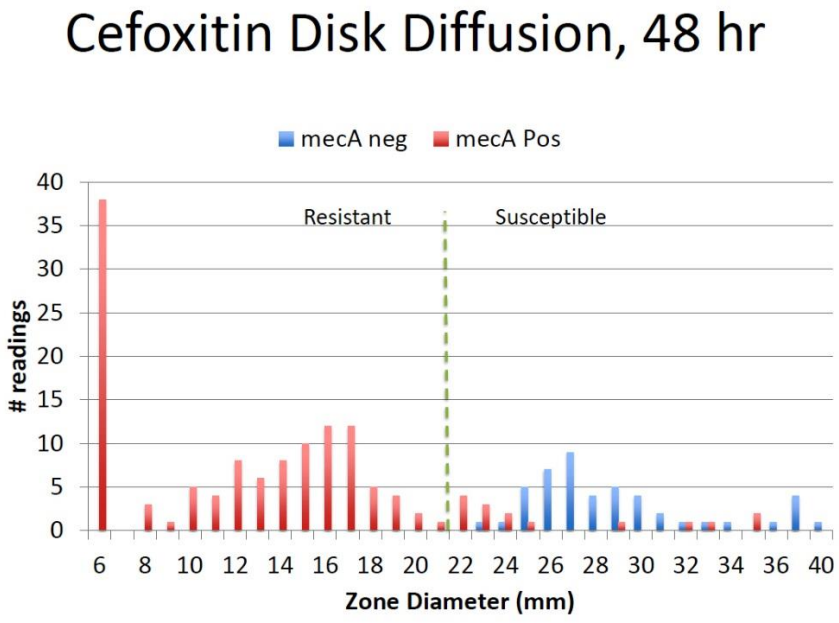
h. Nalidixic Acid (NegGram®) product package insert August 2012 [8].

i. See **3.2.5** of the USCAST Quinolone Rationale Report for details.

Methodology ワーキンググループ

Atypical *S. aureus* Ad Hoc ワーキンググループ

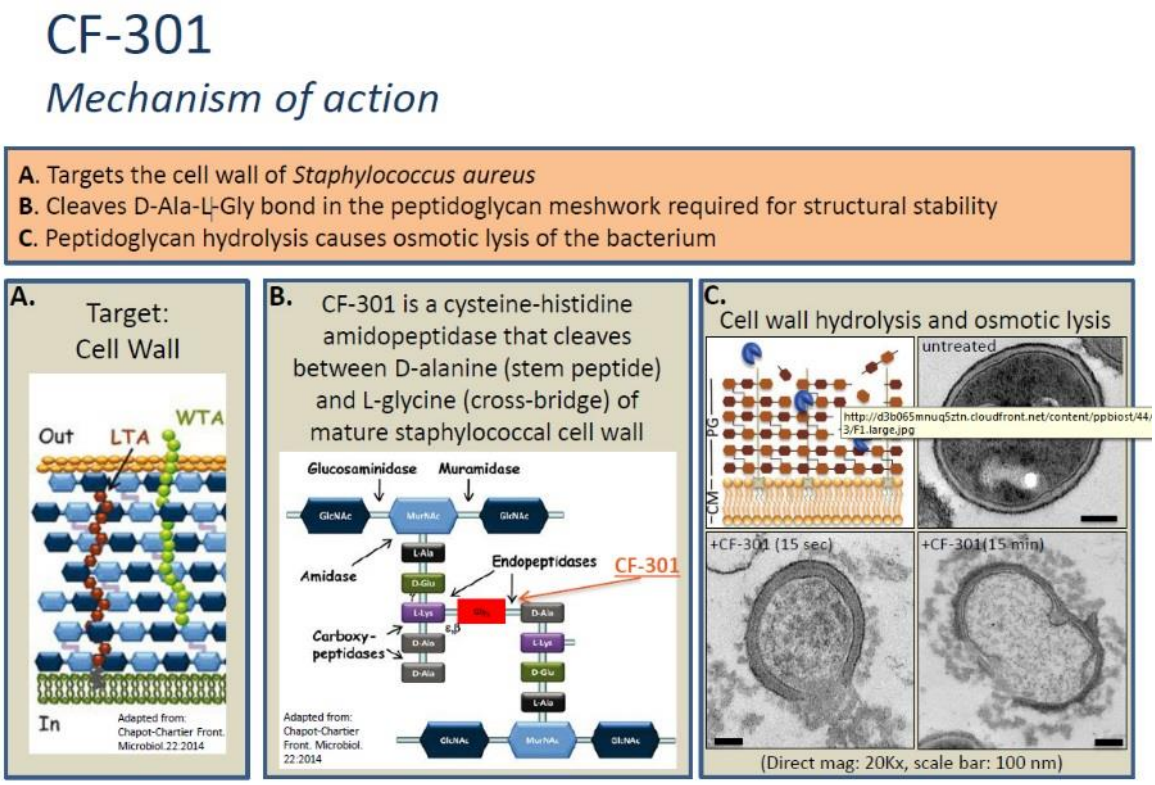
- 前回の会議において，栄養要求性が変化した small-colony variants（SCV_S）の黄色ブドウ球菌（atypical *S. aureus*）の薬剤感受性試験をどのように行うかを検討するワーキンググループが立ち上げられたことを報告した。今回の会議では，①日常検査の薬剤感受性試験用の培地に発育を認めなかった *S. aureus* を atypical *S. aureus* と定義すること，②薬剤感受性試験用の培地として BMHA (MHA with 5% sheep's blood)が候補にあがったが，本培地でも発育が不十分な株が存在したこと，③**Supplemented MHA** が発育支持に優れていたこと，④cefoxitin の MIC 値やディスクを用いた試験では 24 時間と 48 時間後判定ともに *mecA* 陽性の幾つかの株を正しく判定できなかったこと（下図参照），などが報告された。



- 以上のような検討結果から，次のバージョンの Text & Table に以下のような追記を行うことが承認された。**”Cefoxitin MIC and disk tests are not reliable for detecting *mecA* mediated resistance in *S. aureus* isolates that do not grow on MHA or CA-MHA. *mecA* PCR to determine oxacillin susceptibility should be performed.”**
- なお，今回の会議で参考資料とされた論文は以下にリンクする（**論文 No.2** ）。

微量液体希釈法　Ad Hoc ワーキンググループ

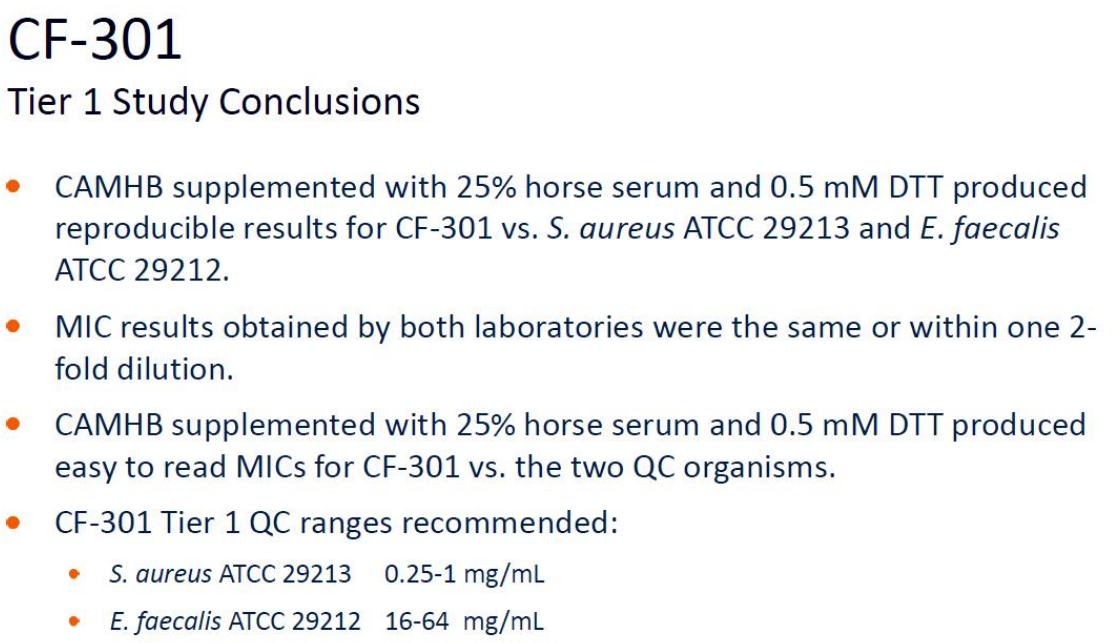
- Lysin CF-31 の微量液体希釈法の確立にあたり，本薬剤の背景，作用機序，MIC 値測定データなどついて Dr. Schuch (ContraFect 社)がプレゼンテーションを行った。**CF-31 の作用機序**については以下にスライドを抜粋して掲載する。



- 微量液体希釈法を行う培地は，Mueller Hinton Broth に **25% horse serum** (トレーリングを減少させるため)と **0.5 mmol/L D-Dithiothreiol (DTT**；フローズンパネルでの薬物保護のため)をサプリメントとして追加することが承認された。
- QC 株とレンジは以下で承認された。

***S. aureus* ATCC 29213；0.25 – 1 µg/mL**

***E. faecalis* ATCC 29212；16 – 64 µg/mL**



- 微量液体希釈法のエンドポイント判定において，**「2 mm button」の記載を削除**すること，具体的な**写真を掲載**することが承認された。
- スキップ現象の具体的な写真を掲載すること，スキップ時の判定で S, I, R の判定が変わるような場合には再測定を行うこと，複数の薬剤でスキップが発生した際の対処方法について以下のように言及することが承認された。**"For a single isolate tested in a broth microdilution panel/tray with a) multiple drugs, or b) multiple formulations, potencies, etc. of a single drug, if more than one row (or two or more rows) or column contains skipped wells, the total results for the panel should be considered at risk and the isolate/test panel be repeated."**
- ***Staphylococci* のテイコプラニンに対するディスク拡散法は不正確であるので，ブレイクポイントの記載を削除**することが承認された。
- Fastidious organisms（栄養要求性の厳しい細菌）の薬剤感受性試験に用いる培地が CLSI と EUCAST とで異なっている。すなわち，**EUCAST** では fastidious organisms すべての細菌に共通して，**MHF = MH + 5% LHB + 20mg/L NAD** を使用している一方，**CLSI は *Streptococci* (MHA + 5% Sheep Blood or MHB + 2.5-5% LYHB)と *Haemophilus* (HTM; MHB + NAD + Hematin + Yeast Extract)**で，これとは異なった処方となっている。今後，両者のデータ比較が必要かを判断したい。
- *mecC* 遺伝子を保有する CNS (coagulase negative *staphylococci*)の検出では，oxacillin と cefoxitin を組み合わせた判定が有効のようなので，今後 Intrinsic Resistance WG と MALDI-TOF ID WG と協力して検討していきたい。

Modified Carbapenemase Inactivation Method (mCIM)

前回の会議報告でカルバペネマーゼ産生グラム陰性桿菌の新たな検出法として，**Carbapenemase Inactivation Method（CIM）**test が提案された。今回の会議では，この **CIM の改良法 (mCIM)**が提案され，予備検討の結果紹介と判定基準の承認が行われた。改良法を以下に示す。変更のポイントは，

①接種菌量は，腸内細菌科細菌は 1μL loop，ブドウ糖比発酵菌は 10μL loop，②TSB で 35℃，4 時間培養すること，③MHB を一昼夜培養後に判定すること，の 3 点である。

B. Isolate Setup

1. For fermenters make a 1µl loopful suspension of the test isolate into 2ml of TSB, MHB (cation adjusted), or sterile water (media selection has been predetermined for each participating site). For non-fermenters the suspension should be equivalent to a 10 µl loopful in 2 ml of TSB. Growth used to make the suspension should be 18 to 24 hours old from a TSA with 5% blood plate.

Note: If a 10µl loopful is used with enteric species, the zones are difficult to read.

Note: Sites 8 and 1 will be conducting with both TSB and cation-adjusted MHB.

Note: Site 7 will conduct the test in both TSB and water

2. Vortex the suspension for 10 to 15 seconds.

3. Add a 10µg meropenem disk into the TSB suspension using a clean pair of forceps, or dispenser and incubate for 4 hours +/- 15 minutes at 35°C.

4. Prepare an inoculated Mueller-Hinton agar (MHA) plate just prior to completion of the 4 hour incubation period.

5. Prepare a 0.5 McFarland suspension of E. coli strain (ATCC 25922)

6. Vortex the suspension for 10 to 15 seconds.

Streak in three directions with a sterile swab dipped in the E.coli ATCC 25922 strain. The entire surface of the plate should be covered at the end of the process. Allow the inoculated plate to dry 3-10 minutes.

7. **Remove** the 10µg meropenem disk from the TSB broth suspension using a 10µl inoculation loop. Drag the loop along the edge of the tube to remove any excess fluid from the loop and disk. Place the disk on the (MHA) plate previously inoculated with the lawn of susceptible E. coli strain (ATCC 25922).

8. A maximum of 8 disks can be placed on a 150mm MHA plate and a maximum of 4 disks can be placed on a 90mm MHA plate.

9. Incubate MHA plates at 35° for 18-24 hours.

10. Read MHA plates using interpretation of results criteria.

判定基準は，以下のとおりに承認された。腸内細菌科細菌（1μL loop TSB, 4 hours）;Positive: 6 – 15 mm，Intermediate: 16 – 18 mm，Negative: ≥ 19 mm

今後，*Acinetobacter* spp. や *P. aeruginosa* で接種菌量を増やす（2 倍量）あるいは培養時間を延長（6 hours），KPC 産生の *Pseudomonas* spp.の菌株なども含めて検討を行い，次回の会議でこれらの検討結果を発表する予定である。

Quality Control ワーキンググループ

今回の会議で承認された薬剤毎の QC 株とそのレンジを以下に示す。

Drug Name:	**S-649266 (Shionogi) 30 µg disk**			
Table 6 information:	Solvent: Saline	Diluent: Saline		
Table 6C information if applicable:	NA	Preparation: NA		Example:
Glossary information:	Class: β-lactam	Subclass: Siderophore cephalosporin	Agent Abbreviation: TBD	Route of Administration: IV

QC Strain (ATCC)	QC Range Approved mm or dil	WG Vote: Y/N/A/NP	% in Range	Mode/ Median	# mm or dilutions	Shoulder %	Footnote to add with drug/range	Variability/Comments
***E. coli* 25922**	**23 – 31**	9/0/2/1	95.3	8	9	NA		Rangefinder 22-32 with 98.7% in range Media Lot C median 28, Lot A & B 26 Lab Medians 26-29 Also considered 23-32
***P. aeruginosa* 27853**	19-31 19-28 20-30 No range **20-30**	NA 4/4/2/2 4/4/2/2 3/4/3/2 6/2/3/1	95.0 80.0 91.3 NA 96.4%	25	13 10 11 NA 11	NA		Medians for Lot A 24, Lot B 22, Lot C 29 Medians for Labs 23-26. Approved range based on 7 labs excluding Lab B & D which were higher Median for Disks 23-26

Drug Name:	**Pexiganan (14-DPX-03)**		
Table 6 information:	Solvent: Water	Diluent: Water	
Table 6C information:	N/A	Preparation: N/A	Example: N/A

Glossary information:	Class: Antimicrobial Peptide	Subclass: Magainins	Agent Abbreviation: PEX	Route of Administration: Topical

QC Strain (ATCC)	QC Range Approved mm or dil	WG Vote: Y/N/A/NP	% in Range	Mode/ Median	# mm or dilutions	Shoulder %	Footnote to add with drug/range	Variability/Comments
S. aureus 29213	8-32	8/0/0/1	100%	16	3	47% @ 8		Some media variability
E. faecalis 29212	16-64	8/0/0/1	100%	32	3			Confirmed with range finder.
S. pneumoniae 49619	16-64	8/0/0/1	96.6-100%	32	3			All labs 96.6% in range, Exclude Lab G 100% in range. Confirmed with range finder. Lab G statistical outlier.
E. coli 25922	2-8	8/0/0/1	100%	4	3	42		Confirmed with range finder.
P. aeruginosa 27853	2-16	8/0/0/1	100%	8	4	63.1% @ 4		Range finder 4-16 (100%) Media lot B mode 4.
H. influenzae 49247	8-32	8/0/0/1	99.7%	16	3			Media lot A mode 8

Drug Name:	**Tedizolid**			
Table 6 information:	Solvent: no change	Diluent: no change		
Table 6C information:	N/A	Preparation: N/A		Example: N/A
Glossary information:	Class: no change	Subclass: no change	Agent Abbreviation: no change	Route of Administration: no change

QC Strain (ATCC)	QC Range Approved mm or dil	WG Vote: Y/N/A/NP	% in Range	Mode/ Median	# mm or dilutions	Shoulder %	Footnote to add with drug/range	Variability/Comments
S. aureus 29213	~~0.25-1 current~~ **0.12-1** new approved	9/0/0/0	97.3% 97.8%	0.5	3 4	76% @ 0.25	Add drug to list in CLSI M7-A10, Section 3.11, Step 3 and troubleshooting guide	Lab variability, Recommended reading instructions: Ignore tiny buttons of growth.
S. aureus 25923	0.12-0.5	7/2/0/0	97.6%	0.25	3	43%	7/1/0/1 Add footnote for drug indicating supplemental QC.	"QC range for S. aureus ATCC 25923 with tedizolid is 0.12-0.5µg/ml which exhibits less trailing and is easier to read. This strain is considered supplemental and not required for routine user QC."

Drug Name:	**Linezolid**			
Table 6 information:	Solvent: no change	Diluent: no change		
Table 6C information if applicable:	no change	Preparation: no change		Example: N/A
Glossary information:	Class: no change	Subclass: no change	Agent Abbreviation: no change	Route of Administration: no change

QC Strain (ATCC)	QC Range Approved mm or dil	WG Vote: Y/N/A/NP	% in Range	Mode/ Median	# mm or dilutions	Shoulder %	Footnote to add with drug/range	Variability/Comments
S. aureus 29213	1-4 current	9/0/0/0	98.9%	2	3	51% @ 4		Confirmed current range.

S. aureus 25923	1-4	7/2/0/0	98.9%	2	3	20% @ 1	7/1/0/1 Add footnote for drug indicating supplemental QC.	"QC range for S. aureus ATCC 25923 with tedezolid is 0.12-0.5µg/ml, exhibits less trailing and is easier to read. This strain is considered supplemental and not required for routine user QC."

Drug Name:	**Meropenem-vaborbactam (RPX7009)**			
Table 6 information:	Solvent: DMSO (No change)	Diluent: Water (No change)		
Table 6C information if applicable:	20/10-µg disk	Preparation: n/a	Example:	
Glossary information:	Class: No change B-lactam/β-lactamase inhibitor combination	Subclass: No change	Agent Abbreviation: TBD	Route of Administration: TBD

QC Strain (ATCC)	QC Range Approved mm or dil	WG Vote: Y/N/A/NP	% in Range	Mode/ Median	# mm or dilutions	Shoulder %	Footnote to add with drug/range	Variability/Comments
S. aureus ATCC 25923	32 – 38	8/0/2/1	97.6%	35	6		See footnote – routine QC.	Range Finder 31 – 39 mm with 99.8% in range. Lab variability median 34-36
E. coli ATCC 25922	31-37	8/0/2/1	99.0%	34	7			Confirmed by Range Finder Lab median 33-35
P. aeruginosa	29 - 35	8/0/2/1	99.3%	32	9		See footnote	Confirmed by Range Finder Lab median 31-33

ATCC 27853							– routine QC.	
K. pneumoniae ATCC 700603	29 – 35	8/0/2/1	99.3%	32	9			Confirmed by Range Finder Lab median 31-33 ESBL producing strain
K. pneumoniae B21 (KP1074)	16-20	8/0/2/1	100%	18	5		See footnote – routine QC. Add organism to Appendix C	Confirmed by Range Finder KPC-producing strain. Publish after strain is deposited with ATCC (projected prior to Dec 2016).
K. pneumoniae ATCC BAA-1705	21 – 27	8/0/2/1	100%	24	7			Lab median 23-25 22 – 27 Range Finder- KPC-producing strain

Drug Name:	**Debio 1452** (active moiety of the prodrug Debio 1450)			
Table 6 information:	Solvent: no change	Diluent: no change		
Table 6C information:	5 µg disk	Preparation: No change		Example
Glossary information:	Class: FabI inhibitor	Subclass: NA	Glossary information: FAB	Class:

QC Strain (ATCC)	QC Range Approved mm or dil	WG Vote: Y/N/A/NP	% in Range	Mode/ Median	# mm or dilutions	Shoulder %	Footnote to add with drug/range	Variability/Comments
S. aureus 25923	~~30-36 (current)~~ ~~29-35~~ ~~28-36~~ 29-36 (revised)	8/0/0/1	~~94%~~ ~~97.6%~~ ~~100%~~ 97.6%	32 32 32 32	7 7 9 8		Remove footnote that indicates only one disk manufacturer used.	Jan 2016 approved range 30-36mm with 96% of results in range (median was 33) New data with 2 disk manufacturers provided.

								Similar results for both disk manufacturers. Lab variability with median and modes range from 30-34.

Tier 3 QC:

QC Strain (ATCC)	Antimicrobic	Method	Current Range	Action Recmd	Concern	Date Reported
E. coli 25922	Cefixime	Disk	23-27	Get original M23, collect additional data	Out low.	NA
K. pneumoniae 700603	βlactam/βlactamase inhibitors	Disk	No range	Collect data	Alternative for E. coli 35218	NA
E. coli 25922	Ciprofloxacin	Disk	30-40	Considered change to 29-37 mm based on 1623 results from 3 disk and 5 MH media manufacturers (large # from one mfg). EUCAST is planning range change. No change approved. Additional information requested.	Wide range (consider narrower range). Zones often in low end with 10% at 30. 1% out @ 29. Only 1% of results at high end at 38-40	Dec-15
P. aeruginosa 27853	Imipenem	Disk	20-28	Collect additional data	Zones in the lower part or below range reported	Dec-15

N. gonorrhoeae 49226	Doxycline	Disk	No range	Include in other study to establish range	Submitted by Mary York	Jan- 16

QC Strain (ATCC)	Antimicrobic	Method	Current Range µg/ml	Action Recmd	Concern	Date Reported
S. pneumo 49619	Cefuroxime	MIC	0.25-1	Request data/feedback	Mode at 0.25	Jun-2013
P. aerug 27853	Etrapenem	MIC	2-8	Monitor	Out low with some labs	NA
E. faecalis 29212	Minocycline	MIC	1–4	Monitor/request feedback	Mode at low end at 16 hrs, bimodal at 18 hrs, at middle of range at 20 hrs	NA
S. aureus 29213	Minocycline	MIC	0.06–0.5	Monitor/request feedback	Mode at low end of current range regardless of read time 16-20 hr	Jun-2013
E. faecalis 29212	Teicoplanin	MIC	0.06-0.25	Monitor	Data in range without tween, some out low with tween. Original data out low with current range.	NA
H. influenzae 49247	Tigecycline	MIC	0.06-0.5	Retain current range	Small number out high	NA
B. fragilis 25285	Pip/tazo	MIC (Agar)	0.12-1	Monitor/request feedback	Out low (control M23 study Jan 2010)	Jun-2013
E. faecalis 29212	Gentamicin	MIC	4-16	Monitor/request feedback	Some out low. Cations, pH in acceptable range (BD)	Jan-2015
E. faecalis 29212	Tobramycin	MIC	8-32	Monitor/request feedback	Some out low. Cations, pH in acceptable range (BD)	Jan-2015
P. aeruginosa 27853	Meropenem	MIC	0.25-1	Expand range to 0.12-1 mg/L.	Tier 2 28% out of range low at 0.12.	June 2016

				QCWG 9/0/0/0 Approved by AST Subcommittee	Tier 2 and 3 combined mode 0.25 with 8% out at 0.12. Tier 3: 337 results from >3 sites, ≥3 lots of media. Tier 3 results reported June 2000 CLSI (many off scale at ≤0.25). Control drug for Pexiganan 110 of 160 at 0.25	

Table 5G. MIC: Troubleshooting Guide

This table provides guidance for troubleshooting and corrective action for out-of-range QC primarily using antimicrobial susceptibility tests with cation-adjusted Mueller-Hinton broth (CAMHB) for broth microdilution. Refer to M07-A10 (MIC), Chapter 4, Quality Control and Quality Assurance.

Out-of-range QC tests are often the result of contamination or the use of an incorrect QC strain; corrective action should first include repeating the test with a pure culture of a freshly subcultured QC strain. If the issue is unresolved, this troubleshooting guide provides additional suggestions for troubleshooting out-of-range QC results and unusual clinical isolate results. In addition, see general corrective action outlined in M07-A10 and notify manufacturers of potential product problems.

Antimicrobial Agent	QC Strain	Observation	Probable Cause	Comments/Suggested Actions
Amoxicillin-Clavulanate and Ticarcillin-clavulanate	*E. coli* ATCC® 35218 *K. pneumoniae* ATCC® 700603	MIC too high	Clavulanate is labile. Antimicrobial agent is degrading.	Use alternative lot. Check storage and package integrity.
Various	*E. coli* ATCC® 35218 *K. pneumoniae* ATCC® 700603	MIC too low	Spontaneous loss of the plasmid encoding the β-lactamase.	See general comment (1) on QC organism maintenance.
Carbapenems	*P. aeruginosa* ATCC® 27853	MIC too high	Antimicrobial agent is degrading.	Use alternative lot. Check storage and package integrity. Repeated imipenem QC results at the upper end of QC range with *P. aeruginosa* ATCC® 27853 may indicate deterioration of the drug.
Chloramphenicol Clindamycin Erythromycin Linezolid Tedizolid Tetracycline	*S. aureus* ATCC®29213 *E. faecalis* ATCC®29212 *S. pneumoniae* ATCC®49619	MIC too high	Trailing endpoint	Read at first well where the trailing begins; tiny buttons of growth should be ignored[1]
Linezolid Tedizolid	*S. aureus* ATCC®29213	MIC too high	Trailing endpoint	*S. aureus* ATCC®25923 may be used as a supplemental QC organism for these drugs. This strain exhibits less trailing and endpoints are easier to interpret.
Dalbavancin Oritavancin Televancin	*S. aureus* ATCC®29213 *E. faecalis* ATCC®29212	MIC too high	Lack of polysorbate-80 in the media	Add polysorbate-80 to CAMHB to final concentration of 0.002% (v/v)[2]

Oritavancin	*S. aureus* ATCC®29213 *E. faecalis* ATCC®29212	MIC too high	Lack of polysorbate-80 in the solvent and diluent	Dissolve antimicrobial powder and prepare dilutions in water containing 0.002% polysorbate-80 (v/v)[3]
Oritavancin	*S. aureus* ATCC®29213 *E. faecalis* ATCC®29212	MIC too high	Use of tissue-culture treated microtiter plates	Use only untreated microdilution trays to prepare intermediate dilutions and for the final microdilution assay[4]
Various	Any	One QC result is out of range, but the antimicrobial agent is not an agent reported for patient results (eg, not on hospital formulary).	Not Applicable	If antimicrobial agent is not normally reported, no repeat is necessary if adequate controls are in place to prevent reporting of the out-of-range antimicrobial agent.
Various	Any	Many MICs too high or too low	Possible reading/transcription error	Recheck readings. Use alternative lot.

Delete this Row: (combined with amoxicillin-clavulanate above)

Ticarcillin-clavulanate	*E. coli* ATCC® 35218	MIC too high	Clavulanate is labile. Antimicrobial agent is degrading.	Use alternative lot. Check storage and package integrity.

Chair の交代

これまで Jean Patel が議長を遂行してきたが，本会議で任務を終了して，次回の会議から Melvin P. Weinstein が議長に就任することが発表された。Dr. Weinstein は血液培養の重要性に関する多くの業績がある。参考までに JCM に掲載された略歴を以下に示す。

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3719630/pdf/zjm2476.pdf

次回の AST ミーティング

次回の CLSI（Clinical and Laboratory Standards Institute） AST（Antimicrobial Susceptibility Test）ミーティングは、2017 年 1 月 14 日～1 月 17 日に、米国アリゾナ州テンピで開催されることが報告された。

（文責：大楠清文）