T&T WG

June 2018

San Diego, CA

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Nancy Watz

Mary York

Bold = members present

T&T Agenda

1. Inducible clindamycin resistance testing language
2. Addition of text surrounding 0.125 vs 0.12 reporting - from Methods Application & Interpretation WG
3. Clarification of beta-hemolytic strep/tetracycline comment?
4. *Staphylococcus* Table 2C options

T&T Item 1:

12.	Melissa Jones-UNC Healthcare	Ed	Table 2C; comment 29	Does CLSI have a position on recommending the D-test? If so, suggest stronger encouragement to test in every section where ICR is discussed. For example:	Suggest wording change: **(29)** Detection of inducible clindamycin resistance (ICR) should be performed on all staphylococci. ICR can be detected by

Table 2C, comment (29):

"Inducible clindamycin resistance can be detected by disk diffusion using the D-zone test or by broth microdilution (see Table 3G, Subchapter 3.9 in M02[1], and Subchapter 3.12 in M07[2])."

Comment update – language adapted from "**Supplemental Tests – Required**"

For isolates that test erythromycin resistant and clindamycin susceptible or intermediate, testing for inducible clindamycin resistance is required before reporting clindamycin. See Table 3G, Subchapter 3.9 in M02,[2] and Subchapter 3.12 in M07.[1]

Update will apply to Table 2 comments where ICR is mentioned:

Table 2C, comment (29), Table 2G, comment (23), and Table 2H-1 – comment (14)

T&T Item 1:

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Discussions around confusion or lack of understanding by docs that a lab has tested erythromycin to determine need for ICR testing and also around soft language in Table 3G for optional reporting comments

ICR Ad Hoc: Review language around ICR testing/reporting comments to help convey this information

Outreach WG: Suggestion that this is a good topic to include in an ORWG newsletter

T&T Item 2:
Additional text for reporting 0.125µg/mL as 0.12µg/mL

From Methods Application WG call:

It would be helpful to have the comment regarding reporting 0.125 as 0.12 in other places in the document – particularly other strep tables and other organisms that are mentioned in the endocarditis guidelines…should it be added in all places we have 0.12 as a breakpoint since it also applies to other drugs?

Additional comments from Dr. Samir Patel:

"This confusion arises from European endocarditis guidelines, which suggest 0.125 rather than 0.12. The IDSA/AHA states 0.12. As some labs are doing E-test which has 0.125, the confusion arises when they get 0.125. I found this paper that shows that reporting 0.125 instead of 0.12 does affect on choice of antibiotics. So I would recommend having a stronger statement."

T&T Item 2:
Additional text for reporting 0.125µg/mL as 0.12µg/mL

Current language

Table 2H-2. *Streptococcus* spp. Viridans Group (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm			Interpretive Categories and MIC Breakpoints, µg/mL			Comments
			S	I	R	S	I	R	
PENICILLINS									
A A	Penicillin Ampicillin	–	–	–	–	≤0.12 ≤0.25	0.25–2 0.5–4	≥4 ≥8	**(5)** Viridans streptococci isolated from normally sterile body sites (eg, CSF, blood, bone) should be tested for penicillin susceptibility using an MIC method. **(6)** A penicillin MIC of ≤0.125 µg/mL is the same as a penicillin MIC of ≤0.12 µg/mL and both should be interpreted as susceptible. Laboratories should report an MIC of ≤0.125 µg/mL as ≤0.12 µg/mL. **(7)** ***Rx:*** Penicillin- or ampicillin-intermediate isolates may necessitate combined therapy with an aminoglycoside for bactericidal action.

Table 7 language

When serial twofold dilution minimal inhibitory concentrations are being prepared and tested, the actual dilution scheme is:

128, 64, 32, 16, 8, 4, 2, 1, 0.5, 0.25, 0.125, 0.0625, 0.03125, 0.015625, 0.0078125, 0.0039063, 0.0019531 µg/mL, etc.

For convenience only, and not because these are the actual concentrations tested, it was decided to use the following values in these tables:

128, 64, 32, 16, 8, 4, 2, 1, 0.5, 0.25, 0.12, 0.06, 0.03, 0.016, 0.008, 0.004, 0.002 µg/mL, etc.

The values that appear in the tables are equivalent to the actual values tested, eg, 0.12 µg/mL = 0.125 µg/mL, 0.016 µg/mL = 0.015625 µg/mL.

T&T Item 2:

Add lang
III. Repo

III. Reporting Results

A. Organisms Included in Table 2

The MIC values determined as described in M07[2] may be reported directly to clinicians for patient care purposes. However, it is essential that an interpretive category result (S, I, or R) also be provided routinely to facilitate understanding of the MIC report by clinicians. Zone diameter measurements without an interpretive category should not be reported. Recommended interpretive categories for various MIC and zone diameter values are included in tables for each organism group and are based on the evaluation of data as described in CLSI document M23.[4]

Laboratories should only report results for agents listed in Table 2 specific to the organism being tested. It is not appropriate to apply disk

D. MIC Reporting Concentrations

When serial twofold dilution minimal inhibitory concentrations are being prepared and tested, the actual dilution scheme is, for example:

16, 8, 4, 2, 1, 0.5, 0.25, 0.125, 0.0625, 0.03125 µg/mL, etc. (See Table 7 for additional dilutions)

For convenience only, and not because these are the actual concentrations tested, it was decided to use the following values in these tables:

16, 8, 4, 2, 1, 0.5, 0.25, 0.12, 0.06, 0.03 µg/mL, etc.

The values that appear in the tables are equivalent to the actual values tested, eg, 0.12 µg/mL = 0.125 µg/mL, and laboratories should report an MIC of ≤0.125 µg/mL as ≤0.12 µg/mL.

16, 8, 4, 2, 1, 0.5, 0.25, 0.125, 0.0625, 0.03125 µg/mL, etc. (See Table 7 for additional dilutions)

For convenience only, and not because these are the actual concentrations tested, it was decided to use the following values in these tables:

16, 8, 4, 2, 1, 0.5, 0.25, 0.12, 0.06, 0.03 µg/mL, etc.

The values that appear in the tables are equivalent to the actual values tested, eg, 0.12 µg/mL = 0.125 µg/mL, and laboratories should report an MIC of ≤0.125 µg/mL as ≤0.12 µg/mL

T&T Item 3: Tetracycline comment clarification

Comment from DivC forwarded to T&T:

*For **beta hemolytic strep and tetracyclines** comment 13 (Table 2H-1), we have a physician requesting doxycycline sensitivities on a beta strep isolate. Tetracycline is on our panel and tested "R". **So does that mean you can interpret isolates "R" to tetracycline to also be "R" to doxycycline? Or this only works for "S" results?***

Current Table 2H-1, comment (13):
"Organisms that are susceptible to tetracycline are also considered susceptible to doxycycline and minocycline."

Is additional wording recommended to clarify that resistance to tetracycline does not imply resistance to doxycycline or minocycline?

Caveat: no testing recommendations for doxycycline or minocycline for β–hemolytic strep or Viridans strep

T&T Item 3: Tetracycline comment clarification

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Optional additional text:

"Organisms that are susceptible to tetracycline are also considered susceptible to doxycycline and minocycline. However, resistance to doxycycline and minocycline cannot be inferred from tetracycline resistance."

Is additional wording recommended to clarify that resistance to tetracycline does not imply resistance to doxycycline or minocycline?

Caveat: no testing recommendations for doxycycline or minocycline for β–hemolytic strep or Viridans strep

T&T Item 4: Table 2C *Staphylococcus* options

Goal is to improve the table formatting as testing recommendations continue to get more complicated, particularly with oxacillin and non-*S. aureus* species

Version 1
Table 2C-1 *S. aureus* only
Table 2C-2 Other staphylococci with option to group species based on testing recommendations

Version 2
Table 2C: Column added for specific indications

Version 3
Table 2C-1 Oxacillin/cefoxitin and vancomycin only
Table 2C-2 All other antimicrobials

Version 1

Table 2C-1. Zone Diameter and MIC Breakpoints for *Staphylococcus aureus*

Test/Report Group	Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm			Interpretive Categories and MIC Breakpoints, µg/mL			Comments [Removed for brevity]
			S	I	R	S	I	R	
PENICILLINASE-STABLE PENICILLINS (Continued)									
A	Oxacillin		–	–	–	≤ 2 (oxacillin)	–	≥ 4 (oxacillin)	
		30 µg cefoxitin (surrogate test for oxacillin)	≥ 22	–	≤ 21	≤ 4 (cefoxitin)	–	≥ 8 (cefoxitin)	

Table 2C-2. Zone Diameter and MIC Breakpoints for *Staphylococcus* spp., other than *S. aureus*

Test/Report Group	Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm			Interpretive Categories and MIC Breakpoints, µg/mL			Comments [Removed for brevity]
			S	I	R	S	I	R	
PENICILLINASE-STABLE PENICILLINS (Continued)									
A	Oxacillin (For Group 1)		–	–	–	≤ 2 (oxacillin)	–	≥ 4 (oxacillin)	
		30 µg cefoxitin (surrogate test for oxacillin)	≥ 22	–	≤ 21	≤ 4 (cefoxitin)	–	≥ 8 (cefoxitin)	
A	Oxacillin (For Group 2)	1 µg oxacillin	≥ 18	–	≤ 17	≤ 0.25	–	≥ 0.5	
A	Oxacillin (For Group 3)	–	–	–	–	≤ 0.25 (oxacillin)	–	≥ 0.5 (oxacillin)	
		30 µg cefoxitin (surrogate test for oxacillin)	≥ 25	–	≤ 24	–	–	–	

In General Comments section of Table 2C-2, include grouping designations:

Groups	*Staphylococcus* spp.	Acceptable Methods
Group 1	*S. lugdunensis*	• Cefoxitin MIC • Cefoxitin disk diffusion • Oxacillin MIC
Group 2	*S. pseudintermedius* and *S. schleiferi*	• Oxacillin MIC • Oxacillin disk diffusion
Group 3	Other *Staphylococcus* spp. (except *S. lugdunensis, S. pseudintermedius, S. schleiferi,* and *S.epidermidis).*	• Cefoxitin disk diffusion • Oxacillin MIC

Version 2

Table 2C. Zone Diameter and MIC Breakpoints for *Staphylococcus* spp.

Test/Report Group	Antimicrobial Agent	Staphylococcus species interpretation restrictions	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm S	I	R	Interpretive Categories and MIC Breakpoints, µg/mL S	I	R	Comments [Removed for brevity]
PENICILLINASE-STABLE PENICILLINS (Continued)										
A	Oxacillin	For reporting of *S. aureus* and *S. lugdunensis*		–	–	–	≤ 2 (oxacillin)	–	≥ 4 (oxacillin)	
			30 µg cefoxitin (surrogate test for oxacillin)	≥ 22	–	≤ 21	≤ 4 (cefoxitin)	–	≥ 8 (cefoxitin)	
A	Oxacillin	For reporting of *S. pseudintermedius* and *S. schleiferi*	1 µg oxacillin	≥ 18	–	≤ 17	≤ 0.25	–	≥ 0.5	
A	Oxacillin	For reporting of CoNS except *S. lugdunensis*, *S. pseudintermedius*, and *S. schleiferi*	–	–	–	–	≤ 0.25 (oxacillin)	–	≥ 0.5 (oxacillin)	
			30 µg cefoxitin (surrogate test for oxacillin)	≥ 25	–	≤ 24	–	–	–	
CEPHEMS (PARENTERAL)										
B	Ceftaroline	Only, for reporting against *S. aureus* only, including Methicillin Resistant S. aureus.(MRSA)	30 µg	≥ 24	21–23	≤ 20	≤ 1	2	≥ 4	
GLYCOPEPTIDES (19) For *S. aureus*, vancomycin-susceptible isolates may become vancomycin intermediate during the course of prolonged therapy.										
B	Vancomycin	For reporting against *S. aureus* only	–	–	–	–	≤ 2	4–8	≥ 16	
B	Vancomycin	CoNS	–	–	–	–	≤ 4	8–16	≥ 32	
Inv.	Teicoplanin	none	–	–	–	–	≤ 8	16	≥ 32	
LIPOGLYCOPEPTIDES										
C	Dalbavancin	For reporting against *S. aureus* only, including Methicillin Resistant S. aureus.(MRSA)	–	–	–	–	≤ 0.25	–	–	
C	Oritavancin		–	–	–	–	≤ 0.12	–	–	
C	Telavancin		–	–	–	–	≤ 0.12	–	–	
LIPOPEPTIDES										
B	Daptomycin	none	–	–	–	–	≤ 1	–	–	

Version 3

Option 1

- New column for species indications

Table 2C-1 (or 2C-2). Zone Diameter and MIC Breakpoints (oxacillin and vancomycin only) for *Staphylococcus* spp.

Test/Report Group	Antimicrobial Agent	*Staphylococcus* species Indications	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm			Interpretive Categories and MIC Breakpoints, µg/mL			Comments [Removed for brevity]
				S	I	R	S	I	R	
PENICILLINASE-STABLE PENICILLINS (Continued)										
A	Oxacillin	*S. aureus* and *S. lugdunensis*	–	–	–	–	≤ 2 (oxacillin)	–	≥ 4 (oxacillin)	
			30 µg cefoxitin (surrogate test for oxacillin)	≥ 22	–	≤ 21	≤ 4 (cefoxitin)	–	≥ 8 (cefoxitin)	
A	Oxacillin	*S. pseudintermedius* and *S. schleiferi*	1 µg oxacillin	≥ 18	–	≤ 17	≤ 0.25	–	≥ 0.5	
A	Oxacillin	*S. epidermidis*	1 µg oxacillin	≥ 18 (oxacillin)	–	≤ 17 (oxacillin)	≤ 0.25 (oxacillin)	–	≥ 0.5 (oxacillin)	
			30 µg cefoxitin (surrogate test for oxacillin)	≥ 25 (cefoxitin)	-	≤ 24 (cefoxitin)	-	-	-	
A	Oxacillin	Other *Staphylococcus* spp.	–	–	–	–	≤ 0.25 (oxacillin)	–	≥ 0.5 (oxacillin)	
			30 µg cefoxitin (surrogate test for oxacillin)	≥ 25	–	≤ 24	–	–	–	
GLYCOPEPTIDES (19) For *S. aureus*, vancomycin-susceptible isolates may become vancomycin intermediate during the course of prolonged therapy.										
B	Vancomycin	*S. aureus*	–	–	–	–	≤ 2	4–8	≥ 16	
		Other *Staphylococcus* spp.	–	–	–	–	≤ 4	8–16	≥ 32	

Version 3

Option 2

- Separate MIC/DD
- List species indications

Table 2C-1 (or 2C-2). Zone Diameter and MIC Breakpoints (oxacillin and vancomycin only) for *Staphylococcus* spp.

Test/Report Group	Antimicrobial Agent	*Staphylococcus* Species Indications	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm S	I	R	Interpretive Categories and MIC Breakpoints, µg/mL S	I	R	Comments [Removed for brevity]
PENICILLINASE-STABLE PENICILLINS										
A	Oxacillin, MIC	*S. aureus* *S. lugdunensis*	-	- -	- -	- -	≤2 ≤4 (cefoxitin)	-	≥4 ≥8 (cefoxitin)	
		Other *Staphylococcus* spp	-	-	-	-	≤0.25	-	≥0.5	
A	Oxacillin, DD	*S. aureus* *S. lugdunensis*	30 µg cefoxitin (surrogate test for oxacillin)	≥22	-	≤21	-	-	-	
		S. pseudintermedius, *S. schleiferi*, *S. epidermidis*	1 µg oxacillin	≥18	-	≤17	-	-	-	
		CoNS (except *S. lugdunensis*, *S. pseudintermedius*, and *S. schleiferi*)	30 µg cefoxitin (surrogate test for oxacillin)	≥25	–	≤24	–	–	–	
GLYCOPEPTIDES **(19)** For *S. aureus*, vancomycin-susceptible isolates may become vancomycin intermediate during the course of prolonged therapy.										
B	Vancomycin	*S. aureus*	–	–	–	–	≤2	4–8	≥16	
		Other *Staphylococcus* spp.	–	–	–	–	≤4	8–16	≥32	