# Test/Report Group B:
# Disconnect between M100 Instructions for Use and Tables 1

**Group B** includes antimicrobial agents that may warrant primary testing, but they may be reported only selectively, such as when the organism is resistant to agents of the same antimicrobial class, as in Group A.

Table 1A. Suggested Groupings of Antimicrobial Agents With US Food and Drug Administration Clinical Indications That Should Be Considered for Routine Testing and Reporting on Nonfastidious Organisms by Clinical Microbiology Laboratories in the United States

| | | | | |
|---|---|---|---|---|
| **GROUP B PRIMARY TEST REPORT SELECTIVELY** | Amikacin[d,e] | Amikacin | Ceftaroline[i,j] | *Daptomycin[k,l] |
| | | | *Daptomycin[k,l] | |
| | | Aztreonam | Linezolid | Linezolid |
| | Amoxicillin-clavulanate<br>Ampicillin-sulbactam<br>Piperacillin-tazobactam<br>Ticarcillin-clavulanate | Cefepime | Doxycycline<br>Minocycline[b]<br>Tetracycline[a] | |
| | Cefuroxime | | | Vancomycin |
| | | Ciprofloxacin<br>Levofloxacin | *Vancomycin | |
| | Cefepime | Doripenem<br>Imipenem<br>Meropenem | Rifampin[h,j] | |
| | Cefotetan<br>Cefoxitin | Piperacillin-tazobactam | | |
| | Cefotaxime[d,e,f] or<br>ceftriaxone[d,e,f] | | | |
| | Ciprofloxacin[d,e]<br>Levofloxacin[d,e] | | | |
| | Doripenem<br>Ertapenem<br>Imipenem<br>Meropenem | | | |
| | Piperacillin | | | |
| | Trimethoprim-sulfamethoxazole[d,e] | | | |

# Tables 1

| GROUP B<br>OPTIONAL PRIMARY TEST<br>REPORT SELECTIVELY | | | | |
|---|---|---|---|---|
| | Amikacin[d,e] | Amikacin | Ceftaroline[i] | *Daptomycin[k] |
| | | | *Daptomycin[k] | |
| | | Aztreonam | Linezolid | Linezolid |
| | Amoxicillin-clavulanate<br>Ampicillin-sulbactam<br>Piperacillin-tazobactam<br>Ticarcillin-clavulanate | Cefepime | Doxycycline<br>Minocycline[b]<br>Tetracycline[a] | |
| | Cefuroxime | | | Vancomycin |
| | | Ciprofloxacin<br>Levofloxacin | *Vancomycin | |
| | Cefepime | Doripenem<br>Imipenem<br>Meropenem | Rifampin[h,j] | |
| | Cefotetan<br>Cefoxitin | Piperacillin-tazobactam | | |
| | Cefotaxime[d,e,f] or<br>ceftriaxone[d,e,f] | | | |
| | Ciprofloxacin[d,e]<br>Levofloxacin[d,e] | | | |
| | Doripenem<br>Ertapenem<br>Imipenem<br>Meropenem | | | |
| | Piperacillin | | | |
| | Trimethoprim-sulfamethoxazole[d,e] | | | |

# T&T WG

June 14-16, 2015

# T&T WG

Members : Jana Swenson (co-chair), Maria Traczewski (co-chair), Carey-Ann Burnham* (secretary), Dale Schwab, Peggy Kohner, Dyan Luper, Linda Mann, Melissa Miller*, Janet Hindler,  Flavia Rossi*, Tom Thomson, Nancy Watz, Mary York

*absent

# T&T June 2015

- Comment from user that comments in Tables 2 may be difficult to find.

# M100-S25
# Table 2H-2 p. 96

| Test/Report Group | Antimicrobial Agent | Disk Content | Zone Diameter Interpretive Criteria (nearest whole mm) | | | MIC Interpretive Criteria (µg/mL) | | | Comments |
|---|---|---|---|---|---|---|---|---|---|
| | | | S | I | R | S | I | R | |
| **FLUOROQUINOLONES** | | | | | | | | | |
| O | Levofloxacin | 5 µg | ≥17 | 14–16 | ≤13 | ≤2 | 4 | ≥8 | |
| O | Ofloxacin | 5 µg | ≥16 | 13–15 | ≤12 | ≤2 | 4 | ≥8 | |
| O | Gatifloxacin | 5 µg | ≥21 | 18–20 | ≤17 | ≤1 | 2 | ≥4 | |
| O | Grepafloxacin | 5 µg | ≥19 | 16–18 | ≤15 | ≤0.5 | 1 | ≥2 | |
| O | Trovafloxacin | 10 µg | ≥19 | 16–18 | ≤15 | ≤1 | 2 | ≥4 | |
| **PHENICOLS** | | | | | | | | | |
| C | Chloramphenicol | 30 µg | ≥21 | 18–20 | ≤17 | ≤4 | 8 | ≥16 | See comment (8). |
| **LINCOSAMIDES** | | | | | | | | | |
| C | Clindamycin | 2 µg | ≥19 | 16–18 | ≤15 | ≤0.25 | 0.5 | ≥1 | See comment (8). |
| **STREPTOGRAMINS** | | | | | | | | | |
| O | Quinupristin-dalfopristin | 15 µg | ≥19 | 16–18 | ≤15 | ≤1 | 2 | ≥4 | |
| **OXAZOLIDINONES** | | | | | | | | | |
| C | Linezolid | 30 µg | ≥21 | – | – | ≤2 | – | – | |

# M100-S25
# Table 2H-2 p. 95

| Test/Report Group | Antimicrobial Agent | Disk Content | Zone Diameter Interpretive Criteria (nearest whole mm) | | | MIC Interpretive Criteria (µg/mL) | | | Comments |
|---|---|---|---|---|---|---|---|---|---|
| | | | S | I | R | S | I | R | |
| **PENICILLINS** | | | | | | | | | |
| A | Penicillin | – | – | – | – | ≤0.12 | 0.25–2 | ≥4 | (4) Viridans streptococci isolated from normally sterile body sites (eg, CSF, blood, bone) should be tested for penicillin susceptibility using an MIC method. (5) ***Rx:*** Penicillin- or ampicillin-intermediate isolates may require combined therapy with an aminoglycoside for bactericidal action. |
| A | Ampicillin | | | | | ≤0.25 | 0.5–4 | ≥8 | |
| **CEPHEMS (PARENTERAL) (Including cephalosporins I, II, III, and IV. Please refer to Glossary I.)** | | | | | | | | | |
| B | Cefepime | 30 µg | ≥24 | 22–23 | ≤21 | ≤1 | 2 | ≥4 | |
| B | Cefotaxime | 30 µg | ≥28 | 26–27 | ≤25 | ≤1 | 2 | ≥4 | |
| B | Ceftriaxone | 30 µg | ≥27 | 25–26 | ≤24 | ≤1 | 2 | ≥4 | |
| **CARBAPENEMS** | | | | | | | | | |
| O | Doripenem | – | – | – | – | ≤1 | – | – | |
| O | Ertapenem | – | – | – | – | ≤1 | – | – | |
| O | Meropenem | – | – | – | – | ≤0.5 | – | – | |
| **GLYCOPEPTIDES** | | | | | | | | | |
| B | Vancomycin | 30 µg | ≥17 | – | – | ≤1 | – | – | |
| **LIPOPEPTIDES** | | | | | | | | | |
| O | Daptomycin | – | – | – | – | ≤1 | – | – | (6) Daptomycin should not be reported for isolates from the respiratory tract. |
| **MACROLIDES** (7) Susceptibility and resistance to azithromycin, clarithromycin, and dirithromycin can be predicted by testing erythromycin. (8) Not routinely reported on isolates from the urinary tract. | | | | | | | | | |
| C | Erythromycin | 15 µg | ≥21 | 16–20 | ≤15 | ≤0.25 | 0.5 | ≥1 | |
| O | Azithromycin | 15 µg | ≥18 | 14–17 | ≤13 | ≤0.5 | 1 | ≥2 | |
| O | Clarithromycin | 15 µg | ≥21 | 17–20 | ≤16 | ≤0.25 | 0.5 | ≥1 | |
| O | Dirithromycin | 15 µg | ≥18 | 14–17 | ≤13 | ≤0.5 | 1 | ≥2 | |
| **TETRACYCLINES** (9) Organisms that are susceptible to tetracycline are also considered susceptible to doxycycline and minocycline. | | | | | | | | | |
| O | Tetracycline | 30 µg | ≥23 | 19–22 | ≤18 | ≤2 | 4 | ≥8 | |

# Confusing comment placement

- Move all comments that appear in the grayed boxes to the right so that they are in the Comment column. No
- Bold the all the comment numbers so that they are easier to see and lighten the shading in the greyed boxes. Agreed
- Consider handling these kinds of comment differently so that there are fewer in Tables 2.

# Confusing comments

- Felt that it might be helpful to take some of these comments out of Tables 2 and put them some where else (especially ones that occur often, such as the one that states a drug should not be reported on urinary isolates). WG agreed
- Create a small ad hoc group to create a table with body site specific information. This table could be put into the Instructions for Use of Tables in M100.

# T&T WG

- Request to add information on reading linezolid MICs to M100
- Information on disk testing is included in M100 but not MIC testing.
- Create a new general comment in Table 2C.
  WG agreed.

# Table 2C

**General Comments**

1) For disk diffusion, test a maximum of 12 disks on a 150-mm plate and **no more than** 6 disks on a 100-mm plate; disks should be placed no less than 24 mm apart, center to center (see M02, Chapter **3.6**). Each zone diameter should be clearly measurable; overlapping zones prevent accurate measurement. Measure the diameter of the zones of complete inhibition (as judged by the unaided eye), including the diameter of the disk. Hold the Petri plate a few inches above a black background illuminated with reflected light, except for linezolid, which should be read with transmitted light (plate held up to light source). The zone margin should be considered the area showing no obvious, visible growth that can be detected with the unaided eye. Ignore faint growth of tiny colonies that can be detected only with a magnifying lens at the edge of the zone of inhibited growth. With trimethoprim and the sulfonamides, antagonists in the medium may allow some slight growth; therefore, disregard slight growth (20% or less of the lawn of growth) and measure the more obvious margin to determine the zone diameter. For linezolid, any discernible growth within the zone of inhibition is indicative of resistance to the respective agent.

# Table 2C
# New General Comment

(2) For gram-positive cocci when testing chloramphenicol, clindamycin, erythromycin, linezolid, and tetracycline by MIC, trailing growth can make end-point determination difficult. In such cases, read the MIC at the first spot where the trailing begins. Tiny buttons of growth should be ignored (see M07 Figures 3 and 4). With trimethoprim and the sulfonamides, antagonists in the medium may allow some slight growth; therefore, read the end point at the concentration in which there is ≥ 80% reduction in growth as compared to the control (see M07 Figure 2).

# *Salmonella* and FQs

- M100-S25 recommendations are confusing
- T&T asked to clarify wording in Table 2A for use of peflox and nalidixic as surrogates for FQ resistance.
- Considered several options, including removing the tests from Table 2 and putting them into a new Table 3.
- Decided best option to create 2 separate sections for FQs in Table 2A, one for *Salmonella* and one for rest of Enterobacteriaceae.

# *Salmonella* and FQs

**QUINOLONES and FLUOROQUINOLONES for *Salmonella* spp. (Please refer to Glossary I)**

(37) For testing and reporting of *Salmonella* spp. (including *S.* Typhi and *S.* Paratyphi A–C). Routine susceptibility testing is not indicated for nontyphoidal *Salmonella* spp. isolated from intestinal sources.

**NOTE:** Reevaluation of fluoroquinolones is ongoing**.**
See Comment (2).

| Test/Report Group | Antimicrobial Agent | Disk Content | Zone Diameter Interpretive Criteria (nearest whole mm) | | | | MIC Interpretive Criteria (µg/mL) | | | | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | S | SDD | I | R | S | SDD | I | R | |
| B | Ciprofloxacin | 5 µg | ≥31 | | 21-30 | ≤20 | ≤0.06 | | 0.06-0.5 | ≥1 | (38) For *Salmonella* spp., MIC testing of fluoroquinolones is preferred. If a ciprofloxacin, levofloxacin, or ofloxacin MIC cannot be done, ciprofloxacin disk diffusion testing can be done. Alternatively, pefloxacin, if available, may be used as a surrogate test for fluoroquinolone resistance mechanisms. (See below).<br><br>(39) Strains of *Salmonella* that test intermediate or resistant to ciprofloxacin, levofloxacin or ofloxacin may be associated with clinical failure or delayed response in fluoroquinolone-treated patients with salmonellosis. |
| B | Levofloxacin | - | - | | - | - | ≤0.12 | | | ≥0.25 | |
| O | Ofloxacin | - | - | | - | - | ≤0.12 | | | ≥0.25 | |
| O | Nalidixic acid (surrogate test for fluoroquinolone resistance) | 30 µg | ≥19 | | 14-18 | ≤13 | ≤16 | | – | ≥32 | (40) Pefloxacin and nalidixic acid disk diffusion tests are surrogate tests for detecting resistance to fluoroquinolones.<br><br>Pefloxacin may not detect less common fluoroquinolone resistance mechanisms identified in *Salmonella* spp. (e.g., *aac'6-lb-cr*).<br><br>Nalidixic acid will not detect all fluoroquinolone resistant isolates and may overcall fluoroquinolone resistance in some isolates of *Salmonella* spp.<br><br>Report any isolate that tests resistant to pefloxacin or nalidixic acid as resistant to ciprofloxacin, levofloxacin, and ofloxacin.<br><br>See comments (38) and (39). |
| Inv. | Pefloxacin (surrogate test for fluoroquinolone resistance) | 5 µg | ≥24 | | - | ≤23 | - | | - | - | |

# *Enterobacteriaceae* and FQs

| Test/Report Group | Antimicrobial Agent | Disk Content | Zone Diameter Interpretive Criteria (nearest whole mm) | | | | MIC Interpretive Criteria (µg/mL) | | | | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | S | SDD | I | R | S | SDD | I | R | |
| **QUINOLONES and FLUOROQUINOLONES for *Enterobacteriaceae* except *Salmonella* spp. (Please refer to Glossary I)**<br><br>**NOTE:** reevaluation of quinolones is ongoing | | | | | | | | | | | |
| B | Ciprofloxacin | 5 µg | ≥21 | | 16–20 | ≤15 | ≤1 | | 2 | ≥4 | |
| B | Levofloxacin | 5 µg | ≥17 | | 14–16 | ≤13 | ≤2 | | 4 | ≥8 | |
| O | Cinoxacin | 100 µg | ≥19 | | 15–18 | ≤14 | ≤16 | | 32 | ≥64 | See comment (25). |
| O | Enoxacin | 10 µg | ≥18 | | 15–17 | ≤14 | ≤2 | | 4 | ≥8 | |
| O | Gatifloxacin | 5 µg | ≥18 | | 15–17 | ≤14 | ≤2 | | 4 | ≥8 | |
| O | Gemifloxacin | 5 µg | ≥20 | | 16–19 | ≤15 | ≤0.25 | | 0.5 | ≥1 | (41) FDA-approved for *Klebsiella pneumoniae.* |
| O | Grepafloxacin | 5 µg | ≥18 | | 15–17 | ≤14 | ≤1 | | 2 | ≥4 | |
| O | Lomefloxacin | 10 µg | ≥22 | | 19–21 | ≤18 | ≤2 | | 4 | ≥8 | |
| O | Nalidixic acid | 30 µg | ≥19 | | 14–18 | ≤13 | ≤16 | | – | ≥32 | See comment (25). |
| O | Ofloxacin | 5 µg | ≥16 | | 13–15 | ≤12 | ≤2 | | 4 | ≥8 | |
| U | Norfloxacin | 10 µg | ≥17 | | 13–16 | ≤12 | ≤4 | | 8 | ≥16 | |
| Inv. | Fleroxacin | 5 µg | ≥19 | | 16–18 | ≤15 | ≤2 | | 4 | ≥8 | |

# Revision of M02 and M07

- Create an ad hoc group to do this who would report to T&T by January 2016
- Goal would be to have a near complete draft available in January 2017 and a final draft in agenda book in June 2017
- Final publication for January 2018
- Call for volunteers to be done soon.

# *Salmonella* and FQs

**QUINOLONES and FLUOROQUINOLONES for *Salmonella* spp. (Please refer to Glossary I)**

(37) For testing and reporting of *Salmonella* spp. (including *S.* Typhi and *S.* Paratyphi A–C). Routine susceptibility testing is not indicated for nontyphoidal *Salmonella* spp. isolated from intestinal sources.

**NOTE:** Reevaluation of fluoroquinolones is ongoing.
See Comment (2).

| Test/Report Group | Antimicrobial Agent | Disk Content | Zone Diameter Interpretive Criteria (nearest whole mm) | | | | MIC Interpretive Criteria (µg/mL) | | | | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | S | SDD | I | R | S | SDD | I | R | |
| B<br>B<br>O | Ciprofloxacin<br>Levofloxacin<br>Ofloxacin | 5 µg<br>-<br>- | ≥31<br>-<br>- | | 21-30<br>-<br>- | ≤20<br>-<br>- | ≤0.06<br>≤0.12<br>≤0.12 | | 0.06-0.5 | ≥1<br>≥0.25<br>≥0.25 | (38) For *Salmonella* spp., MIC testing of fluoroquinolones is preferred. If a ciprofloxacin, levofloxacin, or ofloxacin MIC cannot be done, ciprofloxacin disk diffusion testing can be done. Alternatively, pefloxacin, if available, may be used as a surrogate test for fluoroquinolone resistance mechanisms. (See below).<br><br>(39) Strains of *Salmonella* that test intermediate or resistant to ciprofloxacin, levofloxacin or ofloxacin may be associated with clinical failure or delayed response in fluoroquinolone-treated patients with salmonellosis. |
| O<br><br>Inv. | Nalidixic acid (surrogate test for fluoroquinolone resistance)<br><br>Pefloxacin (surrogate test for fluoroquinolone resistance) | 30 µg<br><br>5 µg | ≥19<br><br>≥24 | | -<br><br>- | ≤18<br><br>≤23 | ≤16<br><br>- | | –<br><br>- | ≥32<br><br>- | (40) Pefloxacin and nalidixic acid disk diffusion tests are surrogate tests for detecting resistance to fluoroquinolones.<br><br>Pefloxacin may not detect less common fluoroquinolone resistance mechanisms identified in *Salmonella* spp. (e.g., *aac'6-Ib-cr*).<br><br>Nalidixic acid will not detect all fluoroquinolone resistant isolates and may overcall fluoroquinolone resistance in some isolates of *Salmonella* spp.<br><br>Report any isolate that tests resistant to pefloxacin or nalidixic acid as resistant to ciprofloxacin, levofloxacin, and ofloxacin.<br><br>See comments (38) and (39). |

Also edit current (M100-S25) comment 41 for nalidixic acid

(41) These interpretive criteria are for urinary tract isolates of *Enterobacteriaceae* ~~and for all isolates of *Salmonella*~~.