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# Evaluation of the Precept Microdilution MIC System for Single-Drug Testing in Individual Trays

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This study presents an evaluation of a commercial system for the MIC testing of single drugs dehydrated in disposable plastic trays (Precept, Austin Biological Laboratories, Inc., Austin, Tex.). The commercial system was compared with a reference agar dilution method, and 203 clinical bacterial isolates were tested by each method. For a total of 767 determinations, there was 94.2% agreement between the two methods, and of the discrepancies encountered, 0.8% were very major, 2.1% were major, and 2.9% were minor. The results suggest that the Precept system may provide a practical and reliable method for MIC determinations of individual antimicrobial agents.

Most commercially available microdilution MIC testing systems utilize multiwell trays containing dilutions of several antimicrobial agents (1, 4–6). When a single-drug MIC determination is requested, the laboratory must prepare a dilution series for that drug or use an entire tray containing multiple drugs to test the single agent requested. In addition, many newer antimicrobial agents are not available in commercial microdilution panels. An alternative approach is provided by the Precept system (Austin Biological Laboratories, Inc., Austin, Tex.). This system utilizes a single-drug microdilution tray containing varied concentrations of a dehydrated antimicrobial agent. In the present study, the Precept system was evaluated by comparison with a reference agar dilution method (8). The results indicate excellent agreement between the two methods.

## MATERIALS AND METHODS

**Organisms.** A total of 203 isolates were tested, including strains of the following: *Escherichia coli*, 29; *Pseudomonas aeruginosa*, 32; *Klebsiella* sp., 30; *Enterobacter* sp., 21; *Citrobacter* sp., 6; *Serratia marcescens*, 16; *Providencia alcalifaciens*, 2; *Providencia stuartii*, 5; *Staphylococcus aureus*, 21; coagulase-negative staphylococci, 20; and enterococci, 21. This group of test organisms included 161 fresh clinical isolates, 34 stock cultures of clinical isolates, and 8 lyophilized control strains. The susceptibility of each of the strains to selected antimicrobial agents was determined by the Precept method and the agar dilution method.

**Microdilution susceptibility tests.** Susceptibility tests were performed with the commercially available Precept trays. This system is a simplified version of the broth microdilution technique (3) for determining the MIC of selected antimicrobial agents. The Precept tray is a covered, self-contained, polystyrene tray molded into 10 inoculating troughs and wells. The wells contain doubling dilutions of a single dehydrated antimicrobial agent in concentrations recommended by the National Committee for Clinical Laboratory Standards (7). The trays contain nine dilutions of each antimicrobial agent and a growth control well. The concentration ranges (in micrograms per milliliter) of each drug tested were as follows: gentamicin and tobramycin, 16 to 0.06; amikacin, 128 to 0.5; cefoperazone, 64 to 0.25, cefoxitin, 32 to 0.13; and vancomycin, 16 to 0.06. Antimicrobial susceptibility tests with this system were performed according to the instructions of the manufacturer. The inoculum was prepared by picking three to four isolated colonies from a plate and placing them into a tube containing 5 ml of tryptic soy broth. This broth was incubated at 35°C for 4 to 6 h to obtain a turbidity that was visually comparable to a 0.5 McFarland standard. The inoculum was then diluted by placing 0.001 ml of the tryptic soy broth culture into a tube containing 5 ml of Mueller-Hinton cation-supplemented broth (2). One drop of a surfactant solution was added to the tube to aid in distributing the inoculum evenly into the wells containing antimicrobial agents. One milliliter of this inoculum suspension was pipetted into the inoculating trough of the Precept tray. The tray was then tilted forward until the inoculum flowed into the wells containing antimicrobial agents, resulting in a broth inoculum volume of 0.1 ml per well. The final inoculum concentration in each well is ca. $5 \times 10^4$ CFU/ml. The trays were incubated at 35°C for 16 to 18 h and then examined for bacterial growth in each well.

**Agar dilution method.** Agar dilution testing was done as described by Washington and Sutter (8).

**Interpretation of results.** Broth and agar dilution results were interpreted as susceptible, moderately susceptible, and resistant according to established criteria, using recently published breakpoint drug concentrations (7). Interpretative category discrepancies between the broth and agar dilution results were considered to be very major (Precept susceptible-agar dilution resistant), major (Precept resistant-agar dilution susceptible), or minor (Precept moderately susceptible-agar dilution susceptible or resistant; Precept susceptible or resistant-agar dilution moderately susceptible).

## RESULTS

The 203 organisms included in the study had the expected patterns of susceptibility to the drugs tested. A total of 1,534 susceptibility tests was performed by the two methods, and 97% of the Precept results were within one doubling dilution of the agar dilution results (Table 1). There was a 94.2% interpretive category agreement between the two methods. The 44 (5.8%) interpretive category discrepancies between the two methods consisted of 6 (0.8%) very major discrepancies, 16 (2.1%) major discrepancies, and 22 (2.9%) minor discrepancies. The largest number of discrepancies (15) was

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TABLE 1. Doubling dilution differences for MIC values determined by the Precept system compared with agar dilution

| Antimicrobial agent | No. (%)[a] | | | | | | |
|---|---|---|---|---|---|---|---|
| | −3 | −2 | −1 | 0 | +1 | +2 | +3 |
| Amikacin | 0 | 0 | 31 (22) | 87 (62) | 23 (16) | 0 | 0 |
| Cefoperazone | 2 | 5 (4) | 45 (32) | 73 (52) | 16 (11) | 0 | 0 |
| Cefoxitin | 1 (<1) | 1 (<1) | 39 (28) | 97 (69) | 3 (2) | 0 | 0 |
| Gentamicin | 0 | 4 | 36 (26) | 44 (31) | 51 (36) | 6 (4) | 0 |
| Tobramycin | 0 | 0 | | | | | |
| Vancomycin | 0 | 0 | 5 (8) | 55 (89) | 2 (3) | 0 | 0 |
| Total | 3 (1) | 10 (1) | 196 (26) | 423 (55) | 124 (16) | 11 (1) | 0 |

[a] Negative numbers indicate Precept MICs less than agar dilution MICs by the stated doubling dilution, positive numbers indicate Precept MICs greater than agar dilution MICs by the stated doubling dilution, and 0 indicates identical results.

noted with gentamicin testing (Table 2). Eleven discrepancies occurred with cefoperazone testing, and nine occurred with cefoxitin. Five or fewer discrepancies were encountered with tobramycin, amikacin, and vancomycin. Among the organisms tested, *P. aeruginosa* accounted for 21 testing discrepancies, and 16 of the discrepancies were major (Table 3). Other organisms associated with an excess of testing discrepancies included *E. coli* (seven total, four very major) and *S. marcescens* (nine total, all minor). No discrepancies were observed with any of the gram-positive cocci tested.

## DISCUSSION

This study demonstrates that the Precept system performed with excellent accuracy in comparison with an agar dilution reference method. There was a 94% interpretive category agreement between the two methods, and 97% of the results were within ± 1 $\log_2$ dilution of the reference method. These results compare favorably with evaluations of other microdilution susceptibility testing systems (4, 5). Of the 44 total discrepancies observed, 50% (22) represent only minor discrepancies. Since there were no discrepancies detected with the gram-positive isolates, testing of the gram-negative bacilli accounted for all discrepancies. Of the observed discrepancies, ca. 36% were detected with isolates of *P. aeruginosa*, and testing of gentamicin accounted for 34% of all discrepancies. The divalent cation content of broth media may affect susceptibility testing results for aminoglycosides and *P. aeruginosa* (8), but the broth used with the Precept system is supplemented with calcium and magnesium. Another potential explanation is an inoculum effect with *P. aeruginosa* (8). The exact explanation of the testing discrepancies observed with *P. aeruginosa* and gentamicin will require further investigation.

In addition to its excellent performance, the Precept system is convenient to use with its self-inoculating design. The cost of the system is about one-half that of commercially available microdilution panels. The Precept system may provide an economical alternative to standard microdilution panels when MIC data are needed for a single antimicrobial agent. This may especially be true when the primary testing method in use in a laboratory does not generate MIC data and microdilution testing is performed only in selected instances. An added advantage of the Precept system is the availability of dilution panels for new or unusual drugs upon request. Overall, the Precept system is a reliable and efficient microdilution system for MIC determinations of individual antimicrobial agents.

TABLE 2. Distribution of susceptibility testing discrepancies by antimicrobial agent

| Category | No. of discrepancies in: | | | | | |
|---|---|---|---|---|---|---|
| | Amikacin | Cefoperazone | Cefoxitin | Gentamicin | Tobramycin | Vancomycin |
| Very major | 1 | 0 | 0 | 1 | 4 | 0 |
| Major | 3 | 0 | 0 | 12 | 1 | 0 |
| Minor | 0 | 11 | 9 | 2 | 0 | 0 |

TABLE 3. Distribution of susceptibility testing discrepancies by organism

| Organism | No. of tests | No. of discrepancies | | |
|---|---|---|---|---|
| | | Very major | Major | Minor |
| *E. coli* | 145 | 4 | 0 | 3 |
| *P. aeruginosa* | 160 | 0 | 16 | 5 |
| *Klebsiella* sp. | 150 | 0 | 0 | 2 |
| *Enterobacter* sp. | 105 | 0 | 0 | 2 |
| *Citrobacter* sp. | 30 | 0 | 0 | 1 |
| *S. marcescens* | 80 | 0 | 0 | 9 |
| *Providencia* spp. | 35 | 2 | 0 | 0 |
| *S. aureus* | 21 | 0 | 0 | 0 |
| Staphylococci, coagulase negative | 20 | 0 | 0 | 0 |
| Enterococci | 21 | 0 | 0 | 0 |

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