JOURNAL OF CLINICAL MICROBIOLOGY, Nov. 1985, p. 793–798
0095-1137/85/110793-06$02.00/0

Vol. 22, No. 5

Evaluation of the BIOGRAM Antimicrobial Susceptibility Test System

RICHARD F. D'AMATO,[1]* LISA HOCHSTEIN,[1] JOHN R. VERNALEO,[1] DENNIS J. CLERI,[1] ANDREW A. WALLMAN,[1] M. STEPHEN GRADUS,[2]† AND CLYDE THORNSBERRY[2]

The Catholic Medical Center of Brooklyn and Queens, Jamaica, New York 11432,[1] and The Centers for Disease Control, Atlanta, Georgia 30333[2]

Received 31 May 1985/Accepted 31 July 1985

BIOGRAM is an antimicrobial susceptibility test system for the determination of MICs from the standard disk diffusion test zone diameters. The system was challenged with 511 recent clinical isolates of members of the family *Enterobacteriaceae*, nonfermentative gram-negative bacteria, staphylococci, and enterococci. Results were compared with those obtained with the broth microdilution method. Appropriate control organisms were included with each test series. A total of 10,085 organism-drug combinations were evaluated. BIOGRAM demonstrated an overall correlation of 95.9% with the reference broth microdilution method.

The agar disk diffusion test described by Bauer et al. (2) and currently recommended with minor modifications by the U.S. Food and Drug Administration (4) and the National Committee for Clinical Laboratory Standards (NCCLS) (8) is used in most clinical microbiology laboratories in the United States. However, it has become increasingly important that laboratories using this test have the ability to perform quantitative antimicrobial susceptibility tests when requested or clinically warranted. The commercial availability of broth microdilution susceptibility test systems brings this capability to even the smallest laboratory, but if the laboratory performs disk tests initially, the request for or the decision to do a quantitative test often comes after the disk diffusion test has been performed. This causes a delay in reporting and increased expense for the laboratory. Additionally, adequate quality control of the test system may require more test panels than the number of clinical isolates being tested.

The categories of interpretation of the standard disk diffusion test are based on the correlation between zone diameters, MICs, and blood levels (for some drugs, urine levels), and there is an inverse linear relationship between the zone diameter and an MIC. Therefore, any zone diameter obtained by the standardized disk diffusion test can be correlated to a specific MIC. The BIOGRAM System (Giles Scientific Inc., New York, N.Y.) was developed on this principle.

The disk diffusion susceptibility test, when performed as described by the NCCLS, yields highly reproducible results. In 1982, Murray et al. (7) reported that the magnitude of differences on retesting bacteria-antimicrobial combinations in the disk test was small, a mean of only 1.3 mm.

In 1983, Jones (5), using data from The College of American Pathologists surveys, reported an overall rate of acceptable disk test performance of 95.2% and that this rate had increased 3 to 5% between 1976 and 1981.

Therefore, MICs calculated from zone diameters obtained with the standard disk diffusion test (8) should be both reproducible and reliable. This report summarizes a comparison of the BIOGRAM system with a standard broth microdilution method (9).

MATERIALS AND METHODS

Organisms. A total of 264 recent clinical isolates, representing approximately the normal distribution of bacteria encountered in medical practice, were tested at The Catholic Medical Center, Jamaica, N.Y. (Table 1). An additional 247 selected bacteria with known susceptibility patterns and mechanisms of resistance were evaluated at the Centers for Disease Control (Table 1). The bacteria were isolated and identified in accordance with the approaches outlined in the *Manual of Clinical Microbiology* (6).

Antimicrobial susceptibility tests. All inocula were prepared from pure cultures of bacteria cultivated for 18 to 20 h on Trypticase soy agar with 5% defibrinated sheep blood (BBL Microbiological Systems, Cockeysville, Md.) at 35°C.

(i) Broth microdilution method. Portions of four to five colonies were suspended in 0.5 ml of brain heart infusion broth (Prepared Media Laboratory, Tualatin, Oregon). The broth was incubated for 5 h at 35°C, after which a 0.05-ml portion was placed in 15 ml of distilled water with 0.02% Tween 80 (Prepared Media Laboratory). With the use of the multipronged inoculator supplied with the system, the diluted inoculum was added to each well of a microdilution tray (Prepared Media Laboratory) containing Mueller-Hinton (MH) broth and the antimicrobial agents and dilution ranges shown in Table 2. Cation-supplemented MH broth was used for the aminoglycoside antimicrobic agents. Sodium chloride was not added to the MH broth containing methicillin, oxacillin, or nafcillin. The final concentration of inoculum in each well was 1×10^5 to 2×10^5 CFU/ml. After 18 to 20 h of incubation at 35°C, results were determined by visual inspection with a convex-mirror-enlarged image. The MIC was that concentration of each antimicrobial agent that prevented discernible growth of the test organism.

(ii) BIOGRAM. The disk diffusion susceptibility test was performed as outlined in the NCCLS performance standard (8). All zones were measured at 18 to 20 h and, when growth was sufficient, also at 5 to 6 h of incubation. All antimicrobial disks (BBL) (Table 2) and MH agar plates (Prepared Media Laboratory) were of one lot. The BIOGRAM system consists of a preprogrammed computer, electronic calipers,

* Corresponding author.
† Present address: Milwaukee Public Health Laboratories, Milwaukee, WI 53202.

TABLE 1. Distribution of bacteria by institution

Organism	No. of clinical isolates from[a]:	
	CMC	CDC
Acinetobacter spp.		5
Citrobacter freundii	6	2
Citrobacter spp.	2	6
Edwardsiella spp.		2
Enterobacter aerogenes	1	10
Enterobacter cloacae	11	8
Enterobacter spp.		3
Escherichia coli	75	27
Hafnia alvei		2
Klebsiella pneumoniae	20	10
Klebsiella oxytoca	3	3
Morganella morganii	4	1
Proteus mirabilis	21	13
Proteus vulgaris	1	7
Providencia stuartii	2	3
Providencia rettgeri	3	6
Providencia spp.		4
Pseudomonas aeruginosa	31	29
Pseudomonas cepacia		2
Pseudomonas maltophilia	1	3
Salmonella spp.	4	4
Serratia marcescens	10	6
Serratia spp.	1	7
Shigella spp.	4	5
Staphylococcus aureus	32	29
Coagulase-negative staphylococci	12	19
Streptococcus faecalis	20	28

[a] A total of 264 isolates were tested at The Catholic Medical Center (CMC), and 247 isolates were tested at The Centers for Disease Control (CDC).

printer, and standard light source (Fig. 1). After incubation, the MH agar plates were placed on the light box, which provides a uniform, illuminated background, for reading zones of inhibition. Zones of inhibition were measured with the electronic caliper, and results were automatically fed into the computer and converted into an MIC based on regression line analysis. Only the most accurate portion of each regression line was incorporated into the BIOGRAM data base. MICs are not limited to a predetermined dilution scheme because they are calculated from zones of inhibition established by the continuous gradient disk diffusion method. Therefore, results are reported as MICs calculated to the nearest 0.1 μg/ml. The range of the MICs for BIOGRAM are shown in Table 2. Inhibitory quotients (3), a multiple of the MIC based on achievable antimicrobial agent concentrations in serum, urine, bile, and cerebrospinal fluid and relative antimicrobial agent costs which consider cost per gram and administration costs, are also computed and printed for each drug tested. Antimicrobial agent tissue levels were modified from those of Ellner and Neu (3). Interpretative categories (S, I, MS, and R) based on the NCCLS guidelines are included for each antimicrobial agent (8).

Quality control. *Escherichia coli* ATCC 25922, *E. coli* ATCC 35218, *Pseudomonas aeruginosa* ATCC 27853, *Staphylococcus aureus* ATCC 29213, *S. aureus* ATCC 25923, and *Streptococcus faecalis* ATCC 29212 were used daily to control the performance of both systems (8, 9).

Interpretation of results. Results expressed as MIC ratios were calculated by dividing the BIOGRAM MIC by the microdilution MIC (BIOGRAM MIC/microdilution MIC). When the two MICs were identical, the ratio was 1; when the BIOGRAM MIC was greater than the microdilution MIC, the ratios were 2, 4, etc.; and when the BIOGRAM MIC was less than the microdilution MIC, the ratios were 0.5, 0.25, etc. The two systems were considered in agreement when the MIC ratios ranged from 0.5 to 2.0 (± 1 doubling dilution). Because BIOGRAM MICs were calculated to the nearest 0.1 μg/ml, MIC ratios did not always match the doubling dilution values of the microdilution test. For analysis of results, ratios which fell between 0.25 and 0.5 were expressed as 0.5; ratios between 0.5 and 1.9 were expressed as 1; ratios between 2 and 3.9 were considered to be 2.

RESULTS

The MIC correlations between BIOGRAM and the broth microdilution method, based on a total of 10,085 test results, are shown in Tables 3 through 7. Table 3 shows the results for staphylococci. The agreement ranged from 82.0% for nafcillin to 100% for sulfisoxazole and trimethoprim-sulfamethoxazole. For oxacillin and nafcillin, the trend was towards higher MICs for BIOGRAM, with 14.6 and 18.0%, respectively, with ratios >2. Twenty-five oxacillin-resistant *S. aureus* isolates and twelve oxacillin-resistant *Staphylococcus epidermidis* isolates were included in the study, and all were detected by BIOGRAM; however, the broth microdilution method failed to detect ten oxacillin-resistant *S. aureus* isolates and two oxacillin-resistant *S. epidermidis*

TABLE 2. Antimicrobial agents and dilution ranges

Antimicrobial agent	Dilution range (μg/ml) by:	
	Broth microdilution[a]	BIOGRAM[b]
Cefazolin	0.5–64	0.7–64
Cephalothin	1–64	0.7–64
Cefotaxime	0.5–64	0.6–84
Cefoperazone	1–128	1.1–230
Cefoxitin	1–64	0.9–48
Moxalactam	1–64	0.8–69
Cefamandole	0.5–64	0.6–60
Ceftazidime	1–64	1.1–64
Penicillin G	0.125–16	0.12–12
Oxacillin	0.25–8	0.2–7
Nafcillin	0.25–8	0.2–7
Methicillin	0.5–16	0.5–15
Ticarcillin	4–128	4–128
Carbenicillin	4–256	4–240
Mezlocillin	4–256	3.5–240
Piperacillin	2–256	1.8–330
Ampicillin	0.25–32	0.12–46
Azlocillin	4–256	4–256
Vancomycin	1–16	1–20
Amoxacillin-clavulanate	2–64	2–64
Cinoxacin	16–64	16–64
Gentamicin	0.5–16	0.5–18
Amikacin	2–64	2–61
Netilmicin	1–64	1–56
Tobramycin	0.5–16	0.8–18
Erythromycin	0.25–32	0.25–40
Clindamycin	0.5–4	0.5–3.5
Sulfisoxazole	100–400	100–350
Trimethoprim-sulfamethoxazole	0.5-9.5–8-152	0.5-9.5–8-152
Trimethoprim	4–16	4–16
Chloramphenicol	2–32	3–40
Tetracycline	0.5–16	0.6–16
Nitrofurantoin	0.5–32	0.15–64

[a] Log base 2 (doubling dilution) MIC.
[b] Continuous range MIC derived from regression analysis.

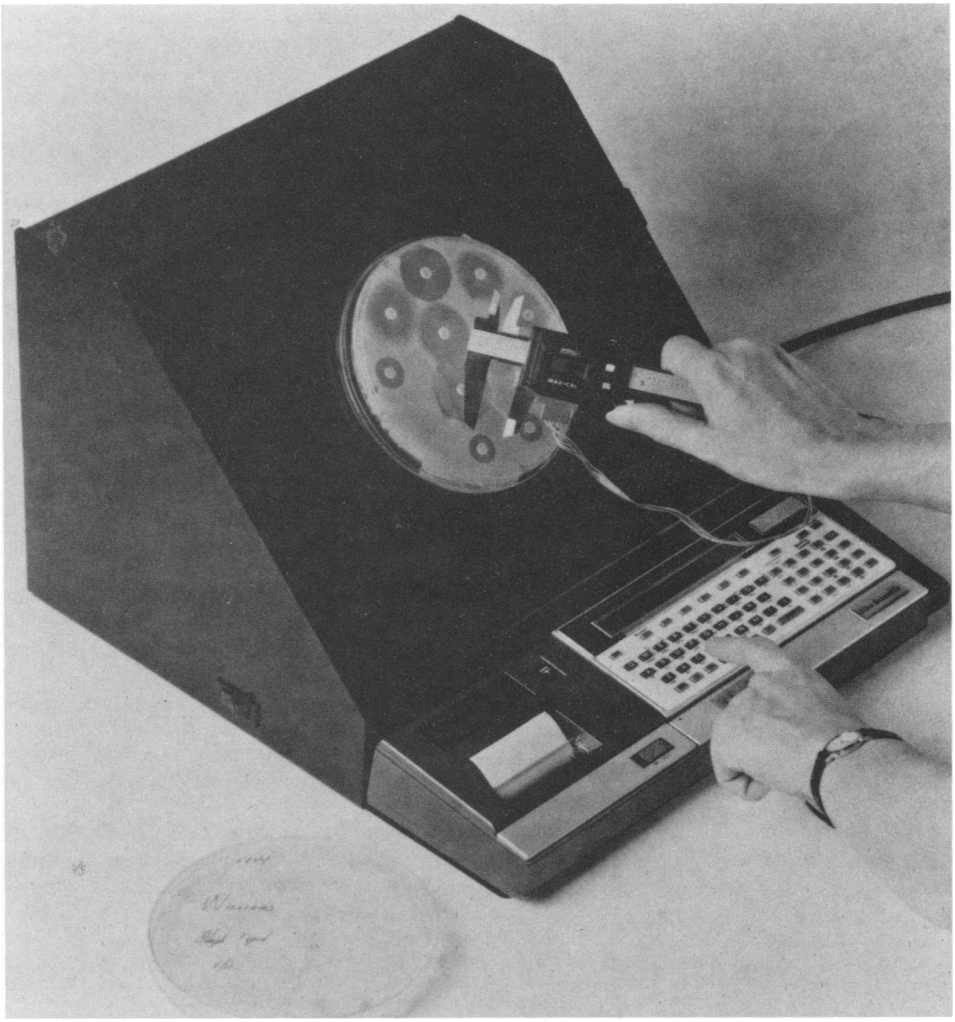

FIG. 1. The BIOGRAM system consists of a preprogrammed computer, electronic calipers, printer, and light source. Zones of inhibition are measured with the calipers, and results are automatically fed into the computer and converted into an MIC.

TABLE 3. Ratios of MICs obtained by microdilution and BIOGRAM for staphylococci[a]

Antimicrobial agent	% Tests with following MIC ratios[b]					% Agreement[c]
	≤0.25	0.5	1	2	≥4	
Amikacin	2.2	5.4	77.2	10.9	4.3	93.5
Amoxacillin-clavulanate	1.1	0.0	78.3	18.5	2.2	96.8
Cephalothin	1.1	5.4	81.5	6.5	5.4	93.4
Chloramphenicol	4.3	4.3	90.2	1.1	0.0	95.6
Clindamycin	1.1	0.0	98.9	0.0	0.0	98.9
Erythromycin	1.1	7.8	90.0	1.1	0.0	98.9
Gentamicin	4.3	1.1	90.3	4.3	0.0	95.7
Sulfisoxazole	0.0	1.2	96.5	2.3	0.0	100.0
Methicillin	2.0	15.7	72.5	7.8	2.0	96.0
Trimethoprim	2.4	4.7	92.9	0.0	0.0	97.6
Nafcillin	0.0	2.0	50.0	30.0	18.0	82.0
Netilmicin	1.1	2.2	93.4	3.3	0.0	98.9
Nitrofurantoin	11.0	16.5	67.0	5.5	0.0	89.0
Oxacillin	1.1	0.0	60.7	23.6	14.6	84.3
Penicillin G	8.0	6.0	82.0	2.0	2.0	90.0
Tobramycin	1.2	1.2	96.5	1.2	0.0	98.9
Tetracycline	1.1	5.7	93.2	0.0	0.0	98.9
Trimethoprim-sulfamethoxazole	0.0	0.0	100.0	0.0	0.0	100.0
Vancomycin	0.0	4.5	94.4	0.0	1.1	98.9

[a] A total of 92 staphylococci isolates, including 61 *S. aureus* and 31 coagulase-negative staphylococci isolates (1,708 drug-organism combinations) were evaluated.

[b] BIOGRAM MIC/reference MIC (see the text).

[c] Overall percent agreement was 95.5% for ratios of 0.5 to 2. When only on-scale results were considered, the percent agreement was 89.9%.

TABLE 4. Ratios of MICs obtained by microdilution and BIOGRAM for *S. faecalis*[a]

Antimicrobial agent	% Tests with following MIC ratios[b]:					% Agreement[c]
	≤0.25	0.5	1	2	≥4	
Ampicillin	2.2	41.3	56.5	0.0	0.0	97.8
Erythromycin	4.2	8.3	81.3	6.3	0.0	95.9
Nitrofurantoin	33.3	60.4	4.2	0.0	2.1	64.6
Tetracycline	0.0	0.0	100.0	0.0	0.0	100.0
Vancomycin	2.1	25.0	72.9	0.0	0.0	97.9

[a] A total of 51 *S. faecalis* isolates (255 drug-organism combinations) were evaluated.
[b] BIOGRAM MIC/reference MIC (see the text).
[c] Overall percent agreement was 91.1% for ratios of 0.5 to 2. When only on-scale results were considered, the percent agreement was 78.8%. When nitrofurantion results were removed, these values were 97.9 and 96.9%.

isolates. For nitrofurantoin and penicillin G, the trends were toward lower ratios, with 11.0 and 8.0%, respectively, <0.5. Overall agreement between the two methods for staphylococci was 95.5%. When only on-scale results were considered, the percent agreement was 89.9%.

Table 4 summarizes the results with 51 isolates of *S. faecalis*. The two systems demonstrated excellent agreement for all antimicrobial agents except nitrofurantoin, which showed a 64.6% correlation. The trend was towards lower MICs for BIOGRAM with this antimicrobial agent. If the nitrofurantoin results are removed, the overall agreement rises from 91.1 to 97.9%.

The MIC ratios for members of the family *Enterobacteriaceae* (Table 5) indicate a high level of correlation between the two methods. Tetracycline (88.7%) and cefamandole (84.9%) were the only antimicrobial agents which demonstrated less than 90% agreement. Tetracycline discrepancies were predominately with *E. coli*, *Citrobacter freundii*, and indole-positive *Protease*. The reference method generally demonstrated higher MICs than BIOGRAM, i.e., lower ratios.

Table 6 summarizes the results for the nonfermentative gram-negative bacteria. Greater than 90% correlation was noted for all antimicrobial agents except netilmicin (81.7%), cefotaxime (86.6%), and cefoperazone (89.6%), with the disagreement ratios being <0.5 (18.3, 13.4, and 10.4%, respectively). Two other aminoglycosides, amikacin and tobramycin, had 9.0% of their ratios at <0.5.

A summary of the agreement between the two methods for 10,085 organism-drug combinations is shown in Table 7. The overall agreement was 95.9%, but when only on-scale results were considered, the overall agreement was 92.4%. The drugs with <90% agreement were cefamandole (84.9%), nafcillin (82.0%), and oxacillin (84.3%). For cefamandole, the reference MICs tended to be higher, and for nafcillin and oxacillin, they tended to be lower.

Table 8 indicates the level of agreement between the two methods when BIOGRAM MICs were calculated after 5 to 6 h of incubation of the MH agar plates and compared with microdilution MICs determined after 18 to 20 h of incubation. A total of 68 organisms (1,615 organism and drug combinations) grew sufficiently at 5 to 6 h for analysis. Overall agreement after 5 to 6 h of incubation was 88.6%. When only on-scale results were considered, the agreement was 90.3%. The largest numbers of discrepancies were with ceftazidime, tobramycin, cefazolin, cefoperazone, and cefamandole; all showed <80% agreement. Most of these discrepancies were with the specially selected group of organisms tested at the Centers for Disease Control.

TABLE 5. Ratios of MICs obtained by microdilution and BIOGRAM for members of the *Enterobacteriaceae*[a]

Antimicrobial agent	% Tests with following MIC ratios[b]:					% Agreement[c]
	≤.025	0.5	1	2	≥4	
Amikacin	2.7	11.4	77.1	7.6	1.1	96.1
Ampicillin	2.4	3.1	85.0	7.2	2.4	95.3
Amoxacillin-clavulanate	1.3	6.1	83.8	7.4	1.3	97.3
Carbenicillin	2.5	5.0	86.1	5.5	0.8	96.6
Cefamandole	14.4	14.0	64.0	6.8	0.7	84.8
Cefazolin	2.7	5.5	78.5	11.9	1.4	95.9
Cefoperazone	6.8	14.7	73.9	4.3	0.3	92.9
Cefotaxime	3.3	5.8	87.9	2.7	0.3	96.4
Cefoxitin	3.0	5.4	76.8	14.1	0.7	96.3
Ceftazidime	0.8	1.9	89.0	8.0	0.3	98.9
Cephalothin	3.4	8.8	80.7	6.8	0.3	96.3
Chloramphenicol	0.5	6.8	87.9	4.7	0.0	99.4
Cinoxacin	0.7	0.7	97.6	1.0	0.0	99.3
Gentamicin	3.0	11.2	70.3	14.7	0.8	96.2
Sulfisoxazole	0.0	3.0	96.2	0.8	0.0	100.0
Mezlocillin	3.3	8.5	85.1	2.5	0.6	96.1
Trimethoprim	0.0	4.8	95.2	0.0	0.0	100.0
Moxalactam	1.1	2.5	94.2	1.7	0.6	98.4
Netilmicin	3.6	12.0	80.4	3.6	0.3	96.0
Nitrofurantoin	3.1	15.8	76.6	4.5	0.0	96.9
Piperacillin	4.7	13.6	73.4	7.2	1.1	94.2
Tobramycin	2.5	8.2	65.5	21.1	2.7	94.8
Tetracycline	11.3	35.3	52.4	1.0	0.0	88.7
Trimethoprim-sulfamethoxazole	0.0	0.3	99.3	0.3	0.0	100.0

[a] A total of 297 *Enterobacteriaceae* isolates (7,128 organism-drug combinations) were evaluated.
[b] BIOGRAM MIC/reference MIC (see the text).
[c] Overall percent agreement was 96.1% for ratios of 0.5 to 2. When only on-scale results were considered, the percent agreement was 93.0%.

TABLE 6. Ratios of MICs obtained by microdilution and BIOGRAM for nonfermentative gram-negative bacteria[a]

Antimicrobial agent	% Tests with following MIC ratios[b]:					% Agreement[c]
	≤0.25	0.5	1	2	≥4	
Amikacin	9.0	31.3	56.7	3.0	0.0	91.0
Azlocillin	1.5	4.5	87.9	4.5	1.5	96.9
Carbenicillin	0.0	3.0	86.6	9.0	1.5	98.6
Cefoperazone	10.4	41.8	46.3	1.5	0.0	89.6
Cefotaxime	13.4	19.4	61.2	6.0	0.0	86.6
Ceftazidime	0.0	6.0	82.1	11.9	0.0	100.0
Chloramphenicol	0.0	0.0	100.0	0.0	0.0	100.0
Gentamicin	3.0	22.4	74.6	0.0	0.0	97.0
Mezlocillin	3.0	4.5	85.1	4.5	3.0	94.1
Moxalactam	3.0	7.6	89.4	0.0	0.0	97.0
Netilmicin	18.3	43.3	38.3	0.0	0.0	81.6
Piperacillin	4.5	20.9	73.1	1.5	0.0	95.5
Tobramycin	9.0	17.9	71.6	1.5	0.0	91.0
Ticarcillin	1.5	23.9	71.6	1.5	1.5	97.0

[a] A total of 66 nonfermentative gram-negative bacteria (924 drug-organism combinations) were evaluated.
[b] BIOGRAM MIC/reference MIC (see the text).
[c] Overall percent agreement was 94.1% for ratios of 0.5 to 2. When only on-scale results were considered, the percent agreement was 92.3%.

DISCUSSION

All antimicrobial agents which can be tested by the agar disk diffusion method have an established regression line based on MIC and disk diffusion results. There is an inverse relationship between the zone diameter and the corresponding MIC; e.g., as the zone of inhibition increases, the MIC decreases. The point in the zone at which growth inhibition occurs corresponds to the MIC for the test organism. A problem with the newer β-lactam antimicrobial agents is that some portion of the regression line is parabolic (1). In the BIOGRAM data base, only the linear portion of each regression line was used.

The results indicate a high level of correlation between the reference method and BIOGRAM. In some instances, the microdilution test failed to detect oxacillin-resistant *S. aureus* and *S. epidermidis* isolates, although the MIC ratios imply errors by the BIOGRAM system. This can be explained by the lack of sodium chloride supplementation of the MH broth containing oxacillin, methicillin, and nafcillin in the microdilution trays. The only other antimicrobial agents which demonstrated less than 90% correlation between the two methods were nitrofurantoin, tetracycline, and cefamandole. Discrepant results with nitrofurantoin were limited to *S. faecalis*. MICs for the broth microdilution test were usually higher than the BIOGRAM MICs. Tetracycline discrepancies were noted predominately with *E. coli* and *C. freundii*. Again, the trend was toward higher MICs for the broth microdilution method.

In addition to reporting MICs and category interpretative results, BIOGRAM interprets MICs by reporting inhibitory quotients based on achievable antimicrobic agent concentrations in serum, urine, bile, and cerebrospinal fluid. This permits an easier interpretation of MICs because the relative activity of each antimicrobial agent in the aforementioned body compartments can be more readily compared.

A cost factor is also reported for each antimicrobial agent. This factor, ranked A (least costly) to D (most costly), was determined with broad-category national-average patient costs and considered variables such as dosing schedules, administration costs, and cost per gram. This may prove useful in reducing the unnecessary use of more expensive antimicrobial agents when a less expensive one can be substituted.

BIOGRAM MICs calculated at 5 to 6 h of incubation permit an early reporting of MIC results. However, some of the antimicrobial agents evaluated demonstrated a lower correlation with the reference method than readings determined after 18 to 20 h of incubation. Therefore, MICs obtained from early readings should be confirmed after overnight incubation of the MH agar plates.

It has been reported that clerical or reporting mistakes are a common source of error associated with the disk diffusion test (8). The caliper and reporting system of BIOGRAM eliminates this problem and also eliminates the need to refer to the interpretive charts for determining S-I-R and QC results, as these are automatically performed. Although it was not shown in this study, this is a potential time saver.

This evaluation indicates that the BIOGRAM system provides a reliable alternative method for the determination of quantitative antimicrobial susceptibility. It permits laboratories routinely using the disk diffusion test to report quantitative results without time delay or additional expense

TABLE 7. Summary of ratios of MICs obtained by microdilution and BIOGRAM[a]

Antimicrobial agent	% Tests with following MIC ratios[b]:					% Agreement[c]
	≤0.25	0.5	1	2	≥4	
Amikacin	2.6	10.2	77.1	8.3	1.7	95.6
Ampicillin	2.3	8.2	81.3	6.1	2.0	95.6
Amoxacillin-clavulanate	1.3	4.6	82.5	10.0	1.5	97.2
Azlocillin	1.4	4.3	85.5	7.2	1.4	97.1
Carbenicillin	2.5	5.6	86.1	5.5	0.8	96.7
Cefamandole	14.4	14.0	64.0	6.8	0.7	84.9
Cefazolin	2.7	5.5	78.5	11.9	1.4	95.9
Cefoperazone	6.8	14.7	73.9	4.3	0.3	92.9
Cefotaxime	3.3	5.8	87.9	2.7	0.3	96.4
Cefoxitin	3.0	5.4	76.8	14.1	0.7	96.3
Ceftazidime	0.8	1.9	89.0	8.0	0.3	98.9
Cephalothin	2.8	8.0	80.9	6.7	1.5	95.6
Chloramphenicol	1.3	6.3	88.4	3.9	0.0	98.7
Clindamycin	1.1	0.0	98.9	0.0	0.0	98.9
Cinoxacin	0.7	0.7	97.6	1.0	0.0	99.3
Erythromycin	2.0	8.1	87.2	2.7	0.0	98.0
Gentamicin	3.3	9.1	74.3	12.6	0.7	96.1
Sulfisoxazole	0.0	2.6	96.3	1.1	0.0	100.0
Methicillin	2.0	15.7	72.5	7.8	2.0	96.1
Mezlocillin	3.3	8.5	85.1	2.5	0.6	96.1
Trimethoprim	0.5	4.8	94.7	0.0	0.0	99.5
Moxalactam	1.1	2.5	94.2	1.7	0.6	98.3
Nafcillin	0.0	2.0	50.0	30.0	18.0	82.0
Netilmicin	3.1	10.0	83.0	3.6	0.2	96.7
Nitrofurantoin	8.3	21.2	66.1	4.2	0.2	91.5
Oxacillin	1.1	0.0	60.7	23.6	14.6	84.3
Penicillin G	8.0	6.0	82.0	2.0	2.0	90.0
Piperacillin	4.7	13.6	73.4	7.2	1.1	94.2
Tobramycin	2.2	6.9	71.3	17.3	2.2	95.6
Tetracycline	7.9	25.1	66.3	0.7	0.0	92.1
Ticarcillin	1.4	22.9	72.9	1.4	1.4	97.1
Trimethoprim-sulfamethoxazole	0.0	0.3	99.5	0.3	0.0	100.0
Vancomycin	0.7	11.4	87.1	0.0	0.7	98.6

[a] A total of 511 isolates (10,085 organism-drug combinations) were evaluated.
[b] BIOGRAM MIC/reference MIC (see the text).
[c] Overall percent agreement was 95.9% for ratios of 0.5 to 2. When only on-scale results were considered, the percent agreement was 92.4%.

TABLE 8. Ratios of MICs obtained by microdilution and early BIOGRAM readings[a]

Antimicrobial agent	% Tests with following MIC ratios[b]:					% Agreement[c]
	≤0.25	0.5	1	2	≥4	
Amikacin	0.0	1.4	33.9	49.3	15.5	84.5
Ampicillin	1.5	10.8	78.5	7.7	1.5	96.9
Amoxacillin-clavulanate	1.4	2.9	68.1	24.6	2.9	95.7
Carbenicillin	2.9	10.0	68.1	14.5	4.3	92.8
Cefamandole	16.4	4.5	47.8	25.4	6.0	77.6
Cefazolin	14.9	6.0	44.8	22.4	11.9	73.1
Cefoperazone	7.5	6.0	40.3	28.4	17.9	74.6
Cefotaxime	0.0	1.5	52.2	31.3	14.9	85.1
Cefoxitin	1.5	0.0	59.1	25.8	13.6	84.8
Ceftazidime	1.5	0.0	37.9	28.8	31.8	66.7
Cephalothin	7.0	14.1	57.7	21.1	0.0	93.0
Chloramphenicol	1.4	2.8	76.1	19.7	0.0	98.6
Clindamycin	0.0	0.0	100.0	0.0	0.0	100.0
Cinoxacin	0.0	0.0	100.0	0.0	0.0	100.0
Erythromycin	0.0	0.0	100.0	0.0	0.0	100.0
Gentamicin	1.4	0.0	34.8	46.4	17.4	81.2
Sulfisoxazole	0.0	4.9	95.1	0.0	0.0	100.0
Mezlocillin	4.4	4.4	69.1	17.6	4.4	91.2
Trimethoprim	0.0	4.7	95.3	0.0	0.0	100.0
Moxalactam	0.0	1.5	52.3	38.5	7.7	92.3
Netilmicin	0.0	1.5	42.6	50.0	5.9	94.1
Nitrofurantoin	0.0	11.8	83.8	4.4	0.0	100.0
Oxacillin	0.0	0.0	100.0	0.0	0.0	100.0
Piperacillin	4.6	7.7	49.2	23.1	15.4	80.0
Tobramycin	1.5	1.5	33.8	32.3	30.8	67.7
Tetracycline	6.3	27.0	61.9	4.8	0.0	93.7
Trimethoprim-sulfamethoxazole	0.0	0.0	100.0	0.0	0.0	100.0
Vancomycin	0.0	0.0	100.0	0.0	0.0	100.0

[a] Results are based on a total of 68 isolates (1,615 organism-drug combinations). BIOGRAM MICs were calculated at 5 to 6 h of incubation and compared with the reference method results obtained after 18 to 20 h of incubation.

[b] BIOGRAM MIC/reference MIC (see the text).

[c] Overall percent agreement was 88.6% for ratios of 0.5 to 2. When only on-scale results were considered, the percent agreement was 90.3%.

over the initial cost of the BIOGRAM system. Additionally, it offers the advantage of flexibility in antimicrobial agent selection and the reproducibility of the disk diffusion test. As new antimicrobic agents and NCCLS data become available, the system can be easily updated to accommodate them by insertion of a new keyboard overlay code and computer data base chip.

LITERATURE CITED

1. **Barry, A. L., C. Thornsberry, R. E. Badal, C. N. Baker, R. N. Jones, and E. H. Gerlach.** 1979. Piperacillin susceptibility tests by the single-disk agar diffusion technique. Antimicrob. Agents Chemother. **16**:378–385.
2. **Bauer, A. W., M. M. Kirby, J. C. Sherris, and M. Truck.** 1966. Antibiotic susceptibility testing by a standardized single disk method. Am. J. Clin. Pathol. **45**:493–496.
3. **Ellner, P. D., and H. C. Neu.** 1981. The inhibitory quotient. A method for interpreting minimum inhibitory concentration data. J. Am. Med. Assoc. **246**:1575–1578.
4. **Federal Register.** 1972. Rules and regulations: antibiotic susceptibility disks. Fed. Regist. **37**:20525–20529.
5. **Jones, R. N.** 1983. Antimicrobial susceptibility testing: a review of changing trends, quality control guidelines, test accuracy and recommendations for testing of beta-lactam drugs. Diagn. Microbiol. Infect. Dis. **1**:1–24.
6. **Lennette, E. H., A. Balows, W. J. Hausler, Jr., and J. P. Truant (ed.).** 1980. Manual of clinical microbiology, 3rd ed. American Society for Microbiology, Washington, D.C.
7. **Murray, P. R., J. R. Zeitinger, and D. J. Krogstad.** 1982. Reliability of disc diffusion susceptibility testing. Infect. Control **3**:230–237.
8. **National Committee for Clinical Laboratory Standards.** 1984. Performance standards for antimicrobial disk susceptibility test, M2-A3. National Committee for Clinical Laboratory Standards, Villanova, Pa.
9. **National Committee for Clinical Laboratory Standards.** 1983. Methods for dilution antimicrobial susceptibility tests for bacteria that grow aerobically. M7-T. National Committee for Clinical Laboratory Standards, Villanova, Pa.