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Letter to the Editor

Quality Control Parameters for Broth Microdilution Tests of Anidulafungin

Anidulafungin (Vicuron, King of Prussia, Pa.), a new echinocandin, inhibits β-glucan synthesis during fungal cell wall formation and has potential therapeutic use for infections with *Candida* and *Aspergillus* spp. (1). A study was performed to propose quality control (QC) ranges for microdilution susceptibility tests of anidulafungin according to National Committee for Clinical Laboratory Standards (NCCLS) recommendations (2). Eight different laboratories performed replicate testing of serial dilutions of anidulafungin in trays prepared by a central facility from three different lots of RPMI 1640 broth provided from three different manufacturers (Sigma, Mediatech, and Irvine Scientific). Drug concentrations ranged from 0.008 to 32 μg/ml. Fluconazole, the control drug, was diluted in one lot of RPMI 1640 over a range of 0.06 to 128 μg/ml. On separate days of testing, each of the three QC strains *Candida parapsilosis* ATCC 22019, *Candida krusei* ATCC 6258, and *Candida albicans* ATCC 90028 was inoculated into MIC trays. *C. albicans* ATCC 90028 data are not shown, since the MICs were too variable for QC purposes. The MIC trays were incubated at 35°C in ambient air and read visually at 24 h and again at 48 h. Results were interpreted at both 50 and 100% inhibition of growth compared to the growth control (2).

The distribution of MIC results is represented in Table 1. Results with modal MICs four- to eightfold higher than all other modal results at a 100% endpoint were considered reading errors and were excluded from analysis. No major differences in overall results occurred among the three lots of RPMI 1640. Fluconazole MICs were within the established QC ranges recommended by the NCCLS for 95% of the values observed with *C. parapsilosis* and 100% of the values observed with *C. krusei.* During the study, laboratories also verified inoculum concentrations. The median colony counts were 1.5×10^3 cells/ml (range, 2.0×10^2 to 2.2×10^4 cells/ml) for *C. parapsilosis* ATCC and 1×10^3 cells/ml (range, 1.0×10^1 to 4.2×10^3 cells/ml) for *C. krusei* ATCC 6258. Variation in inoculum concentration appeared to have no effect on the MIC results.

The most appropriate endpoint for defining microdilution MICs of anidulafungin has not yet been determined. For QC purposes, the MICs based on a 50% inhibition of growth were more reproducible. Use of an endpoint involving complete inhibition resulted in greater differences between laboratories, presumably because pinpoint growth was not interpreted correctly. That was not a problem when the MIC was defined as 50% inhibition of growth compared to that in the growth control well. Until supportive clinical data are available for selecting the endpoint criteria, we propose MIC ranges for both categories of MIC endpoints.

TABLE 1. Proposed anidulafungin MIC ranges for two QC strains when MICs were read as 50 or 100% inhibition of growth

Control strain	Incubation time (h)	Proposed MIC range in μg/ml (% of MICs included)	
		50% inhibition	100% inhibition
C. parapsilosis ATCC 22019	24	0.25–2.0 (95.0)	1.0–4.0 (97.6)[a]
	48	0.5–2.0 (95.0)	1.0–8.0 (97.5)
C. krusei ATCC 6258	24	0.03–0.12 (97.9)	0.06–0.25 (96.2)[b]
	48	0.03–0.12 (97.5)	0.06–0.5 (99.2)[c]

[a] Excludes data from laboratory 3 (9 of 30 MICs were 0.016 to 0.12 μg/ml).
[b] Excludes data from laboratory 5 (29 of 30 MICs were 0.5 to 2.0 μg/ml).
[c] Excludes data from laboratory 5 (17 of 30 MICs were 1.0 or 2.0 μg/ml).

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