

MAY 10 1998

DADE BEHRING

DADE MICROSCAN INC.
 1584 Enterprise Boulevard
 West Sacramento, CA 95691
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510(k) Summary

510(k) Submission Information:

Device Manufacturer: Dade MicroScan Inc.
 Contact name: Sharolyn Lentsch, Regulatory Affairs Manager
 Fax: 916-374-3144
 Date prepared: September 25, 1998
 Product Name: Microdilution Minimum Inhibitory Concentration (MIC) Panels
 Trade Name: MicroScan[®] Dried Gram-Negative and Gram-Positive MIC/Combo Panels
 Intended Use: To determine antimicrobial agent susceptibility
 510(k) Notification: New antimicrobial - Trovafloxacin
 Predicate device: NCCLS Frozen Trovafloxacin Reference Panels

510(k) Summary:

The proposed MicroScan[®] Dried Gram-Negative and Gram-Positive MIC/Combo Panel with Trovafloxacin demonstrated substantially equivalent performance when compared with an NCCLS frozen Trovafloxacin Reference Panel, as defined in the FDA DRAFT document "Review Criteria for Assessment of Antimicrobial Susceptibility Devices" (dated May 31, 1991).

The Premarket Notification (510[k]) presents data in support of the new antimicrobial, Trovafloxacin, for the MicroScan[®] Dried Gram Negative and Gram Positive MIC/Combo Panels.

Both the gram-negative and gram-positive external evaluations were conducted with fresh and stock Efficacy isolates and stock Challenge strains. The external evaluations were designed to confirm the acceptability of the proposed Dried Trovafloxacin panels by comparing their performance with an NCCLS frozen Trovafloxacin Reference panel.

The Dried gram-negative Trovafloxacin panel demonstrated acceptable performance with an overall Essential Agreement of 99.7% when compared with the frozen Trovafloxacin Reference panel. The Dried gram-positive Trovafloxacin panel demonstrated acceptable performance with an overall Essential Agreement of 98.7% when compared with the frozen Trovafloxacin Reference panel.

Inoculum and instrument reproducibility testing was conducted: both the gram-negative and the gram-positive Dried Trovafloxacin panels demonstrated acceptable reproducibility and precision, regardless of which inoculum method (i.e., Turbidity and Prompt), or instrument (autoScan-4[®] and WalkAway[®]) was used.

Quality Control performance was acceptable for both the gram-negative and the gram-positive Dried Trovafloxacin panels.

Section 1. SUMMARY OF CLINICAL STUDIES

Purpose/Scope

The purpose of the clinical studies was to demonstrate that MicroScan[®] Dried Gram-Negative and Gram-Positive MIC/Combo panels with Trovafloxacin (Test panels) are substantially equivalent to frozen NCCLS reference panels (Reference panels). Device performance was evaluated in a clinical trial that included gram-negative and gram-positive isolates. The study is summarized in this Premarket Notification. The clinical trial panels also included 2 other gram-negative antibiotics and 3 other gram-positive antibiotics. Only the Trovafloxacin data are included in this Premarket Notification submission.

Trovafloxacin - Indications & Usage, Microbiology, and Mechanisms of Resistance

In general, Trovafloxacin is a new fluoronaphthyridone related to the fluoroquinolones. The bactericidal action of Trovafloxacin results from inhibition of DNA gyrase and topoisomerase IV. DNA gyrase is an essential enzyme that is involved in the replication, transcription and repair of bacterial DNA. Topoisomerase IV is an enzyme known to play a key role in the partitioning of the chromosomal DNA during bacterial cell division. The mechanism of action of fluoroquinolones including Trovafloxacin is different from that of penicillins, cephalosporins, aminoglycosides, macrolides, and tetracyclines. Therefore, fluoroquinolones may be active against pathogens that are resistant to these antibiotics. Resistance to Trovafloxacin *in vitro* develops slowly via multiple-step mutation in a manner similar to other fluoroquinolones. Although cross-resistance has been observed between Trovafloxacin and some other fluoroquinolones, some microorganisms resistant to other fluoroquinolones may be susceptible to Trovafloxacin.¹

Trovafloxacin is indicated for treatment of pneumonia, bronchitis, acute sinusitis, various internal and skin infections, prostatitis, urethral gonorrhea, cervicitis, and pelvic inflammatory disease, when caused by susceptible strains.

Figure 1 presents the aerobic and facultatively anaerobic gram-negative and gram-positive genera listed under the **Indications and Usage** section for the antimicrobial Trovafloxacin (as taken from the Pfizer Trovan product insert, issued: December 1997). Also highlighted in the table are the bacteria listed under the **Microbiology** section of the same product insert.

¹ Pfizer Trovan[™] (Trovafloxacin) Package Insert. Issued December 1997.

Figure 1
Trovafloxacin Intended Use Isolates²

Gram-Negatives	
Indications and Usage Isolates	Microbiology Isolates
<i>Escherichia coli</i>	<i>Citrobacter freundii</i>
<i>Klebsiella pneumoniae</i>	<i>Enterobacter aerogenes</i>
<i>Proteus mirabilis</i>	<i>Morganella morganii</i>
<i>Pseudomonas aeruginosa</i>	<i>Proteus vulgaris</i>

Gram-Positives	
Indications and Usage Isolates	Microbiology Isolates
<i>Enterococcus faecalis</i>	<i>Streptococcus pneumoniae</i> (penicillin resistant)
<i>Staphylococcus aureus</i> (Methicillin-susceptible)	
<i>Staphylococcus epidermidis</i> (Methicillin-susceptible)	
<i>Streptococcus agalactiae</i> (Gp B)	
<i>Streptococcus pyogenes</i> (Gp A)	
<i>Streptococcus pneumoniae</i> (penicillin susceptible)	
Viridans group streptococci	

Clinical Investigations

A copy of the Clinical Trial protocol is provided in **Section 2.:Clinical Trial Protocol**. The Clinical Trial protocol called for an Efficacy phase (stock and fresh isolates), a CDC Challenge (CDC challenge strains), and Reproducibility (inoculum and instrument). The Reproducibility isolates are provided in **Section 2.: Inoculum and Instrument Reproducibility Amendment**. Throughout each phase Quality Control isolates were also tested. Performance was evaluated by comparing both proposed devices (gram-negative and gram-positive) with frozen NCCLS reference panels and clinical isolates with a broad range of susceptibilities for the 3 gram-negative antibiotics and 4 gram-positive antibiotics on the clinical trial panel. The type and number of isolates tested was in compliance with the FDA guidance "Review Criteria for Assessment of Antimicrobial Susceptibility Devices: Draft May 1991".

After completion of the gram-negative clinical trial, a decision was made to map the dilution range from 0.002 - 8 mcg/ml to 0.03 - 8 mcg/ml due to variable performance with the low end dilutions. Similarly, a decision was made to map several gram-positive dilutions due to variable performance; the 0.002 - 8 mcg/ml range was mapped up to 0.06 - 8 mcg/ml.

² Pfizer Trovan™ (Trovafloxacin) Package Insert. Issued December 1997.

The clinical study was conducted between June and September 1998. A description of each clinical site and their role in the testing is presented in the clinical trial protocol, **Section 2.**

The MicroScan[®] Dried Gram-Negative and Gram-Positive Panels (Test panels) contained doubling dilutions of Trovafloxacin from 0.002 to 8 mcg/ml. Data are presented on the gram-negative panel for the 9 dilutions (i.e., 0.03 - 8 mcg/ml), and on the gram-positive panel for the 8 dilutions (i.e., 0.06 - 8 mcg/ml) for which approval is requested.

The manufacturing process for both Test panels called for Trovafloxacin dehydrated in Mueller-Hinton broth. During testing each well was inoculated/rehydrated with the organisms suspended in distilled water with Pluronic^{®*}. Test panels were read visually after 16-20 hours of incubation at 35° C in a non-CO₂ incubator.

Reference panels were made according to NCCLS recommendations found in NCCLS Document M7-A4 (*Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically*, fourth edition; Approved Standard. Pennsylvania, NCCLS, 1997), using cation adjusted Mueller-Hinton broth. The Reference panels were read visually after 16-20 hours of incubation at 35° C in a non-CO₂ incubator (see **Section 2.: Clinical Trial Protocol**, for the specific read times).

Each MIC was determined by comparing growth results in antibiotic wells with the growth patterns expressed in the 2 control wells (identified as the "Growth well" and the "Control well"). Initial data analysis was performed by comparing the initial Test MIC results with the initial Reference MIC results. As indicated in the Clinical Trial protocol, isolates that exhibited a ≥ 2 dilution error (discrepancy) between the Test and the Reference panel were repeated in triplicate. Final data analysis was performed by comparing the initial Test results to the repeat Reference results. Discrepancies were considered resolved when the repeat Reference result was in Essential Agreement with the initial Test result. An additional data analysis was also performed using repeat results from both the Reference and the Test panels. The Initial, Final, and Additional Data Analyses summaries are presented separately and are identified accordingly.

Both Clinical Trials consisted of 3 different test phases; Efficacy, CDC Challenge, and Reproducibility. Quality Control was performed daily. Data from the Efficacy and CDC Challenge phases were evaluated using the same Error and Agreement definitions.

*BASF, Parsippany, NJ.



MAY 10 1999

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

Sharolyn J. Lentsch
Regulatory Affairs Manager
Dade Microscan, Inc.
1584 Enterprise Boulevard
West Sacramento, CA 95691

Re: K983408
Trade Name: Dried Gram-Negative and Gram-Positive MIC/Combo
Panels/Trovafloxacin
Product Code: JWY
Dated: March 31, 1999
Received: April 1, 1999

Dear Ms. Lentsch:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (Premarket Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially equivalent determination assumes compliance with the Current Good Manufacturing Practice requirements, as set forth in the Quality System Regulation (QS) for Medical Devices: General regulation (21 CFR Part 820) and that, through periodic QS inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal laws or regulations.

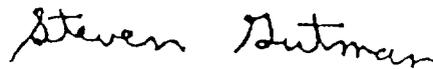
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Under the Clinical Laboratory Improvement Amendments of 1988 (CLIA-88), this device may require a CLIA complexity categorization. To determine if it does, you should contact the Centers for Disease Control and Prevention (CDC) at (770)488-7655.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4588. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at its toll free number (800) 638-2041 or at (301) 443-6597 or at its internet address "<http://www.fda.gov/cdrh/dsmamain.html>"

Sincerely yours,

A handwritten signature in black ink that reads "Steven Gutman". The signature is written in a cursive style with a large, prominent "S" and "G".

Steven I. Gutman, M.D., M.B.A.
Director
Division of Clinical Laboratory Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure

Intended Use Statement

510(k) No.: K 983408

Device Name: MicroScan[®] Dried Gram-Negative and Gram-Positive MIC/Combo Panels with Trovafloxacin (0.03 - 8 mcg/ml on the gram-negative panels and 0.06 - 8mcg/ml on the gram-positive panels)

Indications for Use: To determine gram-negative and gram-positive bacterial susceptibility against the antimicrobial agent Trovafloxacin.

Organisms with indications for testing* include:

<u>Gram-Negative Bacteria</u>	<u>Gram-Positive Bacteria</u>
<i>Escherichia coli</i>	Methicillin susceptible
<i>Klebsiella pneumoniae</i>	<i>Staphylococcus aureus</i>
<i>Proteus mirabilis</i>	Methicillin susceptible
<i>Pseudomonas aeruginosa</i>	<i>Staphylococcus epidermidis</i>
	<i>Enterococcus faecalis</i>
	<i>Streptococcus agalactiae</i> (Gp.B)
	<i>Streptococcus pyogenes</i> (Gp.A)

* As taken from the Indications and Usage section of the manufacturer's package insert (Issued: December 1997).

The MicroScan[®] Dried Gram-Negative and Gram-Positive MIC/Combo Panels with Trovafloxacin are not intended for use with *Streptococcus pneumoniae* and viridans streptococci.

 Woody Dubois
(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K 983408

Prescription Use X OR Over-The Counter Use
(Per 21 CFR 801.109)

(Optional Format 1-2-96)