Antimicrobial Activity of LBM415 (NVP PDF-713) Against a Recent (2003) International Collection of Gram-Positive and Respiratory Tract Pathogens

1552
ECCMID 2005

AA WATTERS, RN JONES, MG STILWELL, TR FRITSCHE
JMI Laboratories, North Liberty, IA, USA

JMI Laboratories
North Liberty, IA, USA
www.jmilabs.com
319.665.3370, fax 319.665.3371
ronald-jones@jmilabs.com

AMENDED ABSTRACT

Objective: To evaluate the spectrum and potency of LBM415 (LBM; formerly NVP PDF-713) when tested against an international collection of common bacterial pathogens comprising the 2003 LBM surveillance program. LBM is the first member of the peptide deformylase inhibitor (PDI) class being considered for clinical trials for treatment of community-acquired respiratory tract infections and serious infections caused by antimicrobial-resistant Gram-positive cocci.
Methods: Non-duplicate, clinically-significant bacterial isolates (10,903 strains) were collected from more than 70 medical centers participating in the global surveillance program, and originated from North America, Europe, and South America geographic areas. All isolates were susceptibility (S) tested using NCCLS broth microdilution methods and interpretive criteria, where applicable. LBM was compared with representative agents used in the empiric or directed therapy of the targeted indications or species.
Results: The antimicrobial activity of LBM is shown in the table:

Organisms (no. tested)	MIC (mg/L)		Cum. % of strains inhibited at MIC (mg/L)			
	50%	90%	≤1	2	4	8
S. aureus (SA; 3,955)	0.5	1	99	99	100	-
Coag-neg staphylococci (CoNS; 1,485)	0.5	1	95	99	100	-
S. pneumoniae (SPN; 736)	1	2	76	93	100	-
Viridans group streptococci (134)	0.25	1	99	100	-	-
Beta-haemolytic streptococci (356)	0.5	1	96	100	-	-
Enterococci (ENT; 2,062)	2	4	48	87	99	100
E. faecalis (1,432)	2	4	37	83	99	100
E. faecium (553)	1	2	70	96	100	-
H. influenzae (HI; 1,855)	2	4	49	78	93	99
M. catarrhalis (MCAT; 108)	0.25	0.5	99	100	-	-

Antibiogram characteristics of the collection include: 28% oxacillin-resistant (OR) SA, 76% OR CoNS, 34% penicillin-non-susceptible SPN, 22% vancomycin-R ENT, and 21% ampicillin-R HI. LBM was highly active against staphylococci, streptococci, enterococci and MCAT, resulting in ≥ 99% inhibition at ≤ 4 mg/L, the results in 93% inhibition of HI strains at the same concentration. No differences were noted in the activity of LBM between S and R subsets of SA, CoNS, SPN, ENT and HI for antimicrobials such as oxacillin, penicillin, ampicillin, macrolides, vancomycin and fluoroquinolones. While regional differences were apparent with some comparator agents, activity of LBM did not vary between geographic samples.
Conclusions: LBM displays a broad-spectrum of activity against the common Gram-positive pathogens, including R subsets, with no regional differences in potency. Some fastidious Gram-negative species (HI, MCAT) were also inhibited by LBM. As a class of antimicrobials, the PDI compounds exhibit a spectrum of activity and unique mode of action that promises to be a significant advance in chemotherapy.

INTRODUCTION

The emergence of resistance to currently marketed antimicrobial agents has become a significant medical management crisis, responsible for increased morbidity, mortality and health-care costs in both inpatient and outpatient settings. The limited number of antimicrobial classes and the common occurrence of cross resistance within and between classes creates an urgent need to identify new classes of compounds with which to manage infections refractory to treatment with existing agents.

Peptide deformylase (PDF), a highly conserved metalloprotease, has been observed to be critical to the maturation of proteins during translation in prokaryotic cells. The PDF enzyme can also be present in eukaryotic cells, specifically within mitochondria. However, it remains much less active than in bacteria, thus making it an attractive target for antibacterial agents.

Inhibitors of PDF have been described in recent years with the naturally occurring antibacterial agent actinonin being a typical example. LBM415 (also known as NVP PDF-713) is one of the first PDF inhibitors to advance to clinical trials for the oral and parenteral treatment of respiratory tract and skin and skin structure infections caused by susceptible gram-positive and -negative organisms. Recent studies have described QC guidelines for both disk and broth microdilution methods for use in clinical trial testing. Spectrum of activity evaluations of the targeted species, including resistant subsets, have demonstrated a potential role for LBM415 in the treatment of the indicated infections.

In this report we summarize the results of testing LBM415 and selected comparator agents against a world-wide collection of contemporary (2003) clinical isolates. This collection of 10,903 isolates was tested by standardized reference methodologies (broth microdilution) and categorical interpretations made using current National Committee for Clinical Laboratory Standards (NCCLS) criteria.

MATERIALS AND METHODS

Bacterial strains. The organisms (10,903 strains) included: 5,440 staphylococci (2,252 oxacillin-resistant), 736 *Streptococcus pneumoniae* (486, 116 and 134 penicillin-susceptible, -intermediate and -resistant, respectively), 356 ß-haemolytic streptococci, 134 viridans group *Streptococcus* spp., 1,514 vancomycin-susceptible enterococci, 455 vancomycin-resistant enterococci, 1,836 *Haemophilus influenzae* (390 ampicillin-resistant), 108 *Moraxella catarrhalis*, 21 *Burkholderia cepacia*, 130 *Stenotrophomonas maltophilia* and 61 other gram-positive isolates (see Table 1 for details). All isolates were non-duplicate consecutive clinical isolates submitted from numerous medical centers located in the Americas and Europe that contributed to various surveillance programs for the year 2003. Identifications were performed by the submitting laboratories and confirmed using standard biochemical algorithms, including use of the Vitek System (bioMerieux, Missouri, USA).

Antimicrobial agents and susceptibility testing. Compound LBM415 was obtained from Novartis Pharmaceuticals (NJ, USA). All strains were tested by the broth microdilution method [NCCLS, 2003] in cation-adjusted Mueller-Hinton broth (with 2 - 5% lysed horse blood added for testing of streptococci and Haemophilus Test Medium (HTM) for testing of *H. influenzae*) against a variety of antimicrobial agents representing the most common classes and examples of drugs used in the empiric or directed treatment of the indicated pathogen. Dry-form microdilution panels and broth reagents were purchased from TREK Diagnostics (Ohio, USA). Interpretation of quantitative MIC results was in accordance with NCCLS [2004] criteria.

RESULTS

- Among the most common bacterial agents of community-acquired pneumonia and skin and skin structure infections, ≥ 99% of staphylococci, streptococci, enterococci, and *M. catarrhalis* were inhibited at 4 mg/L or less of LBM415, as were 93% of *H. influenzae* strains (Table 1).
- All LBM415 MIC values were ≤ 4 mg/L for *S. aureus* and coagulase-negative staphylococci with MIC_{50} and MIC_{90} values of 0.5 and 1 mg/L for both oxacillin-susceptible and oxacillin-resistant strains (Table 2).
- Among all *S. pneumoniae* strains tested, regardless of penicillin susceptibility patterns, LBM415 was uniformly active with MIC_{50} values of 0.5 to 1 mg/L and MIC_{90} values of 1 to 2 mg/L (range from ≤ 0.016 to 4 mg/L).
- LBM415 was also uniformly active against beta-haemolytic and viridans-group streptococci with MIC_{90} results of 0.5 and 0.25 mg/L, respectively, and an MIC_{90} of 1 mg/L.
- No difference was noted in the activity of LBM415 against vancomycin-susceptible or resistant enterococci, with MIC_{50} and MIC_{90} results for *E. faecalis* being 2 and 4 mg/L, respectively, and for *E. faecium*, 1 and 2 mg/L.
- LBM415 displayed a broader range (≤ 0.06 to 8 mg/L) of activity against a collection of other Gram-positives including species of *Aerococcus, Bacillus, Corynebacteria, Kocuria*, *Leuconostoc, Listeria, Micrococcus* and *Rothia* species, although the group MIC_{50} and MIC_{90} (0.12 and 2 mg/L, respectively) remained within achievable concentrations.
- LBM415 displayed activity against both *H. influenzae* and *M. catarrhalis* (Table 3), although the MIC_{50} and MIC_{90} of both ampicillin-susceptible and ampicillin-resistant *H. influenzae* (1 and 4 mg/L, and 2 and 8 mg/L, respectively) are 8 to 16-fold higher than those for *M. catarrhalis* (0.25 and 0.5 mg/L, respectively).
- While LBM415 does demonstrate modest activity against *B. cepacia* and *S. maltophilia*, such activity is not consistent with readily achievable concentrations.
- Regional antibiogram differences were apparent with some species. However, activity of LBM415 against targeted species did not vary between geographic samples.

TABLE 1. Summary of antimicrobial activity at individual MIC values of LBM415 tested against 13 organism groups including 10,903 isolates (all regions).

Organisms (no. tested)	Cumulative % inhibited at MIC (mg/L):							
	≤0.25	0.5	1	2	4	8	16	32
Gram-positive								
S. aureus (3,955)	28	78	99	99	100	-	-	-
Coagulase-negative staphylococci (1,485)[a]	42	69	95	99	100	-	-	-
S. pneumoniae (736)	19	47	76	93	100	-	-	-
viridans group streptococci (134)	73	90	99	100	-	-	-	-
ß-haemolytic streptococci (356)	41	64	96	100	-	-	-	-
Enterococci (2,062)[b]	6	17	48	87	99	100	-	-
E. faecalis (1,432)	2	9	37	83	99	100	-	-
E. faecium (553)	13	34	70	96	100	-	-	-
Other Gram-positive species (61)[c]	64	74	85	97	98	100	-	-
Gram-negative								
H. influenzae (1,855)	3	17	50	78	93	99	99	100
M. catarrhalis (108)	63	97	99	100	-	-	-	-
B. cepacia (21)	5	5	5	10	24	76	81	91
S. maltophilia (130)	0	1	2	13	51	84	95	99

a. Includes *S. auricularis* (seven strains), *S. capitis* (22 strains), CoNS (632 strains), *S. cohnii* (one strain), *S. epidermidis* (577 strains), *S. haemolyticus* (80 strains), *S. hominis* (55 strains), *S. intermedius* (four strains), *S. lugdunensis* (10 strains), *S. saprophyticus* (32 strains), *S. schleiferi* (one strain), *S. sciuri* (one strain), *S. simulans* (15 strains), *Staphylococcus* spp. (five strains), *S. warneri* (25 strains) and *S. xylosis* (18 strains).
b. Includes *E. avium* (seven strains), *E. casseliflavus* (10 strains), *E. durans* (10 strains), *E. faecalis* (1,432 strains), *E. faecium* (553 strains), *E. gallinarum* (26 strains), *E. hirae* (four strains), *E. mundtii* (two strains), *Streptococcus group D* (one strain) and *Enterococcus* spp. (17 strains).
c. Isolates include *Aerococcus* spp. (three strains), *Bacillus* spp. (13 strains), *Corynebacterium* spp. (13 strains), *Kocuria* spp. (one strain), *Leuconostoc* spp. (one strain), *Listeria* spp. (14 strains), *Micrococcus* spp. (15 strains) and *Rothia* spp. (one strain).

TABLE 2. Comparative activity screen of LBM415, a deformylase inhibitor, and selected comparison classes of antimicrobial agents tested against staphylococci (5,440 strains), streptococci (1,226 strains) and enterococci (1,969 strains; all regions).

Antimicrobial agent (no. tested)	MIC (mg/L)			% susceptible[a]	% resistant[a]
	50%	90%	Range		
S. aureus					
oxacillin-susceptible (2,834)					
LBM415	0.5	1	≤0.016-4	[b]	[b]
Erythromycin	0.25	>8	≤0.06->8	79.6	19.3
Clindamycin	0.12	0.12	≤0.06->8	95.2	4.3
Doxycycline	≤0.5	≤0.5	≤0.5->4	98.5	1.5
Gentamicin	≤2	≤2	≤2->8	96.4	2.3
Levofloxacin	0.12	0.5	≤0.03->4	93.7	4.5
Linezolid	2	2	0.12-8	≥99.9	≤0.1
Quinupristin/Dalfopristin	≤0.25	0.5	≤0.25->2	99.9	≤0.1
Vancomycin	1	1	≤0.12-4	100.0	0.0
oxacillin-resistant (1,121)					
LBM415	0.5	1	0.03-4	[b]	[b]
Erythromycin	>8	>8	0.12->8	12.8	86.7
Clindamycin	>8	>8	≤0.06->8	35.6	64.0
Doxycycline	≤0.5	4	≤0.5->4	90.0	10.0
Gentamicin	≤2	>8	≤2->8	65.3	32.6
Levofloxacin	>4	>4	0.06->4	12.1	60.8
Linezolid	2	2	0.25-2	100.0	0.0
Quinupristin/Dalfopristin	0.5	1	≤0.25->2	99.6	0.2
Vancomycin	1	1	0.25-4	100.0	0.0
Coagulase-neg. staphylococci					
oxacillin-susceptible (354)					
LBM415	0.5	1	≤0.016-4	[b]	[b]
Erythromycin	0.25	>8	≤0.06->8	70.6	29.4
Clindamycin	≤0.06	0.12	≤0.06->8	93.8	5.6
Doxycycline	≤0.5	2	≤0.5->4	99.1	0.9
Gentamicin	≤2	≤2	≤2->8	94.4	4.0
Levofloxacin	0.25	2	0.06->4	91.5	4.8
Linezolid	1	1	0.25-2	100.0	[b]
Quinupristin/Dalfopristin	≤0.25	≤0.25	≤0.25-0.5	100.0	0.0
Vancomycin	1	2	0.25-4	100.0	0.0
oxacillin-resistant (1,131)					
LBM415	0.5	1	≤0.016-4	[b]	[b]
Erythromycin	>8	>8	≤0.06->8	28.5	71.3
Clindamycin	0.12	>8	≤0.06->8	57.9	41.6
Doxycycline	1	4	≤0.5->4	90.6	9.4
Gentamicin	8	>8	≤2->8	49.9	36.4
Levofloxacin	4	>4	≤0.03->4	44.9	37.3
Linezolid	1	1	0.25-2	100.0	[b]
Quinupristin/Dalfopristin	≤0.25	0.5	≤0.25->2	99.5	0.4
Vancomycin	1	2	≤0.12-4	100.0	0.0
S. pneumoniae					
penicillin-susceptible (486)					
LBM415	1	2	≤0.016-4	[b]	[b]
Ceftriaxone	0.03	0.25	≤0.008-2	99.6	0.0
Erythromycin	≤0.25	2	≤0.25->8	87.0	12.2
Clindamycin	≤0.25	≤0.25	≤0.25->2	94.8	4.8
Quinupristin/Dalfopristin	≤0.5	≤0.5	≤0.5-2	99.8	0.0
Levofloxacin	1	2	0.06->4	99.8	0.2
Chloramphenicol	≤2	4	≤2->16	98.1	1.9
Rifampin	≤0.5	≤0.5	≤0.5->2	99.8	0.2
Vancomycin	0.25	0.5	≤0.12-1	100.0	0.0
penicillin-intermediate (116)					
LBM415	0.5	1	0.06-4	[b]	[b]
Ceftriaxone	0.25	0.5	≤0.008-1	100.0	0.0
Erythromycin	≤0.25	>8	≤0.25->8	54.3	44.8
Clindamycin	≤0.25	>2	≤0.25->2	79.8	20.2
Quinupristin/Dalfopristin	≤0.5	≤0.5	≤0.5-1	100.0	0.0
Levofloxacin	1	2	0.12-2	100.0	0.0
Chloramphenicol	≤2	4	≤2-16	96.5	3.5
Rifampin	≤0.5	≤0.5	≤0.5-1	100.0	0.0
Vancomycin	0.25	0.5	0.12-1	100.0	0.0
penicillin-resistant (134)					
LBM415	0.5	2	0.06-4	[b]	[b]
Ceftriaxone	1	2	≤0.008-8	87.3	6.0
Erythromycin	4	>8	≤0.06->8	39.8	60.2
Clindamycin	≤0.25	>2	≤0.25->2	58.6	41.4
Quinupristin/Dalfopristin	≤0.5	≤0.5	≤0.5-1	100.0	0.0
Levofloxacin	1	2	0.5-2	100.0	0.0
Chloramphenicol	4	8	≤2->16	88.8	11.2
Rifampin	≤0.5	≤0.5	≤0.5-1	100.0	0.0
Vancomycin	0.25	0.5	0.25-1	100.0	0.0

Antimicrobial agent (no. tested)	MIC (mg/L)			% susceptible[a]	% resistant[a]
	50%	90%	Range		
ß-haemolytic streptococci (356)					
LBM415	0.5	1	≤0.016-2	[b]	[b]
Penicillin	≤0.016	0.06	≤0.016-0.12	100.0	[b]
Ceftriaxone	≤0.25	≤0.25	≤0.25-16	99.4	[b]
Erythromycin	≤0.06	2	≤0.06->8	85.1	14.9
Clindamycin	≤0.06	≤0.06	≤0.06->8	94.7	5.1
Quinupristin/Dalfopristin	≤0.25	0.5	≤0.25-0.5	100.0	0.0
Linezolid	1	1	≤0.06-2	100.0	[b]
Levofloxacin	0.5	1	0.06-2	100.0	0.0
Vancomycin	0.25	0.5	≤0.12-1	100.0	[b]
viridans group streptococci (134)					
LBM415	0.25	1	≤0.016-2	[b]	[b]
Penicillin	0.06	2	≤0.016-32	67.9	7.5
Ceftriaxone	≤0.25	1	≤0.25-8	91.0	3.7
Erythromycin	≤0.06	4	≤0.06->8	58.2	36.6
Clindamycin	≤0.06	0.25	≤0.06->8	90.3	8.2
Quinupristin/Dalfopristin	0.5	1	≤0.25-1	100.0	0.0
Linezolid	1	1	≤0.06-2	100.0	[b]
Levofloxacin	1	2	0.06-2	100.0	0.0
Vancomycin	0.5	1	≤0.12-1	100.0	[b]
Enterococcus faecalis					
vancomycin-susceptible (1,324)					
LBM415	2	4	≤0.016-8	[b]	[b]
Ampicillin	2	2	≤1->16	99.2	0.8
Chloramphenicol	8	>16	≤2->16	79.2	19.3
Levofloxacin	1	>4	0.25->4	63.7	35.3
Gentamicin (high-level)	≤500	>1000	≤500->1000	70.5	29.5
Streptomycin (high-level)	<1000	>2000	≤1000->2000	68.8	31.2
Quinupristin/Dalfopristin	>2	>2	≤0.25->2	1.3	93.1
Linezolid	2	2	0.25-4	99.9	0.0
Teicoplanin	≤2	≤2	≤2-8	100.0	0.0
vancomycin-resistant (97)					
LBM415	2	4	0.25-4	[b]	[b]
Ampicillin	2	4	≤1->16	96.9	3.1
Chloramphenicol	8	>16	4->16	73.2	25.8
Levofloxacin	>4	>4	0.5->4	3.1	96.9
Gentamicin (high-level)	1000	>1000	≤500->1000	30.9	69.1
Streptomycin (high-level)	>2000	>2000	≤1000->2000	28.9	71.1
Quinupristin/Dalfopristin	>2	>2	≤0.25->2	2.1	97.9
Linezolid	1	2	1->8	99.0	1.0
Teicoplanin	>16	>16	≤2->16	40.2	56.7
Enterococcus faecium					
vancomycin-susceptible (190)					
LBM415	1	2	0.12-4	[b]	[b]
Ampicillin	>16	>16	≤1->16	20.5	79.5
Chloramphenicol	8	16	≤2->16	78.4	5.8
Levofloxacin	>4	>4	0.5->4	18.9	70.5
Gentamicin (high-level)	≤500	>1000	≤500->1000	73.2	26.8
Streptomycin (high-level)	<1000	>2000	≤1000->2000	51.1	48.9
Quinupristin/Dalfopristin	1	2	≤0.25->2	81.6	6.3
Linezolid	2	2	0.5->8	98.9	1.1
Teicoplanin	≤2	≤2	≤2	100.0	0.0
vancomycin-resistant (358)					
LBM415	1	2	0.12-4	[b]	[b]
Ampicillin	>16	>16	≤1->16	1.4	98.6
Chloramphenicol	8	8	≤2->16	95.0	2.5
Levofloxacin	>4	>4	1->4	1.4	97.8
Gentamicin (high-level)	≤500	>1000	≤500->1000	53.4	46.6
Streptomycin (high-level)	>2000	>2000	≤1000->2000	25.4	74.6
Quinupristin/Dalfopristin	1	1	≤0.25->2	95.3	2.0
Linezolid	2	2	1-8	99.2	0.6
Teicoplanin	>16	>16	≤2->16	7.5	83.0
Other Gram-pos. species (61)[c]					
LBM415	0.12	2	≤0.06-8	[b]	[b]

a. Susceptibility criteria of the NCCLS [2004].
b. No criteria have been established.
c. Isolates include *Aerococcus* spp. (three strains), *Bacillus* spp. (13 strains), *Corynebacterium* spp. (13 strains), *Kocuria* spp. (one strain), *Leuconostoc* spp. (one strain), *Listeria* spp. (14 strains), *Micrococcus* spp. (15 strains) and *Rothia* spp. (one strain).

Table 3. Comparative antimicrobial activity screen of LBM415, a deformylase inhibitor, tested against *H. influenzae* (1,836 strains) and *M. catarrhalis* (108 strains; all regions).

Antimicrobial agent (no. tested)	MIC (mg/L)			% susceptible[a]	% resistant[a]
	50%	90%	Range		
H. influenzae					
ampicillin-susceptible (1,446)					
LBM415	1	4	0.03-32	[b]	[b]
Amoxicillin/Clavulanate	0.5	1	≤0.06-4	100.0	0.0
Ceftriaxone	≤0.008	0.016	≤0.008-1	100.0	[b]
Chloramphenicol	≤2	≤2	≤2-16	99.4	0.3
Rifampin	≤0.5	≤0.5	≤0.5->2	99.3	0.6
Levofloxacin	≤0.03	≤0.03	≤0.03-0.12	100.0	[b]
Azithromycin	1	2	≤0.5->16	99.8	[b]
Clarithromycin	8	16	≤0.25->32	86.7	1.1
Quinupristin/Dalfopristin	4	8	≤0.5->8	[b]	[b]
ampicillin-resistant (390)					
LBM415	2	8	≤0.016-16	[b]	[b]
Amoxicillin/Clavulanate	1	2	0.12->8	99.7	0.3
Ceftriaxone	≤0.008	≤0.008	≤0.008-2	100.0	[b]
Chloramphenicol	≤2	≤2	≤2-16	95.8	3.6
Rifampin	≤0.5	≤0.5	≤0.5->2	99.5	0.5
Levofloxacin	≤0.03	≤0.03	≤0.03-0.06	100.0	[b]
Azithromycin	1	2	≤0.5-16	99.2	[b]
Clarithromycin	8	16	≤0.25->32	80.8	2.3
Quinupristin/Dalfopristin	4	8	≤0.5->8	[b]	[b]
***M. catarrhalis* (108)**					
LBM415	0.25	0.5	0.06-2	[b]	[b]
Penicillin	4	>4	≤0.03->4	4.8[c]	95.2[c]
Amoxicillin/Clavulanate	≤0.06	0.25	≤0.06-1	100.0	0.0
Ceftriaxone	≤0.03	0.06	≤0.03-0.12	100.0	[b]
Azithromycin	≤0.5	≤0.5	≤0.5	100.0	0.0
Clarithromycin	≤0.25	≤0.25	≤0.25	100.0	0.0
Rifampin	≤0.5	≤0.5	≤0.5	100.0	0.0
Tetracycline	≤2	≤2	≤2-16	99.1	0.9
Quinupristin/Dalfopristin	≤0.5	≤0.5	≤0.5-1	[b]	[b]

a. Susceptibility criteria of the NCCLS [2004]. Breakpoints for *H. influenzae* were applied for interpretation of *M. catarrhalis* results.
b. No criteria have been established.
c. Susceptibility predicted by a negative ß-lactamase test result (MIC, ≤ 0.06 mg/L).

CONCLUSIONS

- LBM415 displays a broad-spectrum of activity against the common Gram-positive pathogens, including resistant subsets, with no regional differences in potency apparent.
- The majority of Gram-negative fastidious species (*H. influenzae* and *M. catarrhalis*) were also inhibited by LBM415.
- As a class of antimicrobials, the peptide deformylase inhibitor compounds exhibit a spectrum of activity and unique mode of action that promises to be a significant advance in chemotherapy targeting infections of the respiratory tract and skin and skin structure.
- Examination of additional candidate compounds to optimize spectrum and potency is warranted.

SELECTED REFERENCES

Andersag TR, Biedenbach DJ, Jones RN, The Quality Control Working Group. (2003). Quality control guidelines for MIC susceptibility testing of NVP PDF-713, a novel peptide deformylase inhibitor. *International Journal of Antimicrobial Agents* 22:84-86.

Andersag TR, Jones RN, The Quality Control Working Group. (2004). Disk diffusion quality control guidelines for NVP PDF-713: A novel peptide deformylase inhibitor. *Diagnostic Microbiology and Infectious Disease* 48:55-57.

Apfel CM, Locher H, Evers S, Takacs B, Hubschwerlen C, Pinson W, Page MGP, Keck W. (2001). Peptide deformylase as an antibacterial drug target: Target validation and resistance development. *Antimicrobial Agents and Chemotherapy* 45:1058-1064.

Credito K, Lin G, Edrie LM, Appelbaum PC. (2004). Antistaphylococcal activity of LBM415, a new peptide deformylase inhibitor, compared with those of other agents. *Antimicrobial Agents and Chemotherapy* 48:4033-4036.

Edrie LM, Pankuch G, Appelbaum PC. (2004). Antipneumococcal activity of LBM415, a new peptide deformylase inhibitor, compared with those of other agents. *Antimicrobial Agents and Chemotherapy* 48:4027-4032.

Giglione C, Pierre M, Meinnel T. (2000). Peptide deformylase as a target for new generation, broad spectrum antimicrobial agents. *Molecular Microbiology* 36:1197-1205.

Jones RN, Fritsche TR, Sader HS. (2004). Antimicrobial spectrum and activity of NVP PDF-713, a novel peptide deformylase inhibitor, tested against 1,837 recent Gram-positive clinical isolates. *Diagnostic Microbiology and Infectious Disease* 49:63-65.

National Committee for Clinical Laboratory Standards. (2003). *Methods for dilution antimicrobial susceptibility tests for bacteria that grow aerobically, 6th edition: Approved standard M7-A6.* Wayne, PA:NCCLS.

National Committee for Clinical Laboratory Standards. (2004). *Performance standards for antimicrobial susceptibility testing, M100-S14 Supplemental Tables.* Wayne, PA:NCCLS.

Wise R, Andrews JM, Ashby J. (2002). *In vitro* activities of peptide deformylase inhibitors against gram-positive pathogens. *Antimicrobial Agents and Chemotherapy* 46:1117-1118.

Yuan Z, Trias J, White RJ. (2001). Deformylase as a novel antibacterial target. *Drug Discovery Today* 6:954-961.

Fritsche TR, Moet GJ, Jones RN. (2004). Commercial broth microdilution panel validation and reproducibility trials for NVP PDF-713, a novel inhibitor of bacterial peptide deformylase. *Clinical Microbiology Infection* 10:857-862.