most commonly using Mueller-Hinton (MH) broth for aerobes, supplemented as required for support of factitious organisms and Wilkins-Chalgren (WC) agar for anaerobes. For investigators using broth microdilution methods an inoculum of about 10^5 CFU per milliliter was used in most studies. For investigators using agar dilution an inoculum of about 10^4 CFU per spot for aerobes and 10^5 CFU per spot for anaerobes was used in most studies. Tests for aerobes were read after overnight incubation at 35-37° C, but some anaerobes required up to 48 hours incubation. These agar and inocula are those recommended by the National Committee for Clinical Laboratory Standards (NCCLS).

The NDA holders letter of January 1993 suggested that at least 100 isolates from each species should be tested. Therefore, only species with around 100 isolates will be considered for inclusion in the *in vitro* section (second list) of the package insert. The NDA holders letter also states that in order to be included in the label (second list) a microorganism should be a significant (not anecdotal) pathogen at the body site(s) or in the infection(s) for which clinical effectiveness for other pathogens has been established. Since the sponsor is requesting nosocomial pneumonia; community acquired pneumonia; acute bacterial exacerbation of chronic bronchitis; acute sinusitis; complicated intra-abdominal infections, including post-surgical infections; gynecologic and pelvic infections, including post-surgical infections; surgical prophylaxis; skin and skin structure infections; uncomplicated urinary tract infections; complicated urinary tract infections; bacterial prostatitis; acute, uncomplicated urethral, cervical pharyngeal and rectal gonorrhea; nongonococcal urethritis and cervicitis; pelvic inflammatory disease; and epidemic meningococcal meningitis in children, only potential pathogenic microorganisms usually found at these sites will be included in the second list of the label. The susceptibility breakpoint for trovafloxacin is 1.0 μg/mL (2.0 μg/mL for anaerobes), therefore, in order to be allowed in the *in vitro* list in the label the MIC_{90} value for an organism must be $\leq$ 1.0 μg/mL ($\leq$ 2.0 μg/mL for anaerobes).

The labeling submitted by the sponsor includes the following organisms in the *in vitro* activity (second) list:

Aerobic gram-positive microorganisms:

Bacillus cereus
Corynebacterium jeikeium
Enterococcus faecium (including vancomycin-sensitive and vancomycin-resistant strains)
Staphylococcus saprophyticus

Aerobic gram-negative microorganisms:

Acinetobacter baumannii
Alcaligenes faecalis
Alcaligenes xylosoxidans spp. *denitrificans*
Alcaligenes xylosoxidans spp. *xylosoxidans*
Bordetella bronchiseptica
Brevundimonas diminuta

Burkholderia cepacia
Citrobacter diversus
Citrobacter freundii
Enterobacter aerogenes
Neisseria meningitidis
Morganella morganii
Proteus vulgaris
Providencia rettgeri
Providencia stuartii
Pseudomonas fluorescens putida
Pseudomonas stutzeri
Salmonella enteritidis
Salmonella typhi
Salmonella spp.
Serratia marcescens
Shigella spp.
Stenotrophomonas maltophilia
Vibrio cholerae
Yersinia enterocolitica

Anaerobic microorganisms:

Bacteroides distasonis
Bacteroides ovatus
Bacteroides uniformis
Clostridium difficile
Clostridium perfringens
Clostridium ramosum
Fusobacterium mortiferum
Fusobacterium nucleatum
Prevotella bivia
Prevotella intermedia
Prevotella melaninogenica

Other microorganisms:

Legionella dumoffii
Legionella micdadei
Legionella longbeacheae
Legionella maltophilia??
Mycoplasma hominis
Toxoplasma gondii
Ureaplasma urealyticum

Table 7. Summary Table of All Preclinical Susceptibility Data

Organism	No. Isolate	Compound	MIC Range (μg/mL)	MIC_{90} Range (μg/mL)	Median MIC_{90} (μg/mL)	References
Acinetobacter baumanii	30	Trovafloxacin			>8	59
	30	Ciprofloxacin			>8	59
	30	Ofloxacin			>8	59
Alcaligenes faecalis	25	Trovafloxacin			>8	59
	25	Ciprofloxacin			>8	59
	25	Ofloxacin			>8	59
Alcaligenes xylosoxidans ssp. *denitrificans*	11	Trovafloxacin			4.0	59
	11	Ciprofloxacin			2.0	59
	11	Ofloxacin			4.0	59
Alcaligenes xylosoxidans ssp. xylosoxidans	24	Trovafloxacin			>8.0	59
	24	Ciprofloxacin			>8.0	59
	24	Ofloxacin			>8.0	59
Bacillus cereus	25	Trovafloxacin			0.06	35-36
	25	Ciprofloxacin			0.125	35-36
	25	Ofloxacin			0.25	35-36
	15	Sparfloxacin			0.125	36
Bacteroides distasonsis	245	Trovafloxacin			1.0	60,62-64,66
	245	Ciprofloxacin			32	60,62-64,66
	173	Ofloxacin			16	62,63,66
	127	Metronidazole			1.5	60,62,64
Bacteroides fragilis	1,404	Trovafloxacin			0.5	11,37-39,60-67
	1,339	Ciprofloxacin			16.0	11,37,39,60-64,66-67
	874	Ofloxacin			16.0	38,62-63,66
	515	Metronidazole			1.28	11,60-62,64,66
B. fragilis Group	2,018	Trovafloxacin			1.0	60-61,63-65
	723	Ciprofloxacin			32.0	60-61,64
	723	Metronidazole			2.0	60-61,64
B. ovatus	218	Trovafloxacin			2.0	60,62-64,66
	218	Ciprofloxacin			64	60,62-64,66
	135	Ofloxacin			64	62-63,66
	100	Metronidazole			1.25	60,62,64,66
B. thetaiotaomicron	361	Trovafloxacin			1.0	60,62-64,66
	361	Ciprofloxacin			32	60,62-64,66
	238	Ofloxacin			64	62-63,66
	159	Metronidazole			1.25	60,62,64,66
B. uniformis	74	Trovafloxacin			4.0	62-64,66

Organism	No. Isolate	Compound	MIC Range (μg/mL)	MIC_{90} Range (μg/mL)	Median MIC_{90} (μg/mL)	References
	74	Ciprofloxacin			40	62-64,66
	58	Ofloxacin			64	62-63,66
	54	Metronidazole			1.0	62,64,66
B. vulgatus	150	Trovafloxacin			4.0	60,62-64,66
	150	Ciprofloxacin			64	60,62-64,66
	105	Ofloxacin			64	62,63,66
	95	Metronidazole			1.0	60,62,64,66
Bordetella bronchiseptica	12	Trovafloxacin			1.0	59
	12	Ciprofloxacin			1.0	59
	12	Ofloxacin			1.0	59
Brevundimonas diminuta	11	Trovafloxacin			8.0	59
	11	Ciprofloxacin			8.0	59
	11	Ofloxacin			>8.0	59
Burkholderia cepacia	16	Trovafloxacin			4.0	59
	16	Ciprofloxacin			>8	59
	16	Ofloxacin			>8	59
Chlamydia pneumoniae	13	Trovafloxacin			1.0	57
	13	Ofloxacin			1.0	57
Chlamydia trachomatis	19	Trovafloxacin			0.05	70
	19	Ofloxacin			0.35	70
Citrobacter freundii	123	Trovafloxacin			0.375	11,35-36,39,51, 53
	123	Ciprofloxacin			0.125	11,35-36,39,51, 53
	75	Ofloxacin			1.0	35-36,51-53
	63	Sparfloxacin			0.25	11,36,39
Citrobacter diversus	77	Trovafloxacin			0.06	11,35-36,39,51, 53
	77	Ciprofloxacin			0.015	11,35-36,39,51, 53
	50	Ofloxacin			0.125	35,36,51,53
	37	Sparfloxacin			0.25	11,36,39
Clostridium perfringens	179	Trovafloxacin			0.25	38,60-62,65-66
	161	Ciprofloxacin			0.5	38,60-62
	121	Ofloxacin			0.5	38,62,66
	109	Metronidazole			1.5	60-62,66
C. difficile	71	Trovafloxacin			1.0	38,60-62
	71	Ciprofloxacin			8.0	38,60-62
	44	Ofloxacin			8.0	38,62
	41	Metronidazole			0.25	60-62
C. ramosum	15	Trovafloxacin			0.5	61
	15	Ciprofloxacin			8.0	61

Organism	No. Isolate	Compound	MIC Range (μg/mL)	MIC_{90} Range (μg/mL)	Median MIC_{90} (μg/mL)	References
	15	Metronidazole			1.0	61
Corynebacterium jeikeium	37	Trovafloxacin			2.0	35,51
	37	Ciprofloxacin			16	38,51
	37	Ofloxacin			4	38,51
Enterobacter aerogenes	165	Trovafloxacin			0.125	11,35-36,39,41, 51,53
	165	Ciprofloxacin			0.125	11,35-36,39,41,51,53
	70	Ofloxacin			0.5	35,36,53
	83	Sparfloxacin			0.25	11,36,39
E. agglomerans	45	Trovafloxacin			0.06	35,36,39,53
	45	Ciprofloxacin			0.03	35,36,39,53
	35	Ofloxacin			0.1	35,36,53
	27	sparfloxacin			0.09	36,39
Enterobacter cloacae	242	Trovafloxacin			1.6	11,35-36,39,41-42,51,53
	242	Ciprofloxacin			0.312	11,35-36,39,41-42,51,53
	90	Ofloxacin			2.12	35-36,51,53
	135	Sparfloxacin			0.085	11,36,39,42
Enterobacter spp.	93	Trovafloxacin			0.125	37,38,47
	93	Ciprofloxacin			0.06	37,38,47
	61	Ofloxacin			1.0	38
	10	Sparfloxacin			0.125	37
Enterococcus faecalis (Van-S)	574	Trovafloxacin			2.0	11,33-41,47,51-53,59,107
	537	Ciprofloxacin			2.0	11,34-41,47,51-53
	188	Ofloxacin			4.0	35-36,38,51,53
	89	Sparfloxacin			1.0	11,34,36,37,39
E. faecalis (Van-R)	33	Trovafloxacin			8	33,67,97,107
	19	Ciprofloxacin			16	67,97
	12	Ofloxacin			>8	67
	19	Sparfloxacin			>16	67,97
E. faecium (Van-S)	130	Trovafloxacin			2.0	33,35,37,39,40,51,52,107
	110	Ciprofloxacin			4.0	35,37,39,40,51,52
	20	Ofloxacin			6.0	35,51
	23	Sparfloxacin			1.0	37,39
E. faecium (Van-R)	285	Trovafloxacin			8.0	33,34,36,52,53,67,97,107
	231	Ciprofloxacin			>16	34,36,52,53,67,97
	150	Ofloxacin			>16	36,53,67
	195	Sparfloxacin			>10	34,36,67,97
Escherichia coli	476	Trovafloxacin			0.06	11,35-39,41-42,47,51,53
	476	Ciprofloxacin			0.062	11,35-39,41-42,47,51,52
	193	Ofloxacin			0.125	35-36,38,51,53

Organism	No. Isolate	Compound	MIC Range (μg/mL)	MIC_{90} Range (μg/mL)	Median MIC_{90} (μg/mL)	References
	188	Sparfloxacin			0.062	11,36-37,39,42
Fusobacterium	68	Trovafloxacin			0.375	60-62,66
nucleatum	68	Ciprofloxacin			2.0	60-62,66
	29	Ofloxacin			3.0	62,66
	68	Metronidazole			0.25	60-62,66
Fusobacterium	101	Trovafloxacin			1.0	38,60,61,66
spp.	101	Ciprofloxacin			3.0	38,60,61,66
	37	Ofloxacin			4.0	38,66
	76	Metronidazole			0.5	60,61,66
Gardnerella	23	Trovafloxacin			2.0	38
vaginalis	23	Ciprofloxacin			2.0	38
	23	Ofloxacin			2.0	38
Haemophilus	403	Trovafloxacin			0.015	11,35-42,47
influenzae	403	Ciprofloxacin			0.015	11,35-42,47
	67	Ofloxacin			0.023	38,51
	150	Sparfloxacin			0.015	11,37,39,42,47
Klebsiella	331	Trovafloxacin			0.125	11,35-36,39,41-42,47,53
pneumoniae	331	Ciprofloxacin			0.06	11,35-36,39,41-42,47,53
	95	Ofloxacin			1.0	36,39,53
	141	Sparfloxacin			0.125	11,36,39,42
Klebsiella	94	Trovafloxacin			0.155	11,35-36,39
oxytoca	94	Ciprofloxacin			0.06	11,35-36,39
	36	Ofloxacin			0.185	35-36
	83	Sparfloxacin			0.25	11,36,39
Klebsiella	113	Trovafloxacin			1.0	37,38,51
spp.	113	Ciprofloxacin			0.25	37,38,51
	63	Ofloxacin			4.5	38,51
	50	Sparfloxacin			0.5	37
Legionella	155	Trovafloxacin			0.008	35,38,56
pneumophila	133	Ciprofloxacin			0.038	35,38
	155	Ofloxacin			0.032	35,38,56
Listeria	61	Trovafloxacin			0.25	38,39
monocytogenes	61	Ciprofloxacin			1.5	38,39
	43	Ofloxacin			4.0	38
	18	Sparfloxacin			1.0	39
Moraxella	304	Trovafloxacin			0.03	11,35,37-40,42,47,51
catarrhalis	304	Ciprofloxacin			0.06	11,35,37-40,42,47,51

Organism	No. Isolate	Compound	MIC Range (µg/mL)	MIC_{90} Range (µg/mL)	Median MIC_{90} (µg/mL)	References
	53	Ofloxacin			0.075	38,51
	131	Sparfloxacin			0.031	11,37,39,42,47
Morganella morganii	195	Trovafloxacin			0.5	11,35-37,39,41,47,51,53
	195	Ciprofloxacin			0.125	11,35-37,39,41,47,51,53
	46	Ofloxacin			0.19	35-36,51,53
	93	Sparfloxacin			1.0	11,36,37,39,53
Mycoplasma pneumoniae	50	Trovafloxacin			0.185	38,55
	10	Ciprofloxacin			1.0	38
	50	Ofloxacin			1.0	38,55
	40	Sparfloxacin			0.25	55
Mycoplasma hominis	121	Trovafloxacin			0.03	38,55,104
	79	Ciprofloxacin			0.75	38,104
	121	Ofloxacin			1.0	38,55,104
	42	Sparfloxacin			0.03	55
Neisseria gonorrhoeae (Cip-S)	509	Trovafloxacin			0.006	11,35,37-38,68-69
	509	Ciprofloxacin			0.008	11,35,37-38,68-69
	295	Ofloxacin			0.03	38,68
	70	Sparfloxacin			0.0028	11,37
Neisseria gonorrhoeae (Cip-R)[a]	30	Trovafloxacin			0.06	68
	30	Ciprofloxacin			0.5	68
	30	Ofloxacin			0.5	68
Neisseria meningitidis	71	Trovafloxacin			0.005	37,38
	71	ciprofloxacin			0.005	37,38
	61	Ofloxacin			0.03	38
	10	Sparfloxacin			0.002	37
Peptostreptococci	156	Trovafloxacin			1.0	38,60-61,66
	156	Ciprofloxacin			4.0	38,60-61,66
	55	Ofloxacin			12.0	38,66
	123	Metronidazole			1.0	60-61
Prevotella bivia	118	Trovafloxacin			1.5	60,65,66
	101	Ciprofloxacin			32	60,66
	50	Ofloxacin			16	66
	101	Metronidazole			2.5	60,66
Prevotella intermedia	27	Trovafloxacin			1.0	60,62
	27	Ciprofloxacin			8.25	60,62
	13	Ofloxacin			0.5	62
	27	Metronidazole			2.25	60,62
P. melaninogenica	21	Trovafloxacin			1.5	60,66

Organism	No. Isolate	Compound	MIC Range (μg/mL)	MIC_{90} Range (μg/mL)	Median MIC_{90} (μg/mL)	References
	21	Ciprofloxacin			16.0	60
	10	Ofloxacin			64.0	66
	21	Metronidazole			2.25	60,66
Prevotella spp.	126	Trovafloxacin			1.0	38,61-62,66
	126	Ciprofloxacin			12.0	38,61-62,66
	77	Ofloxacin			16.0	38,62,66
	101	Metronidazole			1.0	61-62,66
Proteus mirabilis	298	Trovafloxacin			0.5	11,35-37,39,41-42,47,51,53
	298	Ciprofloxacin			0.06	11,35-37,39,41-42,47,51,53
	80	Ofloxacin			0.125	35,36,51,53
	166	Sparfloxacin			0.5	11,36-37,39,42
Proteus vulgaris	89	Trovafloxacin			0.5	35,37,39,47,51,53
	89	Ciprofloxacin			0.03	35,37,39,47,51,53
	30	Ofloxacin			0.125	35,51,53
	38	Sparfloxacin			0.5	37,39
Providencia rettgeri	30	Trovafloxacin			0.5	35,39,51
	30	Ciprofloxacin			0.5	35,39,51
	20	Ofloxacin			1.5	35,51
	10	Sparfloxacin			0.5	39
Providencia stuartii	40	Trovafloxacin			2.0	35,39,51
	40	Ciprofloxacin			0.25	35,39,51
	20	Ofloxacin			5.0	35,51
	20	Sparfloxacin			1.0	39
Pseudomonas aeruginosa	566	Trovafloxacin			2.0	11,35-39,41,51,53,58-59
	566	Ciprofloxacin			2.0	11,35-39,41,51,53,58-59
	357	Ofloxacin			>8	35-36,38,51,53,58-59
	256	Sparfloxacin			2.0	11,36-37,39,58
P. fluorescens putida	15	Trovafloxacin			1.0	59
	15	Ciprofloxacin			0.25	59
	15	Ofloxacin			2.0	59
P. stutzeri	23	Trovafloxacin			0.25	59
	23	Ciprofloxacin			0.125	59
	23	Ofloxacin			0.25	59
Salmonella typhi	34	Trovafloxacin			0.03	38,39
	34	Ciprofloxacin			0.03	38,39
	30	Ofloxacin			0.06	38

Organism	No. Isolate	Compound	MIC Range (µg/mL)	MIC_{90} Range (µg/mL)	Median MIC_{90} (µg/mL)	References
Salmonella enteritidis	15	Trovafloxacin			0.075	35,37
	15	Ciprofloxacin			0.045	35,37
	10	Ofloxacin			0.125	35
Salmonella spp.	127	Trovafloxacin			0.09	11,36,38,39
	127	Ciprofloxacin			0.06	11,36,38,39
	79	Ofloxacin			0.25	36,38
	55	Sparfloxacin			0.06	11,36,39
Serratia marcescens	211	Trovafloxacin			2.5	11,35-36,39,41,47,51,53
	211	Ciprofloxacin			1.0	11,35-36,39,41,47,51,53
	100	Ofloxacin			2.25	35-36,51,53
	91	Sparfloxacin			0.5	11,36,39
Shigella spp.	111	Trovafloxacin			0.03	11,35,38,39,42
	111	Ciprofloxacin			0.02	11,35,38,39,42
	58	Ofloxacin			0.09	35,38
	53	Sparfloxacin			0.03	11,39,42
S. aureus MSSA	666	Trovafloxacin			0.06	11,33-41,51,53,98
	646	Ciprofloxacin			0.75	11,34-41,51-53,98
	194	Ofloxacin			0.5	35,36,38,51,53
	130	Sparfloxacin			0.125	11,34,36,37,39
Staphylococcus aureus MRSA CIP-R	487	Trovafloxacin			2.0	33-42,47,51-54,98
	452	Ciprofloxacin			>16	34-42,47,51-54,98
	134	Ofloxacin			16	35-36,38,51,53
	102	Sparfloxacin			8	34,36-37,39,42
S. aureus MRSA CIP-Sus	28	Trovafloxacin			0.06	11,34
	28	Ciprofloxacin			2.25	11,34
	28	Sparfloxacin			0.31	11,34
S. epidermidis Meth-Cip-R	118	Trovafloxacin			2.5	35,36,53,98
	118	Ciprofloxacin			>16	35,36,53,98
	55	Ofloxacin			>16	35,36,53
Staphylococci coagulase-negative Meth-Cip-S	187	Trovafloxacin			0.06	33-35,37,39,51, 52
	167	Ciprofloxacin			0.5	33-35,37,39,51, 52
	160	Sparfloxacin			0.25	34,37,39
Staphylococci coagulase-negative Meth-R Cip-S	260	Trovafloxacin			0.125	37,40,41
	260	Ciprofloxacin			0.5	37,40,41

Organism	No. Isolate	Compound	MIC Range (μg/mL)	MIC_{90} Range (μg/mL)	Median MIC_{90} (μg/mL)	References
Staphylococcus haemolyticus	20	Trovafloxacin			2.0	35,36
	20	Ciprofloxacin			8.0	35,36
	20	Ofloxacin			8.0	35,36
	10	Sparfloxacin			8.0	36
Staphylococcus saprophyticus	35	Trovafloxacin			0.06	34,36,51
	29	Ciprofloxacin			0.5	34,51
	9	Ofloxacin			0.03	51
	26	Sparfloxacin			0.25	34,36
Stenotrophomonas (Xanthomonas) maltophilia	227	Trovafloxacin			2.0	35-37,39,53,58, 59
	227	Ciprofloxacin			>8	35-37,39,53,58
	197	Ofloxacin			>8	35,36,53,58-59
	142	Sparfloxacin			2.0	36,37,39,58
Streptococcus agalactiae (group B)	120	Trovafloxacin			0.25	34-37,39,41,51
	120	Ciprofloxacin			2.0	34-37,39,41,51
	40	Ofloxacin			2.0	36-51
	56	Sparfloxacin			0.75	34,36,37,39
Streptococcus pneumoniae pen-S	1,867	Trovafloxacin			0.125	11,33-50
	1,847	Ciprofloxacin			2.0	11,34-50
	1,427	Ofloxacin			4.0	11,36,38,43,45,46,48-50
	541	Sparfloxacin			0.5	11,34,36,37,39,42-45,47,50
Streptococcus pneumoniae pen-R	498	Trovafloxacin			0.125	11,43,44,46,49
	498	Ciprofloxacin			2.0	11,43,44,46,49
	343	Ofloxacin			4.0	43,46,49
	306	Sparfloxacin			1.25	43,44
Streptococcus pyogenes	242	Trovafloxacin			0.125	11,34-37,39-41,51-52
	242	Ciprofloxacin			0.75	11,34-37,39-41,51-52
	35	Ofloxacin			1.5	36,51
	90	Sparfloxacin			0.5	11,34,36,37,39
viridans streptococci	246	Trovafloxacin			0.25	33-34,36,38-40,47,52
	226	Ciprofloxacin			4.0	34,36,38-40,47, 52
	55	Ofloxacin			6.0	36,38
	56	Sparfloxacin			1.0	34,36,39
Ureaplasma urealyticum	157	Trovafloxacin			0.5	38,55,104
	111	Ciprofloxacin			4.0	38,104
	57	Ofloxacin			3.0	38,55
	46	Sparfloxacin			1.0	55
Vibrio	15	Trovafloxacin			0.03	38

Organism	No. Isolate	Compound	MIC Range (μg/mL)	MIC_{90} Range (μg/mL)	Median MIC_{90} (μg/mL)	References
cholerae	15	Ciprofloxacin			0.004	38
	15	Ofloxacin			0.015	38
Yersinia	45	Trovafloxacin			0.06	35,38
enterocolitica	45	Ciprofloxacin			0.03	35,38
	45	Ofloxacin			0.185	35,38

Each of microorganisms in the in vitro activity list will be discussed below along with the reasons for inclusion in or exclusion from the label.

a. Activity Against Gram-positive Aerobes

Bacillus cereus: Two studies, 25 isolates, MIC range _ MIC_{90} range: median MIC_{90}: 0.06 μg/mL.

In addition to food poisoning, based on many reports and frequent and regular occurrence *Bacillus cereus* is now accepted to be associated with mild to severe, necrotic or gangrenous infected wounds. Even though the median MIC_{90} is acceptable the number of the organisms tested are very few. This organism will not be allowed in the label.

Corynebacterium jeikeium Two studies, 37 isolates, MIC range: , MIC_{90} range: , median MIC_{90}: 2.0 μg/mL.

Corynebacterium jeikeium is the most common corynebacterial pathogen isolated in the clinical laboratory. It is associated with septicemia, endocarditis skin and soft tissue infections, and occasionally, meningitis, peritonitis, and pneumonia, particularly in the compromised and previously treated host. The number of the isolates and the MIC_{90} of 2.0 μg/mL is not acceptable. This organisms will not be allowed in the label.

Enterococcus faecium (Van-S) Eight studies, 130 isolates, MIC range MIC_{90} range: , median MIC_{90}: 2.0 μg/mL.

Enterococcus faecium (Van-R) Eight studies, 285 isolates, MIC range: MIC_{90} range: median MIC_{90}: 8.0 μg/mL.

Enterococci are involved most commonly in urinary tract infections and are implicated in 10% of all such infections. Intra abdominal or pelvic wound infections are the next commonly encountered infections. However, these wound cultures are frequently polymicrobial, and the role of enterococci in this setting remains controversial. Bacteremia is the third most common type of infection, and enterococci are the third leading cause of nosocomial bacteremia. Endocarditis is less common than bacteremia and enterococci is estimated to be the causative agent in , of bacterial endocarditis cases. *E. faecalis* is the most commonly encountered species in this setting, but various other species also have been implicated as causes of endocarditis. The MIC_{90} is above the susceptible breakpoint for both Van-R and Van-S *E. faecium*. This organism will not be

allowed in the label

Staphylococcus saprophyticus Three studies, 35 isolates, MIC range: , MIC_{90} range: , median MIC_{90}: 0.06 µg/mL.

--One study had 20 isolates collected between 1990 and 1991 at Massachusetts General Hospital. MIC range was MIC_{50} was 0.125 µg/mL, and MIC_{90} was 0.125 µg/mL.

--One study had 9 U. S. isolates which according to the authors were neither recent clinical isolates nor typical of a consecutive clinical isolate distribution. They had known quinolone resistance. Neither MIC range nor MIC_{90} was given. The MIC_{50} was 0.03 µg/mL.

--One U.S. study had 6 isolates collected from cancer patients admitted to The University of Texas M. D. Anderson Cancer Center at Houston during the past 5 years. The MIC range was . The MIC_{90} and MIC_{50} was not given.

Staphylococcus saprophyticus is an important opportunistic pathogen in human urinary tract infections, especially in young, sexually active females. It has been proposed as an agent of nongonococcal urethritis in males and prostatitis. Although the median MIC_{90} was 0.06 µg/mL, the number of the isolates are not sufficient to justify inclusion in the label. *Staphylococcus saprophyticus* will not be allowed in the label.

b. Activity Against Gram-negative Aerobes

Acinetobacter baumanii One study, 30 isolates, MIC range: MIC_{50}: ≤0.06 µg/mL, MIC_{90}: >8.0 µg/mL.

--The study was performed in the U.S., 85% of the isolates were collected between 1994-1995 at the Ohio State University Medical Center and 15%, all representing uncommon species, were isolated from 1978-1995 in the same hospital.

There are few isolates and the MIC_{90} is >8.0 µg/mL. *Acinetobacter baumanii* will not be allowed in the label.

Alcaligenes faecalis One study, 25 isolates, MIC range: , MIC_{50}: 4.0 µg/mL, MIC_{90}: >8.0 µg/mL.

--The study was performed in the U.S., 85% of the isolates were collected between 1994-1995 at the Ohio State University Medical Center and 15%, all representing uncommon species, were isolated from 1978-1995 in the same hospital

There is few isolates and the MIC_{90} is >8.0 µg/mL. *Alcaligenes faecalis* will not be allowed in the

label

Alcaligenes xylosoxidans subsp. *denitrificans* — One study, 11 isolates, MIC range 2.0 µg/mL, MIC_{90}: 4.0 µg/mL. MIC_{50}:

--The study was performed in the U.S., 85% of the isolates were collected between 1994-1995 at the Ohio State University Medical Center and 15%, all representing uncommon species, were isolated from 1978-1995 in the same hospital

There are few isolates and the MIC_{90} is 4.0 µg/mL. *Alcaligenes xylosoxidans* subsp. *denitrificans* will not be allowed in the label

Alcaligenes xylosoxidans subsp. *xylosoxidans* — One study, 24 isolates, MIC range >8.0 µg/mL, MIC_{90}: >8.0 µg/mL. MIC_{50}:

--The study was performed in the U.S., 85% of the isolates were collected between 1994-1995 at the Ohio State University Medical Center and 15%, all representing uncommon species, were isolated from 1978-1995 in the same hospital

There is few isolates and the MIC_{90} is >8.0 µg/mL. *Alcaligenes xylosoxidans* subsp. *xylosoxidans* will not be allowed in the label

Bordetella bronchiseptica — One study, 12 isolates, MIC range 0.5 µg/mL, MIC_{90}: 1.0 µg/mL. MIC_{50}:

--The study was performed in the U.S., 85% of the isolates were collected between 1994-1995 at the Ohio State University Medical Center and 15%, all representing uncommon species, were isolated from 1978-1995 in the same hospital

There are data on very few isolates and the MIC_{90} is 1.0 µg/mL. *Bordetella bronchiseptica* will not be allowed in the label

Brevundimonas diminuta — One study, 11 isolates, MIC range µg/mL, MIC_{90}: 8.0 µg/mL. , MIC_{50}: 4.0

--The study was performed in the U.S., 85% of the isolates were collected between 1994-1995 at the Ohio State University Medical Center and 15%, all representing uncommon species, were isolated from 1978-1995 in the same hospital

There are data on very few isolates and the MIC_{90} is 8.0 µg/mL. *Brevundimonas diminuta* will not be allowed in the label

Burkholderia cepacia — One study, 16 isolates, MIC range: MIC_{50}: 2.0 µg/mL, MIC_{90}: 4.0 µg/mL.

--The study was performed in the U.S., 85% of the isolates were collected between 1994-1995 at the Ohio State University Medical Center and 15%, all representing uncommon species, were isolated from 1978-1995 in the same hospital.

There are data on very few isolates and the MIC_{90} is 4.0 µg/mL. *Burkholderia cepacia* will not be allowed in the label

Citrobacter diversus — Six studies, 77 isolates, MIC range , MIC_{90} range median MIC_{90}: 0.06 µg/mL.

--One U.S. study had 17 isolates collected in summer of 1990 at Massachusetts General Hospital and University of Washington. MIC range was , MIC_{50} was 0.062 µg/mL, and MIC_{90} was 0.25 µg/mL.

--One U.S. study had 10 isolates collected at University of Iowa hospitals and clinics in 1991-1992. MIC range was MIC_{50} was 0.03 µg/mL, and MIC_{90} was 0.06 µg/mL.

--One U.S. study had 10 isolates collected at Columbia Presbyterian Medical Center before 1992. MIC range was , MIC_{50} was 0.03 µg/mL, and MIC_{90} was 0.06 µg/mL.

--One study had 10 U. S. isolates which according to the authors were neither recent clinical isolates nor typical of a consecutive clinical isolate distribution. They had known quinolone resistance. The MIC range was not given, the MIC_{50} was 0.008 µg/mL and the MIC_{90} was 0.016 µg/mL.

--One U.S. study had 20 isolates collected at Yale-New Haven Hospital. The age of the isolates were not indicated. MIC range was , MIC_{50} was $\leq$0.015 µg/mL, and MIC_{90} was 0.03 µg/mL.

--One U.S. study had 10 isolates collected from cancer patients admitted to The University of Texas M. D. Anderson Cancer Center at Houston during the past 5 years. The MIC range was , MIC_{50} was 0.03 µg/mL and MIC_{90} was 0.06 µg/mL.

Less than 100 isolates were tested in a number of different centers. However, majority of the isolates were older than 5 years. Even though the median MIC_{90} was 0.06 µg/mL and this organism may be associated with pneumonia, *Citrobacter diversus* will not be allowed into the

label.

Citrobacter freundii

Six studies, 123 isolates, MIC range:
MIC_{90} range: median MIC_{90}: 0.375 µg/mL.

--One U.S. study had 28 isolates collected in summer of 1990 at Massachusetts General Hospital and University of Washington. MIC range was MIC_{50} was 0.125 µg/mL, and MIC_{90} was 0.25 µg/mL.

--One U.S. study had 20 isolates collected at University of Iowa hospitals and clinics in 1991-1992. MIC range was µg/mL, MIC_{50} was 0.06 µg/mL, and MIC_{90} was 0.5 µg/mL.

--One U.S. study had 20 isolates collected at Columbia Presbyterian Medical Center before 1992. MIC range was , MIC_{50} was 0.06 µg/mL, and MIC_{90} was 0.25 µg/mL.

--One study had 15 U. S. isolates which according to the authors were neither recent clinical isolates nor typical of a consecutive clinical isolate distribution. They had known quinolone resistance. The MIC range was not given, the MIC_{50} was 0.06 µg/mL and the MIC_{90} was 0.5 µg/mL.

--One U.S. study had 25 isolates collected at Yale-New Haven Hospital. The age of the isolates were not indicated. MIC range was MIC_{50} was 0.03 µg/mL, and MIC_{90} was 4.0 µg/mL.

--One U.S. study had 15 isolates collected from cancer patients admitted to The University of Texas M. D. Anderson Cancer Center at Houston during the past 5 years. The MIC range was , MIC_{50} was 0.06 µg/mL and MIC_{90} was 0.25 µg/mL.

More than 100 isolates were tested in a number of different centers. Majority of the isolates were older than 5 years. However, the recent study with 15 isolates indicates that *Citrobacter freundii* remains susceptible to trovafloxacin with an MIC_{90} of 0.25 µg/mL. This organism may be associated with pneumonia, *Citrobacter freundii* will be allowed into the label.

Enterobacter aerogenes

Seven studies, 165 isolates, MIC range:
MIC_{90} range median MIC_{90}: 0.125 µg/mL.

--One U.S. study had 38 isolates collected in summer of 1990 at Massachusetts General Hospital and University of Washington. MIC range was MIC_{50} was 0.125 µg/mL, and MIC_{90} was 0.5 µg/mL.

--One U.S. study had 20 isolates collected at University of Iowa

hospitals and clinics in 1991-1992. MIC range was _ MIC_{50} was 0.03 µg/mL, and MIC_{90} was 0.06 µg/mL.

--One U.S. study had 20 isolates collected at Columbia Presbyterian Medical Center before 1992. MIC range was , MIC_{50} was 0.06 µg/mL, and MIC_{90} was 0.125 µg/mL.

--One Saudi study had 27 isolates collected between April, 1995 to September 1995. MIC range was MIC_{50} was <0.03 µg/mL, and MIC_{90} was 0.125 µg/mL.

--One study had 10 U. S. isolates which according to the authors were neither recent clinical isolates nor typical of a consecutive clinical isolate distribution. They had known quinolone resistance. The MIC range was not given, the MIC_{50} was 0.03 µg/mL and the MIC_{90} was 8.0 µg/mL.

--One U.S. study had 25 isolates collected at Yale-New Haven Hospital. The age of the isolates were not indicated. MIC range was , MIC_{50} was 0.03 µg/mL, and MIC_{90} was 0.125 µg/mL.

--One U.S. study had 25 isolates collected from cancer patients admitted to The University of Texas M. D. Anderson Cancer Center at Houston during the past 5 years. The MIC range was MIC_{50} was 0.03 µg/mL and MIC_{90} was 0.06 µg/mL.

This organism may be associated with pneumonia. More than 100 isolates were tested in a number of different centers. However, majority of the isolates were older than 5 years. The two recent studies were performed in Saudi Arabia with 27 isolates and in U.S. with 25 isolates. The MIC_{90}s were 0.125 µg/mL and 0.06 µg/mL respectively. *Enterobacter aerogenes* will be allowed into the label.

Morganella morganii

Nine studies, 195 isolates, MIC range:
MIC_{90} range: , median MIC90: 0.5 µg/mL.

--One U.S. study had 39 isolates collected in summer of 1990 at Massachusetts General Hospital and University of Washington. MIC range was , MIC_{50} was 1.0 µg/mL, and MIC_{90} was 2.0 µg/mL.

--One U.S. study had 10 isolates collected at University of Iowa hospitals and clinics in 1991-1992. MIC range was MIC_{50} was 0.125 µg/mL, and MIC_{90} was 0.25 µg/mL.

--One U.K. study had 25 isolates collected at City Hospital NHS Trust. The age of the isolates was not indicated. MIC range

was , MIC_{50} was 0.25 µg/mL, and MIC_{90} was 1.0 µg/mL

--One U.S. study had 20 isolates collected at Columbia Presbyterian Medical Center before 1992. MIC range was MIC_{50} was 0.125 µg/mL, and MIC_{90} was 0.25 µg/mL.

--One Saudi study had 45 isolates collected between April, 1995 to September 1995. MIC range was , MIC_{50} was 0.125 µg/mL, and MIC_{90} was 2.0 µg/mL.

--One Belgian study had 20 isolates collected in 1993 from ten large hospitals. MIC range was , MIC_{50} was 0.25 µg/mL, and MIC_{90} was 0.25 µg/mL.

--One study had 10 U. S. isolates which according to the authors were neither recent clinical isolates nor typical of a consecutive clinical isolate distribution. They had known quinolone resistance. The MIC range was not given, the MIC_{50} was 0.06 µg/mL and the MIC_{90} was 0.125 µg/mL.

--One U.S. study had 17 isolates collected at Yale-New Haven Hospital. The age of the isolates were not indicated. MIC range was , MIC_{50} was 0.25 µg/mL, and MIC_{90} was 0.5 µg/mL.

--One U.S. study had 9 isolates collected from cancer patients admitted to The University of Texas M. D. Anderson Cancer Center at Houston during the past 5 years. The MIC range was , MIC_{50} and MIC_{90} was not given.

This is an opportunistic organism most commonly associated with urinary tract infections. Close to 200 isolates were tested in a number of different centers. However, majority of the isolates were older than 5 years. The three recent studies were performed in Saudi Arabia, Belgium and the U.S. with 45, 20, and 9 isolates respectively. The MIC_{90} for the Saudi study was 2.0 µg/mL and for the Belgian study was 0.25 µg/mL. None of the U.S. isolated had MICs greater than 0.5 µg/mL. Even though both foreign studies followed NCCLS methodologies, the MIC_{90} results for these studies are at conflict. The small U.S. study indicates that *Morganella morganii* remains susceptible to trovafloxacin and it will be allowed into the label.

Neisseria meningitidis

Two studies, 71 isolates, MIC range: , MIC_{90} range: , median MIC_{90}: 0.005 µg/mL.

--One U.K. study had 10 isolates collected at City Hospital NHS Trust. The age of the isolates was not indicated. MIC range was 0.002 µg/mL, MIC_{50} was 0.002 µg/mL, and MIC_{90} was 0.002 µg/mL.

--One U.K. study had 61 isolates collected in University College Hospital in London. The authors indicate that some of the isolates were recent clinical isolates from the University College Hospital microbiology lab and some were frozen isolates from UK and European centers collected in 1993-1994. . MIC range was MIC_{50} was 0.004 µg/mL, and MIC_{90} was 0.008 µg/mL.

Neisseria meningitidis is an organism that is implicated in community -acquired pneumonia, urethritis, and most importantly in meningitis. Due to the seriousness of meningococcal meningitis and the associated public health issues this organism will be listed ONLY if the efficacy of a drug is studied and demonstrated in well controlled clinical trials. *Neisseria meningitidis* will not be allowed in the label.

Proteus vulgaris

Six studies, 89 isolates, MIC range: MIC_{90} range median MIC_{90}: 0.5 µg/mL.

--One U.S. study had 10 isolates collected at University of Iowa hospitals and clinics in 1991-1992. MIC range was MIC_{50} was 0.06 µg/mL, and MIC_{90} was 0.25 µg/mL.

--One U.K. study had 18 isolates collected at City Hospital NHS Trust. The age of the isolates was not indicated. MIC range was , MIC_{50} was 0.25 µg/mL, and MIC_{90} was 0.5 µg/mL

--One U.S. study had 20 isolates collected at Columbia Presbyterian Medical Center before 1992. MIC range was , MIC_{50} was 0.25 µg/mL, and MIC_{90} was 0.5 µg/mL.

--One Belgian study had 21 isolates collected in 1993 from ten large hospitals. MIC range was , MIC_{50} was 0.25 µg/mL, and MIC_{90} was 0.5 µg/mL.

--One study had 10 U. S. isolates which according to the authors were neither recent clinical isolates nor typical of a consecutive clinical isolate distribution. They had known quinolone resistance. The MIC range was not given, the MIC_{50} was 0.125 µg/mL and the MIC_{90} was 0.25 µg/mL.

--One U.S. study had 10 isolates collected at Yale-New Haven Hospital. The age of the isolates were not indicated. MIC range was , MIC_{50} was 0.125 µg/mL, and MIC_{90} was 1.0 µg/mL.

This organism is most commonly associated with urinary tract infections. Only 89 isolates were

tested in a number of different centers. However, majority of the isolates were older than 5 years. The only recent study was performed in Belgium with 21 isolates and an MIC_{90} of 0.5 µg/mL which indicates that *Proteus vulgaris* remains susceptible to trovafloxacin. Even though the number of isolates are less than 100 given the low frequency by which this organism is isolated from clinical samples, *Proteus vulgaris* will be allowed into the label.

Providencia rettgeri — Three studies, 30 isolates, MIC range: MIC_{90} range: 0.5 µg/mL, median MIC_{90}: 0.5 µg/mL.

There are not enough isolates tested and *Providencia rettgeri* will not be allowed into the label.

Providencia stuartii — Three studies, 40 isolates, MIC range , MIC_{90} range , median MIC_{90}: 2.0 µg/mL.

There are not enough isolates tested and the median MIC_{90} is 2.0 µg/mL. *Providencia stuartii* will not be allowed into the label.

P. fluorescens putida — One study, 15 isolates, MIC range. MIC_{90} range: 1.0 µg/mL, median MIC_{90}: 1.0 µg/mL.

There are not enough isolates tested and *Pseudomonas fluorescens putida* will not be allowed into the label.

Pseudomonas stutzeri — One study, 23 isolates, MIC range , MIC_{90} range: 0.25 µg/mL, median MIC_{90}: 0.25 µg/mL.

There are not enough isolates tested and *Pseudomonas stutzeri* will not be allowed into the label.

Salmonella enteritidis — Two studies, 15 isolates, MIC range MIC_{90} range median MIC_{90}: 0.075 µg/mL.

There are not enough isolates tested and Infectious diarrhea is not an indication for trovafloxacin. *Salmonella enteritidis* will not be allowed into the label.

Salmonella typhi — Two studies, 34 isolates, MIC range , MIC_{90} range: 0.03 µg/mL, median MIC_{90}: 0.03 µg/mL.

There are not enough isolates tested and Infectious diarrhea is not an indication for trovafloxacin. *Salmonella typhi* will not be allowed into the label.

Salmonella spp. — Four studies, 127 isolates, MIC range MIC_{90} range median MIC_{90}: 0.09 µg/mL.

Infectious diarrhea is not an indication for trovafloxacin. *Salmonella* spp. will not be allowed into the label.

Serratia marcescens — Eight studies, 211 isolates, MIC range MIC_{90} range , median MIC_{90}: 2.5 µg/mL.

--One U.S. study had 36 isolates collected in summer of 1990 at Massachusetts General Hospital and University of Washington. MIC range was , MIC_{50} was 2.0 µg/mL, and MIC_{90} was 4.0 µg/mL.

--One U.S. study had 20 isolates collected at University of Iowa hospitals and clinics in 1991-1992. MIC range was µg/mL, MIC_{50} was 0.125 µg/mL, and MIC_{90} was 0.5 µg/mL.

--One U.S. study had 25 isolates collected at Columbia Presbyterian Medical Center before 1992. MIC range was MIC_{50} was 0.5 µg/mL, and MIC_{90} was 1.0 µg/mL.

--One Saudi study had 28 isolates collected between April, 1995 to September 1995. MIC range was MIC_{50} was 0.125 µg/mL, and MIC_{90} was 1.0 µg/mL.

--One Belgian study had 22 isolates collected in 1993 from ten large hospitals. MIC range was MIC_{50} was 0.5 µg/mL, and MIC_{90} was 16 µg/mL.

--One study had 25 U. S. isolates which according to the authors were neither recent clinical isolates nor typical of a consecutive clinical isolate distribution. They had known quinolone resistance. The MIC range was not given, the MIC_{50} was 1.0 µg/mL and the MIC_{90} was >8.0 µg/mL.

--One U.S. study had 25 isolates collected at Yale-New Haven Hospital. The age of the isolates were not indicated. MIC range was , MIC_{50} was 0.25 µg/mL, and MIC_{90} was 4.0 µg/mL.

--One U.S. study had 30 isolates collected from cancer patients admitted to The University of Texas M. D. Anderson Cancer Center at Houston during the past 5 years. The MIC range was MIC_{50} was 0.25 µg/mL and MIC_{90} was 0.25 µg/mL.

Serratia marcescens is an important cause of extraintestinal infections, having caused many nosocomial outbreaks associated with blood transfusions surgery, and the urinary tract. Most of the MIC_{90}s were above the susceptible breakpoint. *Serratia marcescens* will not be allowed in the label.

Shigella spp.

Five studies, 111 isolates, MIC range , MIC_{90} range median MIC_{90}: 0.03 µg/mL.

--One U.S. study had 31 isolates collected in summer of 1990 at

Massachusetts General Hospital and University of Washington. MIC range was MIC_{50} was 0.031 µg/mL, and MIC_{90} was 0.031 µg/mL.

--One U.S. study had 10 isolates collected at University of Iowa hospitals and clinics in 1991-1992. MIC range was MIC_{50} was ≤0.015 µg/mL, and MIC_{90} was ≤0.015 µg/mL.

--One U.K. study had 48 isolates collected at University College Hospital in London and other European centers between 1993 and 1994. MIC range was MIC_{50} was 0.015 µg/mL, and MIC_{90} was 0.03 µg/mL.

--One U.S. study had 12 isolates collected at Columbia Presbyterian Medical Center before 1992. MIC range was MIC_{50} was 0.03 µg/mL, and MIC_{90} was 0.06 µg/mL.

--Reference 42 is an abstract that does not address *Shigella* spp.

Infectious diarrhea is not an indication for trovafloxacin. *Shigella* spp. will not be allowed into the label.

Stenotrophomonas maltophilia Seven studies, 227 isolates, MIC range MIC_{90} range: 0.5->8 µg/mL, median MIC_{90}: 2.0 µg/mL.

--One U.S. study had 10 isolates collected at University of Iowa hospitals and clinics in 1991-1992. MIC range was MIC_{50} was 0.25 µg/mL, and MIC_{90} was 2.0 µg/mL.

--One U.K. study had 10 isolates collected at City Hospital NHS Trust. The age of the isolates was not indicated. MIC range was MIC_{50} was 0.25 µg/mL, and MIC_{90} was 1.0 µg/mL

--One U.S. study had 20 isolates collected at Columbia Presbyterian Medical Center before 1992. MIC range was MIC_{50} was 0.25 µg/mL, and MIC_{90} was 0.5 µg/mL.

--One U.S. study had 25 isolates collected at Yale-New Haven Hospital. The age of the isolates were not indicated. MIC range was MIC_{50} was 0.25 µg/mL, and MIC_{90} was 2.0 µg/mL.

--Reference 58 is an abstract that does not address checkerboard titration with out reference to MIC range, MIC_{50}, or MIC_{90}.

--One U.S. study had 50 isolates. Eighty five percent of the isolates were collected in 1994-1995 and 15% were collected in 1991-1994 at The Ohio State University Medical Center. MIC range was MIC_{50} was 1.0 μg/mL, and MIC_{90} was >8.0 μg/mL.

--One U.S. study had 30 isolates collected from cancer patients admitted to The University of Texas M. D. Anderson Cancer Center at Houston during the past 5 years. The MIC range was MIC_{50} was 0.5 μg/mL and MIC_{90} was 4.0 μg/mL.

Stenotrophomonas maltophilia is ubiquitous in nature and has also been isolated from the hospital environment. It is the third most frequently isolated nonfermentative gram-negative rod in the clinical laboratory. Strains may be colonizers (e.g., in cystic fibrosis) or infecting agents. Septicemia (often associated with intravenous catheters), pneumonia, and wound infections have been reported. Most of the isolates tested are not recent isolates and the MICs were greater than the susceptible breakpoint. The two recent studies with 50 and 30 isolates each reported the MIC_{90} to be >8.0 μg/mL and 4.0 μg/mL respectively. *Stenotrophomonas maltophilia* will not be allowed into the label.

Vibrio cholerae — One study, 15 isolates, MIC range MIC_{90} range: 0.03 μg/mL, median MIC_{90}: 0.03 μg/mL.

There are not enough isolates tested and *Vibrio cholerae* will not be allowed into the label.

Yersinia enterocolitica — Two study, 45 isolates, MIC range MIC_{90} range: 0.06 μg/mL, median MIC_{90}: 0.06 μg/mL.

Infectious diarrhea is not an indication for trovafloxacin and there is not enough isolates tested therefore, *Yersinia enterocolitica* will not be allowed into the label.

c. Activity Against Anaerobes

Bacteroides distasonis — Five studies, 245 isolates, MIC range MIC_{90} range median MIC_{90}: 1.0 μg/mL.

--One U.S. study (reference 60) makes no reference to *Bacteroides distasonis.*

--One U.K. study had 12 isolates collected at Southmead Hospital, Bristol Dental Hospital, the PHLS Anaerobe Reference Unit, Cardiff, and University of Bristol, Department of Medical Microbiology. The age of the isolates was not stated. The MIC range was MIC_{50} was 0.25 μg/mL, and MIC_{90} was 0.5 μg/mL.

--One U.S. study had 118 isolates collected at New England

Medical Center, Danbury Hospital, Duke University Medical Center, Loyola Medical Center, university Medical Center at University of Florida (Jacksonville), University of Michigan Medical Center, the Pittsburgh V.A. Medical Center, and the wadsworth V.A. Medical Center (Los Angeles) between 1992-1994. The MIC range was , MIC_{50} was 1.0 µg/mL, and MIC_{90} was 1.0 µg/mL.

--One U.S. study (reference 64) makes no reference to *Bacteroides distasonis*.

--One U.S. study had 43 isolates collected from several Chicago area medical centers during 1994. The MIC range was not stated, MIC_{50} was 0.5 µg/mL, and MIC_{90} was 1.0 µg/mL.

Bacteroides distasonis as a member of *Bacteroides fragilis* group is recovered from most intra-abdominal infections and may occur in infections at other sites. The MIC_{90} of well over a 100 recent isolates was 1.0 µg/mL. *Bacteroides distasonis* may be included in the label.

Bacteroides ovatus

Five studies, 218 isolates, MIC range MIC_{90} range median MIC_{90}: 2.0 µg/mL.

--One U.S. study (reference 60) makes no reference to *Bacteroides ovatus*.

--One U.K. study had 17 isolates collected at Southmead Hospital, Bristol Dental Hospital, the PHLS Anaerobe Reference Unit, Cardiff, and University of Bristol, Department of Medical Microbiology. The age of the isolates was not stated. The MIC range was MIC_{50} was 0.5 µg/mL, and MIC_{90} was 2.0 µg/mL.

--One U.S. study had 118 isolates collected at New England Medical Center, Danbury Hospital, Duke University Medical Center, Loyola Medical Center, university Medical Center at University of Florida (Jacksonville), University of Michigan Medical Center, the Pittsburgh V.A. Medical Center, and the wadsworth V.A. Medical Center (Los Angeles) between 1992-1994. The MIC range was MIC_{50} was 1.0 µg/mL, and MIC_{90} was 2.0 µg/mL.

--One U.S. study (reference 64) makes no reference to *Bacteroides ovatus*.

--One U.S. study had 24 isolates collected from several Chicago area medical centers during 1994. The MIC range was not stated, MIC_{50} was 1.0 µg/mL, and MIC_{90} was 2.0 µg/mL.

Bacteroides ovatus as a member of *Bacteroides fragilis* group is recovered from most intra-

abdominal infections and may occur in infections at other sites. The MIC_{90} of well over a 100 recent isolates was 2.0 μg/mL. *Bacteroides ovatus* will be allowed in the label.

Bacteroides uniformis

Four studies, 74 isolates, MIC range MIC_{90} range , median MIC_{90}: 4.0 μg/mL.

--One U.K. study had 13 isolates collected at Southmead Hospital, Bristol Dental Hospital, the PHLS Anaerobe Reference Unit, Cardiff, and University of Bristol, Department of Medical Microbiology. The age of the isolates was not stated. The MIC range was MIC_{50} was 0.25 μg/mL, and MIC_{90} was 2.0 μg/mL.

--One U.S. study had 23 isolates collected at New England Medical Center, Danbury Hospital, Duke University Medical Center, Loyola Medical Center, university Medical Center at University of Florida (Jacksonville), University of Michigan Medical Center, the Pittsburgh V.A. Medical Center, and the wadsworth V.A. Medical Center (Los Angeles) between 1992-1994. The MIC range was MIC_{50} was 1.0 μg/mL, and MIC_{90} was 4.0 μg/mL.

--One U.S. study (reference 64) makes no reference to *Bacteroides uniformis*.

--One U.S. study had 23 isolates collected from several Chicago area medical centers during 1994. The MIC range was not stated, MIC_{50} was 1.0 μg/mL, and MIC_{90} was 4.0 μg/mL.

Bacteroides uniformis as a member of *Bacteroides fragilis* group is recovered from most intra-abdominal infections and may occur in infections at other sites. The MIC_{90} of 46 recent isolates was 4.0 μg/mL. *Bacteroides uniformis* will not be allowed in the label.

Bacteroides vulgatus

Five studies, 150 isolates, MIC range , MIC_{90} range: 0.5-4.0 μg/mL, median MIC_{90}: 4.0 μg/mL.

--One U.S. study (reference 60) makes no reference to *Bacteroides vulgatus*.

--One U.K. study had 18 isolates collected at Southmead Hospital, Bristol Dental Hospital, the PHLS Anaerobe Reference Unit, Cardiff, and University of Bristol, Department of Medical Microbiology. The age of the isolates was not stated. The MIC range was MIC_{50} was 0.25 μg/mL, and MIC_{90} was 1.0 μg/mL.

--One U.S. study had 55 isolates collected at New England Medical Center, Danbury Hospital, Duke University Medical Center, Loyola Medical Center, university Medical Center at

University of Florida (Jacksonville), University of Michigan Medical Center, the Pittsburgh V.A. Medical Center, and the wadsworth V.A. Medical Center (Los Angeles) between 1992-1994. The MIC range was 0.125-16.0 μg/mL, MIC_{50} was 0.5 μg/mL, and MIC_{90} was 4.0 μg/mL.

--One U.S. study (reference 64) makes no reference to *Bacteroides vulgatus*.

--One U.S. study had 32 isolates collected from several Chicago area medical centers during 1994. The MIC range was not stated, MIC_{50} was 0.25 μg/mL, and MIC_{90} was 4.0 μg/mL.

Bacteroides vulgatus as a member of *Bacteroides fragilis* group is recovered from most intra-abdominal infections and may occur in infections at other sites. The MIC_{90} of 87 recent isolates was 4.0 μg/mL. *Bacteroides vulgatus* will not be allowed in the label.

Clostridium difficile

Four studies, 71 isolates, MIC range
MIC_{90} range median MIC_{90}: 1.0 μg/mL.

--One U.K. study had 30 isolates collected at University College Hospital in London and other European centers between 1993 and 1994. MIC range was , MIC_{50} was 1.0 μg/mL, and MIC_{90} was 4.0 μg/mL.

--One U.S. study (reference 60) makes no reference to *Clostridium difficile*.

--One U.S. study had 15 isolates collected at the V.A. Wadsworth Medical Center in Los Angeles. The age of the isolates were not indicated except for stating that they were "recent clinical isolates." MIC range was
MIC_{50} was 1.0 μg/mL, and MIC_{90} was 1.0 μg/mL.

--One U.K. study had 14 isolates collected at Southmead Hospital, Bristol Dental Hospital, the PHLS Anaerobe Reference Unit, Cardiff, , and University of Bristol, Department of Medical Microbiology. The age of the isolates was not stated. The MIC range was
MIC_{50} was 0.5 μg/mL, and MIC_{90} was 1.0 μg/mL.

Clostridium difficile is the major cause of antibiotic-associated diarrhea and pseudomembranous colitis. There were less than 100 isolates tested and the one U.K. study with one third of the isolates, reported the MIC_{90} to be 4.0 μg/mL. *Clostridium difficile* will not be allowed in the label.

Clostridium perfringens

Six studies, 179 isolates, MIC range , MIC_{90} range median MIC_{90}: 0.25 μg/mL.

--One U.K. study had 52 isolates collected at University College Hospital in London and other European centers between 1993 and 1994. MIC range was , MIC_{50} was 0.125 µg/mL, and MIC_{90} was 0.25 µg/mL.

--One U.S. study, 1 isolate with MIC of 0.03 µg/mL.

--One U.S. study had 20 isolates collected at the V.A. Wadsworth Medical Center in Los Angeles. The age of the isolates were not indicated except for stating that they were "recent clinical isolates." MIC range was MIC_{50} was 0.125 µg/mL, and MIC_{90} was 0.125 µg/mL.

--One U.K. study had 16 isolates collected at Southmead Hospital, Bristol Dental Hospital, the PHLS Anaerobe Reference Unit, Cardiff, and University of Bristol, Department of Medical Microbiology. The age of the isolates was not stated. The MIC range was MIC_{50} was 0.06 µg/mL, and MIC_{90} was 0.25 µg/mL.

--One U.S. study had 13 isolates. The age and the geographical location from which the isolates were recovered were not indicated. MIC range was MIC_{50} was 0.125 µg/mL, and MIC_{90} was 0.125 µg/mL.

--One U.S. study had 53 isolates collected from several Chicago area medical centers during 1994. The MIC range was not stated, MIC_{50} was 0.125 µg/mL, and MIC_{90} was 0.25 µg/mL.

Clostridium perfringens is encountered in a wide variety of clinical settings ranging from simple contamination of wounds to traumatic or nontraumatic myonecrosis, clostridial cellulitis, intra-abdominal sepsis, gangrenous choleysistitis, postabortion infections, bacteremia in various clinical settings, aspiration pneumonia, necrotizing pneumonia, and brain abscess. Considering that the MIC_{90} for 106 recent isolates is 0.25 µg/mL, *Clostridium perfringens* will be allowed in the label.

Clostridium ramosum — One study, 15 isolates, MIC range. MIC_{90} range: 0.5 µg/mL, median MIC_{90}: 0.5 µg/mL.

There are not enough isolates tested and *Clostridium ramosum* will not be allowed into the label.

Fusobacterium mortiferum — There is no *in vitro* data presented in the NDA to support the inclusion of this organism. *Fusobacterium mortiferum* will not be allowed in the label.

Fusobacterium nucleatum — Four studies, 68 isolates, MIC range: , MIC_{90} range , median MIC_{90}: 0.375 µg/mL.

--One U.S. study (reference 60) makes no reference to *Fusobacterium nucleatum*.

--One U.S. study had 28 isolates collected at the V.A. Wadsworth Medical Center in Los Angeles. The age of the isolates were not indicated except for stating that they were "recent clinical isolates." MIC range was MIC_{50} was 0.5 μg/mL, and MIC_{90} was 0.5 μg/mL.

--One U.K. study had 17 isolates collected at Southmead Hospital, Bristol Dental Hospital, the PHLS Anaerobe Reference Unit, Cardiff, , and University of Bristol, Department of Medical Microbiology. The age of the isolates was not stated. The MIC range was MIC_{50} was 0.25 μg/mL, and MIC_{90} was 0.5 μg/mL.

--One U.S. study had 12 isolates collected from several Chicago area medical centers during 1994. The MIC range was not stated, MIC_{50} was 0.5 μg/mL, and MIC_{90} was 0.5 μg/mL.

There are only 12 isolates that may be considered as "recent" isolates. The reported MIC_{90} was 0.5 μg/mL. There is not enough *in vitro* data presented to justify the inclusion of *Fusobacterium nucleatum* in the label. *Fusobacterium nucleatum* will not be allowed in the label.

Prevotella bivia

Three studies, 118 isolates, MIC range MIC_{90} range median MIC_{90}: 1.5 μg/mL.

--One U.S. study (reference 60) makes no reference to *Prevotella bivia*.

--One U.S. study had 17 isolates. The age and the geographical location from which the isolates were recovered were not indicated. MIC range was , MIC_{50} was 1.0 μg/mL, and MIC_{90} was 1.0 μg/mL.

--One U.S. study had 45 isolates collected from several Chicago area medical centers during 1994. The MIC range was not stated, MIC_{50} was 2.0 μg/mL, and MIC_{90} was 2.0 μg/mL.

Only data for 62 isolates could be found in the NDA. One study with the majority of the isolates reported the MIC_{90} to be 2.0 μg/mL. *Prevotella bivia* will not be allowed in the label.

Prevotella intermedia

Two studies, 27 isolates, MIC range MIC_{90} range: 1.0 μg/mL, median MIC_{90}: 1.0 μg/mL.

--One U.S. study (reference 60) makes no reference to *Prevotella intermedia*.

--One U.K. study had 13 isolates collected at Southmead Hospital, Bristol Dental Hospital, the PHLS Anaerobe Reference Unit, Cardiff, , and University of

Bristol, Department of Medical Microbiology. The age of the isolates was not stated. The MIC range was MIC$_{50}$ was 0.5 µg/mL, and MIC$_{90}$ was 1.0 µg/mL.

Only data for 13 isolates could be found in the NDA. There is not enough *in vitro* data presented to justify the inclusion of *Prevotella intermedia* in the label. *Prevotella intermedia* will not be allowed

Prevotella melaninogenica — Two studies, 21 isolates, MIC range , MIC$_{90}$ range median MIC$_{90}$: 1.5 µg/mL.

--One U.S. study had one isolate with MIC of 1.0 µg/mL.

--One U.S. study had 10 isolates collected from several Chicago area medical centers during 1994. The MIC range was not stated, MIC$_{50}$ was 0.25 µg/mL, and MIC$_{90}$ was 2.0 µg/mL.

Only data for 11 isolates could be found in the NDA. There is not enough *in vitro* data presented to justify the inclusion of *Prevotella melaninogenica* in the label. *Prevotella melaninogenica* will not be allowed

d. Activity Against "Other" Organisms

Legionella dumoffii
Legionella micdadei
Legionella longbeacheae
Legionella maltophilia — There were no *in vitro* data presented in the NDA to support inclusion of *Legionella dumoffii, Legionella micdadei, Legionella longbeacheae,* or *Legionella maltophili*??. These organisms will not be allowed in the label.

Mycoplasma hominis — Three studies, 121 isolates, MIC range: 0.008-0.125 µg/mL, MIC$_{90}$ range median MIC$_{90}$: 0.03 µg/mL.

--One U.K. study had 10 isolates collected at University College Hospital in London and other European centers between 1993 and 1994. MIC range was , MIC$_{50}$ was not reported, and MIC$_{90}$ was 0.125 µg/mL.

--One U.S. study had tested 42 isolates at University of Washington in Seattle. The age and the geographical location of the isolates were not reported. MIC range was MIC$_{50}$ was 0.06 µg/mL, and MIC$_{90}$ was 0.06 µg/mL.

--One U.S. study had tested 69 clinical isolates at University of Alabama at Birmingham. The age of the isolates were not reported. MIC range was , MIC$_{50}$ was 0.016 µg/mL, and MIC$_{90}$ was 0.031 µg/mL.

The role of *Mycoplasma hominis* in genitourinary tract infections is controversial. Difficulty in accepting *Mycoplasma hominis* as cause of disease has arisen either because samples cannot be obtained easily from the affected site (for example, the fallopian tube) or because the organisms are recovered from asymptomatic individuals. Never the less, there is evidence that these species play etiologic role in some genital tract diseases of both men and women. *Mycoplasma hominis* has been isolated from the upper urinary tract only in patients with symptoms of acute pyelonephritis, often with an antibody response. *Mycoplasma hominis* will be included in the label.

Ureaplasma urealyticum

Three studies, 157 isolates, MIC range
MIC_{90} range , median MIC_{90}: 0.5 µg/mL.

--One U.K. study had 10 isolates collected at University College Hospital in London and other European centers between 1993 and 1994. MIC range was MIC_{50} was not reported, and MIC_{90} was 0.5 µg/mL.

--One U.S. study had tested 46 isolates at University of Washington in Seattle. The age and the geographical location of the isolates were not reported. MIC range was MIC_{50} was 0.125 µg/mL, and MIC_{90} was 0.5 µg/mL.

--One U.S. study had tested 101 clinical isolates at University of Alabama at Birmingham. The age of the isolates were not reported. MIC range was MIC_{50} was 0.063 µg/mL, and MIC_{90} was 0.125

The role of *Ureaplasma urealyticum* in genitourinary tract is controversial. Difficulty in accepting *U. urealyticum* as cause of disease has arisen either because samples cannot be obtained easily from the affected site (for example, the fallopian tube) or because the organisms are recovered from asymptomatic individuals. Never the less, there is evidence that these species play etiologic role in some genital tract diseases of both men and women. *Ureaplasma urealyticum* has been associated with nonchlamydial nongonococcal urethritis in men and women. *Ureaplasma urealyticum* will be included in the label.

Toxoplasma gondii

There were no *in vitro* data presented in the NDA to support the inclusion of *Toxoplasma gondii* in the label. *Toxoplasma gondii* will not be allowed in the label.

In the label the *in vitro* organisms with MIC_{90} values $\leq$1.0 µg/mL should, therefore, read as follows:

Aerobic gram-negative microorganisms:
Citrobacter freundii
Enterobacter aerogenes
Morganella morganii
Proteus vulgaris

Anaerobic microorganisms: