CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

50675_S14

STATISTICAL REVIEW(S)

SEP 28 1998

STATISTICAL REVIEW AND EVALUATION

NDA:	50-675/S-014 Vantin® Oral Suspension (5 mg/kg b.i.d. for 5 days)
Generic Name:	Cefpodoxime proxetil
Trademark:	Vantin®
Formulation:	Oral Suspension
Drug Class:	1-S
Applicant:	Pharmacia & Upjohn Trading Corporation.
Indications:	Acute otitis media in pediatric patients
Documents Reviewed:	NDA volumes 21.1 - 21.31 dated December 23, 1997
Type of Review:	Clinical
Medical Officer:	Roopa Viraraghavan, M.D., HFD-520
Statistical Reviewer:	Joel Jiang, Ph.D., HFD-725
Project Manager:	Carmen DeBellas, HFD-520

Review's Note:

1. Reviewer's comments are given in italics throughout the review.

2. Throughout the review, the following term is abbreviated and referred to as:
cefpodoxime = cefpodoxime proxetil

I. INTRODUCTION

The Applicant submitted two studies, 0098-A and 0098-B, as evidence to support cefpodoxime regarding this indication. The general designs of the studies are as follows:

Study 0098-A was a prospective, randomized, evaluator-blind, multicenter, comparative trial which compared the safety and efficacy of cefpodoxime (5 mg/kg b.i.d. for 5 days) versus cefixime (8 mg/kg q.d. for 10 days), for the treatment of pediatric subjects 2 months through 12 years of age with unilateral or bilateral acute suppurative otitis media. It was initiated on November 10, 1993 and completed on August 1, 1996.

Study 0098-B was a prospective, randomized, evaluator-blind, multicenter, comparative trial which compared the safety and efficacy of cefpodoxime (5 mg/kg b.i.d. for 5 days) versus cefixime (8 mg/kg q.d. for 10 days), for the treatment of pediatric subjects 2 months through 12 years of age with unilateral or bilateral acute suppurative otitis media. It was initiated on October 25, 1993 and completed on July 30, 1996.

II. STUDY 0098-A

II.A. METHODS

Approximately 200 evaluable subjects between the age of 2 months and less than 12 years were collectively enrolled (100 subjects in each treatment group). Subjects who met the inclusion/exclusion criteria were randomized to one of the two treatment groups in a 1:1 ratio to either 5-day regimen of cefpodoxime administered b.i.d. at 10 mg/kg/day or 10 day regimen of cefixime administered q.d. at 8 mg/kg/day.

Study visits were scheduled for Pretreatment Visit (Day 0), Phone Call (Day 2-3), Second Visit (Day 7-10), Third Visit (Day 12-15), and Final Visit (Day 25-38). Table 2.1 demonstrates study visit schedules which were specified by the protocol. Subjects were examined for progress of infection and for safety at the later three visits. In addition, safety was also assessed whenever deemed necessary. The measures of data quality assurance were taken to obtain consistent, accurate, and complete data.

TABLE 2.1: STUDY 0098A: SCHEDULE OF STUDY PROCEDURES

Visit Number	Pretreatment	Second Visit	Third Visit	Final Visit
Allowable Study Window	Day 0	Day 7-10	Day 12-15	Day 25-38
Informed Consent	X			
Medical History	X			
Physical Examination	X			
Pneumatic Otoscopy	X	X	X	X
Microbiology Culture & Sensitivity Testing	X	X	X	X
Clinical Observation	X	X	X	X
Drug Compliance			X	

EFFICACY EVALUATION

The efficacy criteria were clinical and bacteriologic responses. The progress of infection for each ear was determined by evaluating the degree of change from the previous visit.

The overall clinical evaluation was based only on clinical signs and symptoms and was independent of any bacteriologic culture that might have been obtained. The progress of infection was recorded for both of each patient's ears. Subjects were evaluated by ear each follow-up visit and categorized as cure, improved, unchanged, and worsened. An overall bacteriologic evaluation was obtained for each subject at each post pretreatment visit, which was classified as presumptive cure, presumptive failure, side effect failure, non-investigational antibiotic, and not reported. The by pathogen bacteriologic evaluation was obtained using information from both ears, which was coded as eradication, persistence, recurrence, and not reported.

The primary efficacy endpoints defined in the pivotal protocol were clinical success and bacteriologic cure at End of Therapy and at Test of Cure. The End of Therapy window corresponded to Visit 2 for the cefpodoxime treated subjects and Visit 3 for the cefixime treated subjects. The Test of Cure window was retrospectively defined as 4 to 21 days post treatment, inclusive. The primary efficacy measures included overall clinical evaluations, overall bacteriologic evaluations, and by pathogen bacteriologic evaluations at

these two endpoints. Clinical and bacteriologic evaluations at Visit 2, Visit 3, and Final Visit were the second efficacy measures.

Reviewer's Note: The Medical Officer agreed with Applicant's definition of evaluable population, and consented with the Applicant's assessment for clinical and bacteriologic outcomes. However, overall bacteriologic responses of the evaluable subjects at Test of Cure were considered by the Medical Officer as the primary efficacy measure, and all the other efficacy measures were the secondary. The Medical Officer also defined another group of subjects called the Medical Officer sub-population in terms of certain evaluable criteria.

Please refer to the Medical Officer's review for detailed descriptions of the Applicant's and Medical Officer's efficacy outcome definitions.

SAFETY EVALUATION

All medical events that were spontaneously reported by the subjects or directly observed by the investigator during the study were reported to the sponsor, regardless of whether the events were considered to be related to the study medication. Also, any event that occurred subsequent to the study period was reported if the investigator judged it to be related to the study medication.

Safety was evaluated by the frequencies of all medical events, treatment related medical events, serious medical events, and events that led to study discontinuation.

STATISTICAL METHODS

The comparisons of interest in the study were conducted between cefpodoxime and cefixime.

Reviewer's Note: All efficacy analyses were conducted for the Intent-to-treat subjects, the evaluable subjects, and the subjects of the Medical Officer sub-population, among which the evaluable subjects was considered primary for the analysis of efficacy data. All of the subjects in these three groups were assessed for their overall bacteriologic outcomes, by pathogen bacteriologic outcomes, and overall clinical outcomes at Test of Cure. The evaluable subjects and the subjects of the Medical Officer sub-population were also evaluated at End of Therapy, Visit 2, Visit 3, and Final Visit. For analysis purpose, subjects were classified into two general categories: cure/success or failure, and pathogens were classified as eradication or failure. Now that the efficacy parameters outlined by the Applicant and the Medical Officer were not always identical, this reviewer proceeded basically upon the Medical Officer's in efficacy evaluation.

The primary efficacy analysis was the comparison of the treatment groups with respect to the bacteriologic cure rate at Test of Cure in the evaluable population for the purpose of establishing the equivalence of the two treatments. Equivalence between the treatments with respect to efficacy variables was assessed by computing the two-tailed 95% confidence interval of the difference in response rates. The confidence intervals were computed using a normal approximation to binomial, and included a continuity correction. The evaluation of whether the treatment groups were considered equally effective is judged by the draft DAIDP "Points to Consider" document pertaining to results of confidence intervals. The secondary efficacy measures included overall bacteriologic evaluations, by pathogen bacteriologic evaluations, and overall clinical evaluations at End of Therapy, Visit 2, Visit 3, and Final Visit, which were analyzed using the same methods as were used to evaluate the primary efficacy measures.

Subset analyses by gender, age, and race were performed for the primary efficacy variables. Homogeneity of treatment effect across subgroups was assessed via Breslow-Day's test.

Evaluation of safety data was based on review of adverse events within treatment groups for all subjects who received at least one dose of study drug. This reviewer conducted safety analyses with the following variables: the rate of at least one adverse event, the rate of at least one treatment related adverse event, the rate of severe adverse events, and the rate of discontinuation due to adverse events. The statistical comparisons between the two treatment groups were performed using Fisher's exact test.

Prior to performing efficacy analyses, this reviewer assessed the comparability of the treatment groups with respect to pretreatment characteristics, including demographics, baseline disease characteristics, evaluability status, and medication compliance. Quantitative variables were assessed using the t-test. Qualitative variables were assessed using Fisher's exact test.

All tests were two-sided and used a 5% level of significance. A 15% level of significance was applied to the test of homogeneity.

II.B. RESULTS

An actual total of 455 subjects were enrolled at 12 centers in the USA between November 10, 1993 and August 1, 1996. Of these enrolled subjects, 225 (49.5%) cefpodoxime treated subjects and 230 (50.5%) cefixime treated subjects were included in the intent-to-treat analyses, and 88 subjects in the cefpodoxime group and 93 subjects in the cefixime group completed the study. The primary reason for study discontinuation in both treatment groups was failure to meet the protocol eligibility criteria, followed by lack of efficacy, lost to follow-up, nonserious medical events, noncompliance, and personal request. The evaluable group comprised 124 cefpodoxime subjects and 132 cefixime subjects. The primary reason for nonevaluability in each treatment group was no isolated pathogen or resistant pathogens at pretreatment. There were 125 cefpodoxime subjects and 128 cefixime subjects in the Medical Officer sub-population group.

Reviewer's Note: The number and percentage of subjects included in each analysis group are presented in Table 2.2. There were no notable treatment differences with respect to the percentage of subjects included in each analysis group. Demographic data are described for the intent-to-treat subjects, the evaluable subjects, and the subjects of the Medical Officer sub-population in Tables 2.3, 2.4, and 2.5, respectively, and no statistically significant differences were detected in these pretreatment characteristics of the two treatment groups. The pneumatic otoscopy and/or tympanometry data at pretreatment for the intent-to-treat subjects, the evaluable subjects, and the subjects of the Medical Officer sub-population are shown in Tables 2.6, 2.7, and 2.8, respectively, and the two treatment groups were not significantly different with respect to these findings.

TABLE 2.2: STUDY 0098A: SUBJECTS POPULATIONS

Treatment Group for Clinical Response	Subjects Included	
	Cefpodoxime (N=225)	Cefixime (N=230)
Intent-to-Treat	225 (100%)	230 (100%)
Evaluable	124 (55.1%)	132 (57.4%)
MO Sub-Population	125 (55.6%)	128 (55.7%)

TABLE 2.3: STUDY PRT-0098A: SUMMARY OF DEMOGRAPHIC DATA FOR THE ITT SUBJECTS

Number of Subjects	Cefpodoxime (N=225)	Cefixime (N=230)	P-value
Age (yrs.)	3.3 ± 2.5	3.2 ± 2.6	*0.545
< 2 yrs.	91 (40.4%)	102 (44.4%)	0.448
≥ 2 yrs.	134 (59.6%)	128 (55.7%)	
Gender			
Male	121 (53.8%)	135 (58.7%)	0.300
Female	104 (46.2%)	95 (41.3%)	
Race			
White	109 (48.4%)	111 (48.3%)	0.102
Black	17 (7.6%)	22 (9.6%)	
Hispanic	91 (40.4%)	96 (41.7%)	
Other	8 (3.6%)	1 (0.4%)	

* P-value is obtained by t-test, otherwise, by Fisher's exact test

TABLE 2.4: STUDY PRT-0098A: SUMMARY OF DEMOGRAPHIC DATA FOR THE EVALUABLE SUBJECTS

Number of Subjects	Cefpodoxime (N=124)	Cefixime (N=132)	P-value
Age (yrs.)	3.1 ± 2.2	2.8 ± 2.3	*0.433
< 2 yrs.	52 (41.9%)	66 (50.0%)	0.211
≥ 2 yrs.	72 (58.1%)	66 (50.0%)	
Gender			
Male	64 (51.6%)	72 (54.6%)	0.707
Female	60 (48.4%)	60 (45.5%)	
Race			
White	66 (53.2%)	72 (54.6%)	0.381
Black	10 (8.1%)	9 (6.8%)	
Hispanic	43 (34.7%)	50 (37.9%)	
Other	5 (4.0%)	1 (0.8%)	

* P-value is obtained by t-test, otherwise, by Fisher's exact test

TABLE 2.5: STUDY PRT-0098A: SUMMARY OF DEMOGRAPHIC DATA FOR THE SUBJECTS OF THE MO SUB-POPULATION

Number of Subjects	Cefpodoxime (N=125)	Cefixime (N=128)	P-value
Age (yrs.)	3.1 ± 2.3	2.9 ± 2.4	*0.542
< 2 yrs.	54 (43.2%)	64 (50.0%)	0.314
≥ 2 yrs.	71 (56.8%)	64 (50.0%)	
Gender			
Male	64 (51.2%)	69 (53.9%)	0.706
Female	61 (48.8%)	59 (46.1%)	
Race			
White	70 (56.0%)	71 (55.5%)	0.413
Black	10 (8.0%)	10 (7.8%)	
Hispanic	40 (32.0%)	46 (35.9%)	
Other	5 (4.0%)	1 (0.8%)	

* P-value is obtained by t-test, otherwise, by Fisher's exact test

TABLE 2.6: STUDY PRT-0098A: SUMMARY OF PNEUMATIC OTOSCOPY AND/OR TYMPANOMETRY DATA AT PRETREATMENT FOR THE ITT SUBJECTS

Number of Subjects	Cefpodoxime (N=225)	Cefixime (N=230)	P-value
Tympanic Membrane Abnormal	225 (100%)	230 (100%)	NA
Hyperemic			
Yes	217 (96.4%)	216 (93.9%)	0.275
Opaque			
Yes	221 (98.2%)	225 (97.8%)	1.000
Bulging			
Yes	191 (84.9%)	197 (85.7%)	0.895
Light Reflex Absent			
Yes	224 (99.6%)	226 (98.3%)	0.372
Impaired Mobility			
Yes	224 (99.6%)	227 (98.7%)	0.623
Perforation			
Yes	45 (20.0%)	55 (23.9%)	0.365

TABLE 2.7: STUDY PRT-0098A: SUMMARY OF PNEUMATIC OTOSCOPY AND/OR TYMPANOMETRY DATA AT PRETREATMENT FOR THE EVALUABLE SUBJECTS

Number of Subjects	Cefpodoxime (N=124)	Cefixime (N=132)	P-value
Tympanic Membrane Abnormal	124 (100%)	132 (100%)	NA
Hyperemic Yes	117 (94.4%)	122 (92.4%)	0.620
Opaque Yes	123 (99.2%)	130 (98.5%)	1.000
Bulging Yes	105 (84.7%)	116 (87.9%)	0.473
Light Reflex Absent Yes	124 (100%)	131 (99.2%)	1.000
Impaired Mobility Yes	124 (100%)	131 (99.2%)	1.000
Perforation Yes	22 (17.7%)	27 (20.5%)	0.635

TABLE 2.8: STUDY PRT-0098A: SUMMARY OF PNEUMATIC OTOSCOPY AND/OR TYMPANOMETRY DATA AT PRETREATMENT FOR THE SUBJECTS OF THE MO SUB-POPULATION

Number of Subjects	Cefpodoxime (N=125)	Cefixime (N=128)	P-value
Tympanic Membrane Abnormal	125 (100%)	128 (100%)	NA
Hyperemic Yes	119 (95.2%)	118 (92.2%)	0.440
Opaque Yes	124 (99.2%)	127 (99.2%)	1.000
Bulging Yes	102 (81.6%)	114 (89.1%)	0.110
Light Reflex Absent Yes	125 (100%)	128 (100%)	NA
Impaired Mobility Yes	125 (100%)	128 (100%)	NA
Perforation Yes	28 (22.4%)	29 (14.8%)	0.146

Reviewer's Note: *The overall bacteriologic responses at Test of Cure as per the intent-to-treat subjects, the evaluable subjects, and the subjects of the Medical Officer sub-population are presented in Tables 2.9, 2.10, and 2.11, respectively. Comparisons (95% confidence intervals) of the difference between the two treatment groups show that cefpodoxime was therapeutically equivalent to cefixime with respect to overall bacteriologic outcomes.*

Subset analyses by gender, age, and race for the overall bacteriologic cure rates in the evaluable subjects are shown in Table 2.12. Results are consistent across all three demographic aspects.

TABLE 2.9: STUDY 0098A: OVERALL BACTERIOLOGIC RESPONSE OF THE ITT SUBJECTS AT TEST OF CURE

Bacteriological Response	Cefpodoxime (N=225)	Cefixime (N=230)
Cure	89 (39.6%)	80 (34.8%)
Failure	136 (60.4%)	150 (65.2%)
Cefpodoxime vs Cefixime by Cure	4.8%, 95% C.I.: -4.5%, 14.1%	

TABLE 2.10: STUDY 0098A: OVERALL BACTERIOLOGIC RESPONSE OF THE EVALUABLE SUBJECTS AT TEST OF CURE

Bacteriological Response	Cefpodoxime (N=124)	Cefixime (N=132)
Cure	77 (62.1%)	75 (56.8%)
Failure	47 (37.9%)	57 (43.2%)
Cefpodoxime vs Cefixime by Cure	5.3%, 95% C.I.: -7.5%, 18.1%	

TABLE 2.11: STUDY 0098A: OVERALL BACTERIOLOGIC RESPONSE OF THE SUBJECTS OF THE MO SUB-POPULATION AT TEST OF CURE

Bacteriological Response	Cefpodoxime (N=125)	Cefixime (N=128)
Cure	75 (60.0%)	72 (56.3%)
Failure	50 (40.0%)	56 (43.7%)
Cefpodoxime vs Cefixime by Cure	3.8%, 95% C.I.: -9.2%, 16.7%	

TABLE 2.12: STUDY 0098A: SUBSET ANALYSES BY DEMOGRAPHIC ASPECTS OF THE OVERALL BACTERIOLOGICAL CURE RATES OF THE EVALUABLE SUBJECTS AT TEST OF CURE

Subset	Cefpodoxime (N=124)	Cefixime (N=132)	95% C.I.	P-value Breslow-Day's
Male	39/64 (60.9%)	44/72 (61.1%)	(-25.3%, 10.4%)	0.341
Female	38/60 (63.3%)	31/60 (51.7%)	(-14.4%, 24.4%)	
< 2 yrs.	26/52 (50.0%)	32/66 (48.5%)	(-31.6%, 7.9%)	0.700
≥ 2 yrs.	51/72 (70.8%)	43/66 (65.2%)	(-12.9%, 21.7%)	
White	40/66 (60.6%)	42/72 (58.3%)	(-18.5%, 17.2%)	0.633
Black	8/10 (80.0%)	5/9 (55.6%)	NA	
Hispanic	26/43 (60.5%)	27/50 (54.0%)	(-24.1%, 20.3%)	
Other	3/5 (60.0%)	1/1 (100%)	NA	

Reviewer's Note: The pathogen eradication rates for the most common isolated baseline pathogens at Test of Cure are summarized for the intent-to-treat subjects, the Applicant evaluable subjects, and the subjects of the Medical Officer sub-population in Table 2.13, 2.14, and 2.15, respectively.

TABLE 2.13: STUDY 0098A: BY PATHOGEN BACTERIAL ERADICATION RATES OF THE ITT SUBJECTS AT TEST OF CURE (FOR MOST COMMON ISOLATED BASELINE PATHOGENS)

Pathogen	Cefpodoxime	Cefixime	Cefpodoxime vs Cefixime by Eradication
H. influenzae	0/0 (NA)	2/3 (66.7%)	NA
H. influenzae (ß-l. -)	19/29 (65.5%)	19/24 (79.2%)	-13.6%, 95% C.I.: -41.2%, 13.9%
H. influenzae (ß-l. +)	14/21 (66.7%)	13/19 (68.4%)	-1.8%, 95% C.I.: -35.8%, 32.3%
M. catarrhalis	0/1 (0%)	3/5 (50.0%)	NA
M. catarrhalis (ß-l. -)	2/4 (50.0%)	2/3 (66.7%)	NA
M. catarrhalis (ß-l. +)	9/15 (60.0%)	8/19 (42.1%)	17.9%, 95% C.I.: -21.3%, 57.1%
S. pneumoniae	42/64 (65.6%)	31/63 (49.2%)	16.4%, 95% C.I.: -2.1%, 35.0%
S. pyogenes	10/12 (83.3%)	7/13 (53.8%)	29.5%, 95% C.I.: -12.9%, 71.8%

TABLE 2.14: STUDY 0098A: BY PATHOGEN BACTERIAL ERADICATION RATES OF THE EVALUABLE SUBJECTS AT TEST OF CURE (FOR MOST COMMON ISOLATED BASELINE PATHOGENS)

Pathogen	Cefpodoxime	Cefixime	Cefpodoxime vs Cefixime by Eradication
H. influenzae	0/0 (NA)	2/3 (66.7%)	NA
H. influenzae (ß-l. -)	16/25 (64.0%)	18/23 (78.3%)	-14.3%, 95% C.I.: -43.7%, 15.2%
H. influenzae (ß-l. +)	14/19 (73.7%)	13/19 (68.4%)	5.3%, 95% C.I.: -28.8%, 39.3%
M. catarrhalis	0/1 (0%)	3/5 (60.0%)	NA
M. catarrhalis (ß-l. -)	2/3 (66.7%)	2/3 (66.7%)	NA
M. catarrhalis (ß-l. +)	9/15 (60.0%)	7/17 (41.2%)	18.8%, 95% C.I.: -21.5%, 59.2%
S. pneumoniae	35/54 (64.8%)	29/57 (50.9%)	13.9%, 95% C.I.: -6.0%, 33.9%
S. pyogenes	9/11 (81.2%)	6/12 (50.0%)	31.8%, 95% C.I.: -13.2%, 76.9%

TABLE 2.15: STUDY 0098A: BY PATHOGEN BACTERIAL ERADICATION RATES OF THE SUBJECTS OF THE MO SUB-POPULATION AT TEST OF CURE (FOR MOST COMMON ISOLATED BASELINE PATHOGENS)

Pathogen	Cefpodoxime	Cefixime	Cefpodoxime vs Cefixime by Eradication
H. influenzae	0/0 (NA)	2/3 (66.7%)	NA
H. influenzae (ß-l. -)	16/25 (64.0%)	18/22 (81.8%)	-17.8%, 95% C.I.: -46.9%, 11.2%
H. influenzae (ß-l. +)	12/17 (70.6%)	11/17 (64.7%)	5.9%, 95% C.I.: -31.4%, 43.2%
M. catarrhalis	0/1 (0%)	3/5 (60.0%)	NA
M. catarrhalis (ß-l. -)	1/2 (50.0%)	2/3 (66.7%)	NA
M. catarrhalis (ß-l. +)	8/14 (57.1%)	7/16 (43.8%)	13.4%, 95% C.I.: -28.8%, 55.6%
S. pneumoniae	36/55 (65.5%)	29/55 (52.7%)	12.7%, 95% C.I.: -7.3%, 32.8%
S. pyogenes	10/12 (83.3%)	5/11 (45.5%)	37.9%, 95% C.I.: -7.0%, 82.8%

Reviewer's Note: *The 95% confidence intervals for the difference in success rates of the overall clinical responses at Test of Cure between cefpodoxime and cefixime groups indicate the therapeutic equivalence of the two treatment groups as per the intent-to-treat subjects, the evaluable subjects, and the subjects of the Medical Officer sub-population, which are presented in Tables 2.16, 2.17, and 2.18, respectively.*

TABLE 2.16: STUDY 0098A: OVERALL CLINICAL RESPONSE OF THE ITT SUBJECTS AT TEST OF CURE

Clinical Response	Cefpodoxime (N=225)	Cefixime (N=230)
Success Failure	91 (40.4%) 134 (59.6%)	81 (35.2%) 149 (64.8%)
Cefpodoxime vs Cefixime by Success	5.2%, 95% C.I.: -4.1%, 14.6%	

TABLE 2.17: STUDY 0098A: OVERALL CLINICAL RESPONSE OF THE EVALUABLE SUBJECTS AT TEST OF CURE

Clinical Response	Cefpodoxime (N=124)	Cefixime (N=132)
Success Failure	77 (62.1%) 47 (37.9%)	75 (56.8%) 57 (43.2%)
Cefpodoxime vs Cefixime by Success	5.3%, 95% C.I.: -7.5%,18.1%	

TABLE 2.18: STUDY 0098A: OVERALL CLINICAL RESPONSE OF THE SUBJECTS OF THE MO SUB-POPULATION AT TEST OF CURE

Clinical Response	Cefpodoxime (N=125)	Cefixime (N=128)
Success Failure	75 (60.0%) 50 (40.0%)	73 (57.0%) 55 (43.0%)
Cefpodoxime vs Cefixime by Success	3.0%, 95% C.I.: -10.0%, 15.9%	

Reviewer's Note: *The overall bacteriologic responses at End of Therapy are shown for the intent-to-treat subjects, the evaluable subjects, and the subjects of the Medical Officer sub-population in Tables 2.19, 2.20, and 2.21, respectively. All comparisons (95% confidence intervals) of the difference between the two treatment groups illustrate the superiority of cefpodoxime to cefixime.*

TABLE 2.19: STUDY 0098A: OVERALL BACTERIOLOGIC RESPONSE OF THE ITT SUBJECTS AT END OF THERAPY		
Bacteriological Response	Cefpodoxime (N=225)	Cefixime (N=230)
Cure	127 (56.4%)	101 (43.9%)
Failure	98 (43.6%)	129 (56.1%)
Cefpodoxime vs Cefixime by Cure	12.5%, 95% C.I.: 3.0%, 22.1%	

TABLE 2.20: STUDY 0098A: OVERALL BACTERIOLOGIC RESPONSE OF THE EVALUABLE SUBJECTS AT END OF THERAPY		
Bacteriological Response	Cefpodoxime (N=124)	Cefixime (N=132)
Cure	108 (87.1%)	95 (72.0%)
Failure	16 (12.9%)	37 (28.0%)
Cefpodoxime vs Cefixime by Cure	15.1%, 95% C.I.: 4.7%, 25.6%	

TABLE 2.21: STUDY 0098A: OVERALL BACTERIOLOGIC RESPONSE OF THE SUBJECTS OF THE MO SUB-POPULATION AT END OF THERAPY		
Bacteriological Response	Cefpodoxime (N=125)	Cefixime (N=128)
Cure	107 (85.6%)	90 (70.3%)
Failure	18 (14.4%)	38 (29.7%)
Cefpodoxime vs Cefixime by Cure	15.3%, 95% C.I.: 4.5%, 26.1%	

Reviewer's Note: *The pathogen eradication rates for the most common isolated baseline pathogens at End of Therapy are summarized for the intent-to-treat subjects, the evaluable subjects, and the subjects of the Medical Officer sub-population in Table 2.22, 2.23, and 2.24, respectively.*

TABLE 2.22: STUDY 0098A: BY PATHOGEN BACTERIAL ERADICATION RATES OF THE ITT SUBJECTS AT END OF THERAPY (FOR MOST COMMON ISOLATED BASELINE PATHOGENS)			
Pathogen	Cefpodoxime	Cefixime	Cefpodoxime vs Cefixime by Eradication
H. influenzae	0/0 (NA)	2/3 (66.7%)	NA
H. influenzae (ß-l. -)	28/31 (90.3%)	20/24 (83.3%)	7.0%, 95% C.I.: -14.9%, 28.9%
H. influenzae (ß-l. +)	18/22 (81.8%)	16/21 (76.2%)	5.6%, 95% C.I.: -23.3%, 34.6%
M. catarrhalis	0/1 (0%)	4/7 (57.1%)	NA
M. catarrhalis (ß-l. -)	4/5 (80.0%)	3/3 (100%)	NA
M. catarrhalis (ß-l. +)	11/15 (73.3%)	12/19 (63.2%)	10.2%, 95% C.I.: -27.0%, 47.3%
S. pneumoniae	64/69 (92.8%)	44/66 (66.7%)	26.1%, 95% C.I.: 11.7%, 40.5%
S. pyogenes	11/12 (91.7%)	9/13 (69.2%)	22.4%, 95% C.I.: -15.1%, 60.0%

TABLE 2.23: STUDY 0098A: BY PATHOGEN BACTERIAL ERADICATION RATES OF THE EVALUABLE SUBJECTS AT END OF THERAPY (FOR MOST COMMON ISOLATED BASELINE PATHOGENS)			
Pathogen	Cefpodoxime	Cefixime	Cefpodoxime vs Cefixime by Eradication
H. influenzae	0/0 (NA)	2/3 (66.7%)	NA
H. influenzae (ß-l. -)	23/25 (92.0%)	20/24 (83.3%)	8.7%, 95% C.I.: -13.7%, 31.1%
H. influenzae (ß-l. +)	17/19 (89.5%)	15/20 (75.0%)	14.5%, 95% C.I.: -14.1%, 43.1%
M. catarrhalis	0/1 (0%)	4/6 (66.7%)	NA
M. catarrhalis (ß-l. -)	2/3 (66.7%)	3/3 (100%)	NA
M. catarrhalis (ß-l. +)	11/15 (73.3%)	11/18 (61.1%)	12.2%, 95% C.I.: -25.6%, 50.1%
S. pneumoniae	54/57 (94.7%)	40/61 (65.6%)	29.2%, 95% C.I.: 14.2%, 44.1%
S. pyogenes	10/11 (90.9%)	8/12 (66.7%)	24.2%, 95% C.I.: -16.1%, 64.6%

TABLE 2.24: STUDY 0098A: BY PATHOGEN BACTERIAL ERADICATION RATES OF THE SUBJECTS OF THE MO SUB-POPULATION AT END OF THERAPY (FOR MOST COMMON ISOLATED BASELINE PATHOGENS)			
Pathogen	Cefpodoxime	Cefixime	Cefpodoxime vs Cefixime by Eradication
H. influenzae	0/0 (NA)	2/3 (66.7%)	NA
H. influenzae (ß-l. -)	24/26 (92.3%)	19/23 (82.6%)	9.7%, 95% C.I.: -13.0%, 32.4%
H. influenzae (ß-l. +)	15/17 (88.2%)	14/19 (73.7%)	14.6%, 95% C.I.: -16.1%, 45.2%
M. catarrhalis	0/1 (0%)	3/5 (60.0%)	NA
M. catarrhalis (ß-l. -)	2/3 (66.7%)	3/3 (100%)	NA
M. catarrhalis (ß-l. +)	10/14 (71.4%)	10/17 (58.8%)	12.6%, 95% C.I.: -27.2%, 52.4%
S. pneumoniae	55/58 (94.8%)	40/59 (67.8%)	27.0%, 95% C.I.: 12.1%, 42.0%
S. pyogenes	11/12 (91.7%)	7/11 (63.6%)	28.0%, 95% C.I.: -13.1%, 69.2%

Reviewer's Note: *Tables 2.25, 2.26, and 2.27 show clinical responses of the intent-to-treat subjects, the Applicant evaluable subjects, and the subjects of the Medical Officer sub-population at End of Therapy, respectively. Confidence interval results from these populations show that the cefpodoxime was therapeutically superior to cefixime with respect to the success rates at this time point.*

TABLE 2.25: STUDY 0098A: OVERALL CLINICAL RESPONSE OF THE ITT SUBJECTS AT END OF THERAPY		
Clinical Response	Cefpodoxime (N=225)	Cefixime (N=230)
Success	129 (57.3%)	101 (43.9%)
Failure	96 (42.7%)	129 (56.1%)
Cefpodoxime vs Cefixime by Success	13.4%, 95% C.I.: 3.9%, 23.0%	

TABLE 2.26: STUDY 0098A: OVERALL CLINICAL RESPONSE OF THE EVALUABLE SUBJECTS AT END OF THERAPY		
Clinical Response	Cefpodoxime (N=124)	Cefixime (N=132)
Success Failure	108 (87.1%) 16 (12.9%)	94 (71.2%) 38 (28.8%)
Cefpodoxime vs Cefixime by Success	15.9%, 95% C.I.: 5.4%, 26.4%	

TABLE 2.27: STUDY 0098A: OVERALL CLINICAL RESPONSE OF THE SUBJECTS OF THE MO SUB-POPULATION AT END OF THERAPY		
Clinical Response	Cefpodoxime (N=125)	Cefixime (N=128)
Success Failure	107 (85.6%) 18 (14.4%)	90 (70.3%) 38 (29.7%)
Cefpodoxime vs Cefixime by Success	15.3%, 95% C.I.: 4.5%, 26.1%	

Reviewer's Note: *The following twelve tables (Tables 2.28 to 2.39) present other secondary efficacy data as per the evaluable subjects and the subjects of the Medical Officer sub-population, including overall bacteriologic and clinical responses at Visit 2, Visit 3, and Final Visit. Confidence interval results show that the two treatment groups were therapeutically equivalent with respect to the overall bacteriological responses and the overall clinical responses at these time points.*

TABLE 2.28: STUDY 0098A: OVERALL BACTERIOLOGIC RESPONSE OF THE EVALUABLE SUBJECTS AT VISIT 2		
Bacteriological Response	Cefpodoxime (N=124)	Cefixime (N=130)
Cure Failure	108 (87.1%) 16 (12.9%)	107 (81.1%) 25 (18.9%)
Cefpodoxime vs Cefixime by Cure	6.0%, 95% C.I.: -3.7%, 15.7%	

TABLE 2.29: STUDY 0098A: OVERALL BACTERIOLOGIC RESPONSE OF THE SUBJECTS OF THE MO SUB-POPULATION AT VISIT 2		
Bacteriological Response	Cefpodoxime (N=125)	Cefixime (N=128)
Cure Failure	107 (85.6%) 18 (14.4%)	102 (79.7%) 26 (20.3%)
Cefpodoxime vs Cefixime by Cure	5.9%, 95% C.I.: -4.2%, 16.0%	

TABLE 2.30: STUDY 0098A: OVERALL BACTERIOLOGIC RESPONSE OF THE EVALUABLE SUBJECTS AT VISIT 3		
Bacteriological Response	Cefpodoxime (N=124)	Cefixime (N=132)
Cure	87 (70.2%)	95 (72.0%)
Failure	37 (29.8%)	37 (28.0%)
Cefpodoxime vs Cefixime by Cure	-1.8%, 95% C.I.: -13.7%, 10.1%	

TABLE 2.31: STUDY 0098A: OVERALL BACTERIOLOGIC RESPONSE OF THE SUBJECTS OF THE MO SUB-POPULATION AT VISIT 3		
Bacteriological Response	Cefpodoxime (N=125)	Cefixime (N=128)
Cure	86 (68.8%)	90 (70.3%)
Failure	39 (31.2%)	38 (29.7%)
Cefpodoxime vs Cefixime by Cure	-1.5%, 95% C.I.: -13.6%, 10.6%	

TABLE 2.32: STUDY 0098A: OVERALL BACTERIOLOGIC RESPONSE OF THE EVALUABLE SUBJECTS AT FINAL VISIT		
Bacteriological Response	Cefpodoxime (N=124)	Cefixime (N=132)
Cure	72 (58.1%)	79 (59.9%)
Failure	52 (41.9%)	53 (40.1%)
Cefpodoxime vs Cefixime by Cure	-1.8%, 95% C.I.: -14.6%, 11.1%	

TABLE 2.33: STUDY 0098A: OVERALL BACTERIOLOGIC RESPONSE OF THE SUBJECTS OF THE MO SUB-POPULATION AT FINAL VISIT		
Bacteriological Response	Cefpodoxime (N=125)	Cefixime (N=128)
Cure	70 (56.0%)	72 (56.3%)
Failure	55 (44.0%)	56 (43.8%)
Cefpodoxime vs Cefixime by Cure	-0.2%, 95% C.I.: -13.3%, 12.8%	

TABLE 2.34: STUDY 0098A: OVERALL CLINICAL RESPONSE OF THE EVALUABLE SUBJECTS AT VISIT 2		
Clinical Response	Cefpodoxime (N=124)	Cefixime (N=132)
Success Failure	108 (87.1%) 16 (12.9%)	107 (81.1%) 25 (18.9%)
Cefpodoxime vs Cefixime by Success	6.0%, 95% C.I.: -3.7%, 15.7%	

TABLE 2.35: STUDY 0098A: OVERALL CLINICAL RESPONSE OF THE SUBJECTS OF THE MO SUB-POPULATION AT VISIT 2		
Clinical Response	Cefpodoxime (N=125)	Cefixime (N=128)
Success Failure	107 (85.6%) 18 (14.4%)	103 (80.5%) 25 (19.5%)
Cefpodoxime vs Cefixime by Success	5.1%, 95% C.I.: -4.9%, 15.1%	

TABLE 2.36: STUDY 0098A: OVERALL CLINICAL RESPONSE OF THE EVALUABLE SUBJECTS AT VISIT 3		
Clinical Response	Cefpodoxime (N=124)	Cefixime (N=132)
Success Failure	87 (70.2%) 37 (29.8%)	94 (71.2%) 38 (28.8%)
Cefpodoxime vs Cefixime by Success	-1.1%, 95% C.I.: -13.0%, 10.9%	

TABLE 2.37: STUDY 0098A: OVERALL CLINICAL RESPONSE OF THE SUBJECTS OF THE MO SUB-POPULATION AT VISIT 3		
Clinical Response	Cefpodoxime (N=125)	Cefixime (N=128)
Success Failure	86 (68.8%) 39 (31.2%)	90 (70.3%) 38 (29.7%)
Cefpodoxime vs Cefixime by Success	-1.5%, 95% C.I.: -13.6%, 10.6%	

TABLE 2.38: STUDY 0098A: OVERALL CLINICAL RESPONSE OF THE EVALUABLE SUBJECTS AT FINAL VISIT		
Clinical Response	Cefpodoxime (N=124)	Cefixime (N=132)
Success Failure	72 (58.1%) 52 (41.9%)	79 (59.8%) 53 (40.2%)
Cefpodoxime vs Cefixime by Success	-1.8%, 95% C.I.: -14.6%, 11.1%	

TABLE 2.39: STUDY 0098A: OVERALL CLINICAL RESPONSE OF THE SUBJECTS OF THE MO SUB-POPULATION AT FINAL VISIT		
Clinical Response	Cefpodoxime (N=125)	Cefixime (N=128)
Success Failure	70 (56.0%) 55 (44.0%)	73 (57.0%) 55 (43.0%)
Cefpodoxime vs Cefixime by Success	-1.0%, 95% C.I.: -14.0%, 12.0%	

Reviewer's Note: *For all subjects who were randomized to treatment and received at least one dose of study medication, the rates of at least one adverse event, the rates of at least one treatment related adverse event, the rates of serious adverse events, and the rate of discontinued due to adverse events are presented in Table 2.40. No significant differences were detected regarding all these safety parameters between the two treatment groups.*

No deaths were reported during the study.

TABLE 2.40: STUDY 0098A: MEDICAL EVENT RATES

Safety Outcome	Cefpodoxime (N=225)	Cefixime (N=230)	Fisher's P-value
Subject with at Least AE	74 (32.9%)	66 (28.7%)	0.361
Body as a Whole	28 (12.4%)	17 (7.4%)	0.084
Digestive	26 (11.6%)	31 (13.5%)	0.573
Hemic and Lymphatic	2 (0.9%)	2 (0.9%)	1.000
Nervous	2 (0.9%)	2 (0.9%)	1.000
Respiratory	17 (7.6%)	16 (7.0%)	0.858
Skin	12 (5.3%)	15 (6.5%)	0.693
Special Senses	7 (3.1%)	4 (1.7%)	0.377
Urogenital	0 (0)	3 (1.3%)	0.248
Subject with Treatment Related AEs	23 (18.6%)	24 (13.4%)	0.307
Body as a Whole	1 (0.4%)	1 (0.4%)	1.000
Digestive	18 (8.0%)	19 (8.3%)	1.000
Nervous	1 (0.4%)	1 (0.4%)	1.000
Skin	5 (2.2%)	9 (3.9%)	0.417
Urogenital	0 (0)	1 (0.4%)	1.000
Subject with Serious AEs	0 (0)	2 (0.9%)	0.499
Subject Discontinued due to AEs	7 (3.1%)	9 (1.6%)	0.684

Reviewer's Summary and Conclusions: *See Section IV.*

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III. STUDY 0098-B

III.A. METHODS

Approximately 200 evaluable subjects between the age of 2 months and less than 12 years were collectively enrolled (100 subjects in each treatment group). Subjects who met the inclusion/exclusion criteria were randomized to one of the two treatment groups in a 1:1 ratio to either 5-day regimen of cefpodoxime administered b.i.d. at 10 mg/kg/day or 10 day regimen of cefixime administered q.d. at 8 mg/kg/day.

Study visits were scheduled for Pretreatment Visit (Day 0), Phone Call (Day 2-3), Second Visit (Day 7-10), Third Visit (Day 12-15), and Final Visit (Day 25-38), which was exactly the same as Study 0098-A.

Efficacy evaluation, safety evaluation, and statistical method were similar to those described for Study 0098-A in Section II.A.1.

III.B. RESULTS

An actual total of 514 subjects were enrolled at 19 centers in the USA between October 25, 1993 and July 30, 1996. Of these enrolled subjects, 256 (49.8%) cefpodoxime treated subjects and 258 (50.2%) cefixime treated subjects were included in the intent-to-treat analyses, and 107 subjects in the cefpodoxime group and 111 subjects in the cefixime group completed the study. The primary reason for study discontinuation in both treatment groups was failure to meet the protocol eligibility criteria, followed by lack of efficacy, noncompliance, nonserious medical events, and lost to follow-up. The Applicant evaluable group comprised 136 cefpodoxime subjects and 140 cefixime subjects. The primary reason for nonevaluability in each treatment group was no isolated pathogen or resistant pathogens at pretreatment. There were 126 cefpodoxime subjects and 130 cefixime subjects in the Medical Officer sub-population group.

Reviewer's Note: *The number and percentage of subjects included in each analysis group are presented in Table 3.1. There were no notable treatment differences with respect to the percentage of subjects included in each analysis group. Demographic data are described for the intent-to-treat, the evaluable, and the subjects of the Medical Officer sub-population in Tables 3.2, 3.3, and 3.4, respectively, and no statistically significant differences were detected in these pretreatment characteristics of the two treatment groups. The pneumatic otoscopy and/or tympanometry data at pretreatment for the intent-to-treat subjects, the evaluable subjects, and the subjects of the Medical Officer sub-population are shown in Tables 3.5, 3.6, and 3.7, respectively, and the two treatment groups were not significantly different with respect to these findings.*

TABLE 3.1: STUDY 0098B: SUBJECTS POPULATIONS		
Treatment Group for Clinical Response	Subjects Included	
	Cefpodoxime (N=256)	Cefixime (N=258)
Intent-to-Treat	256 (100%)	258 (100%)
Evaluable	136 (53.1%)	140 (54.3%)
MO Sub-population	126 (49.2%)	130 (50.4%)

TABLE 3.2: STUDY 0098B: SUMMARY OF DEMOGRAPHIC DATA FOR THE ITT SUBJECTS			
Number of Subjects	Cefpodoxime (N=256)	Cefixime (N=258)	P-value
Age (yrs.)	3.5 ± 3.1	3.3 ± 2.6	*0.353
< 2 yrs.	107 (41.8%)	104 (40.3%)	0.788
≥ 2 yrs.	149 (58.2%)	154 (59.7%)	
Gender			
Male	136 (53.1%)	148 (57.4%)	0.375
Female	120 (46.9%)	110 (42.6%)	
Race			
White	188 (73.4%)	192 (74.4%)	0.374
Black	41 (16.0%)	42 (16.3%)	
Hispanic	25 (9.8%)	18 (7.0%)	
Other	2 (0.8%)	6 (2.3%)	
* P-value is obtained by t-test, otherwise, by Fisher's exact test			

TABLE 3.3: STUDY 0098B: SUMMARY OF DEMOGRAPHIC DATA FOR THE EVALUABLE SUBJECTS			
Number of Subjects	Cefpodoxime (N=136)	Cefixime (N=140)	P-value
Age (yrs.)	3.4 ± 2.9	3.4 ± 2.7	*0.816
< 2 yrs.	57 (41.9%)	58 (41.4%)	1.000
≥ 2 yrs.	79 (58.1%)	82 (58.6%)	
Gender			
Male	80 (58.8%)	84 (60.0%)	0.903
Female	56 (41.2%)	56 (40.0%)	
Race			
White	110 (80.9%)	114 (81.4%)	0.262
Black	16 (11.8%)	14 (10.0%)	
Hispanic	10 (7.4%)	8 (5.7%)	
Other	0 (0%)	4 (2.9%)	
* P-value is obtained by t-test, otherwise, by Fisher's exact test			

TABLE 3.4: STUDY 0098B: SUMMARY OF DEMOGRAPHIC DATA FOR THE SUBJECTS OF THE MO SUB-POPULATION

Number of Subjects	Cefpodoxime (N=126)	Cefixime (N=130)	P-value
Age (yrs.)	3.4 ± 2.9	3.2 ± 2.7	*0.763
< 2 yrs.	54 (42.9%)	56 (43.1%)	1.000
≥ 2 yrs.	72 (57.1%)	74 (56.9%)	
Gender			
Male	74 (58.7%)	78 (60.0%)	0.899
Female	52 (41.3%)	52 (40.0%)	
Race			
White	100 (79.4%)	105 (80.8%)	0.391
Black	15 (11.9%)	14 (10.8%)	
Hispanic	11 (8.7%)	8 (6.2%)	
Other	0 (0%)	3 (2.3%)	

* P-value is obtained by t-test, otherwise, by Fisher's exact test

TABLE 3.5: STUDY PRT-0098B: SUMMARY OF PNEUMATIC OTOSCOPY AND/OR TYMPANOMETRY DATA AT PRETREATMENT FOR THE ITT SUBJECTS

Number of Subjects	Cefpodoxime (N=256)	Cefixime (N=258)	P-value
Tympanic Membrane Abnormal	256 (100%)	256 (99.2%)	0.499
Hyperemic Yes	235 (91.8%)	231 (89.5%)	0.449
Opaque Yes	232 (90.6%)	227 (88.0%)	0.392
Bulging Yes	223 (87.1%)	218 (84.5%)	0.449
Light Reflex Absent yes	244 (95.3%)	243 (94.2%)	0.693
Impaired Mobility yes	245 (95.7%)	243 (94.2%)	0.547
Perforation yes	48 (18.8%)	47 (18.2%)	0.910

TABLE 3.6: STUDY PRT-0098B: SUMMARY OF PNEUMATIC OTOSCOPY AND/OR TYMPANOMETRY DATA AT PRETREATMENT FOR THE EVALUABLE SUBJECTS

Number of Subjects	Cefpodoxime (N=136)	Cefixime (N=140)	P-value
Tympanic Membrane Abnormal	136 (100%)	138 (98.6%)	0.498
Hyperemic Yes	125 (91.9%)	123 (87.9%)	0.321
Opaque Yes	124 (91.2%)	128 (91.4%)	1.000
Bulging Yes	122 (89.7%)	126 (90.0%)	1.000
Light Reflex Absent Yes	128 (94.1%)	133 (95.0%)	0.796
Impaired Mobility Yes	127 (93.3%)	133 (95.0%)	0.614
Perforation Yes	21 (15.4%)	19 (13.6%)	0.733

TABLE 3.7: STUDY PRT-0098B: SUMMARY OF PNEUMATIC OTOSCOPY AND/OR TYMPANOMETRY DATA AT PRETREATMENT FOR THE SUBJECTS OF THE MO SUB-POPULATION

Number of Subjects	Cefpodoxime (N=126)	Cefixime (N=130)	P-value
Tympanic Membrane Abnormal	126 (100%)	129 (99.2%)	1.000
Hyperemic Yes	116 (92.1%)	116 (89.2%)	0.522
Opaque Yes	114 (90.5%)	119 (91.5%)	0.829
Bulging Yes	112 (88.9%)	118 (90.8%)	0.682
Light Reflex Absent Yes	119 (94.4%)	124 (95.4%)	0.782
Impaired Mobility Yes	117 (92.9%)	124 (95.4%)	0.435
Perforation Yes	21 (16.7%)	17 (13.1%)	0.483

Reviewer's Note: *The overall bacteriologic responses at Test of Cure as per the intent-to-treat subjects, the evaluable subjects, and the subjects of the Medical Officer sub-population are presented in Tables 3.8, 3.9, and 3.10, respectively. Comparisons (95% confidence intervals) of the difference between the two treatment groups show that cefpodoxime was therapeutically equivalent to cefixime with respect to overall bacteriologic outcomes.*

Subset analyses by gender, age, and race for the overall bacteriologic cure rates in the evaluable subjects are shown in Table 3.11. Results are consistent across gender and age subgroups, but race.

TABLE 3.8: STUDY 0098B: OVERALL BACTERIOLOGIC RESPONSE OF THE ITT SUBJECTS AT TEST OF CURE

Bacteriological Response	Cefpodoxime (N=256)	Cefixime (N=258)
Cure	109 (42.6%)	101 (39.2%)
Failure	147 (57.4%)	157 (60.8%)
Cefpodoxime vs Cefixime by Cure	3.4%, 95% C.I.: -5.5%, 12.3%	

TABLE 3.9: STUDY 0098B: OVERALL BACTERIOLOGIC RESPONSE OF THE EVALUABLE SUBJECTS AT TEST OF CURE

Bacteriological Response	Cefpodoxime (N=136)	Cefixime (N=140)
Cure	94 (69.1%)	90 (64.3%)
Failure	42 (30.9%)	50 (35.7%)
Cefpodoxime vs Cefixime by Cure	4.8%, 95% C.I.: -7.0%, 16.7%	

TABLE 3.10: STUDY 0098B: OVERALL BACTERIOLOGIC RESPONSE OF THE SUBJECTS OF THE MO SUB-POPULATION AT TEST OF CURE

Bacteriological Response	Cefpodoxime (N=126)	Cefixime (N=130)
Cure	89 (70.6%)	85 (65.4%)
Failure	37 (29.4%)	45 (34.6%)
Cefpodoxime vs Cefixime by Cure	5.3%, 95% C.I.: -6.9%, 17.4%	

TABLE 3.11: STUDY 0098B: SUBSET ANALYSES BY DEMOGRAPHIC ASPECTS OF THE OVERALL BACTERIOLOGICAL CURE RATES OF THE EVALUABLE SUBJECTS AT TEST OF CURE

Subset	Cefpodoxime (N=136)	Cefixime (N=140)	95% C.I.	P-value Breslow-Day's
Male	58/80 (72.5%)	54/84 (64.3%)	(-12.1%, 18.8%)	0.463
Female	36/56 (64.3%)	36/56 (64.3%)	(-23.4%, 16.3%)	
< 2 yrs.	36/57 (63.2%)	33/58 (56.9%)	(-24.2%, 15.7%)	0.893
≥ 2 yrs.	58/79 (73.4%)	57/82 (69.5%)	(-11.0%, 18.9%)	
White	73/110 (66.4%)	77/114 (67.5%)	(-16.2%, 10.2%)	0.083
Black	12/16 (75.0%)	7/14 (50.0%)	(-36.5%, 47.2%)	
Hispanic	9/10 (90.0%)	4/8 (50.0%)	NA	
Other	0/0 (NA)	2/4 (50.0%)	NA	

Reviewer's Note: *The pathogen eradication rates for the most common isolated baseline pathogens at Test of Cure are summarized for the intent-to-treat subjects, the evaluable subjects, and the subjects of the Medical Officer sub-population in Table 3.12, 3.13, and 3.14, respectively.*

TABLE 3.12: STUDY 0098B: BY PATHOGEN BACTERIAL ERADICATION RATES OF THE ITT SUBJECTS AT TEST OF CURE (FOR MOST COMMON ISOLATED BASELINE PATHOGENS)

Pathogen	Cefpodoxime	Cefixime	Cefpodoxime vs Cefixime by Eradication
H. influenzae	2/2 (100%)	4/7 (57.1%)	NA
H. influenzae (ß-l. -)	11/17 (64.7%)	13/19 (68.4%)	-3.7%, 95% C.I.: -40.2%, 32.7%
H. influenzae (ß-l. +)	11/19 (57.9%)	15/22 (68.2%)	-10.3%, 95% C.I.: -44.7%, 24.1%
M. catarrhalis	2/4 (50.0%)	1/2 (50.0%)	NA
M. catarrhalis (ß-l. -)	1/1 (100%)	0/0 (NA)	NA
M. catarrhalis (ß-l. +)	9/18 (50.0%)	11/15 (73.3%)	-23.3%, 95% C.I.: -61.6%, 14.9%
S. pneumoniae	59/77 (76.6%)	45/72 (62.5%)	14.1%, 95% C.I.: -1.9%, 30.1%
S. pyogenes	13/16 (81.3%)	10/15 (66.7%)	14.6%, 95% C.I.: -22.5%, 51.6%

TABLE 3.13: STUDY 0098B: BY PATHOGEN BACTERIAL ERADICATION RATES OF THE EVALUABLE SUBJECTS AT TEST OF CURE (FOR MOST COMMON ISOLATED BASELINE PATHOGENS)

Pathogen	Cefpodoxime	Cefixime	Cefpodoxime vs Cefixime by Eradication
H. influenzae	1/1 (100%)	4/6 (66.7%)	NA
H. influenzae (ß-l. -)	11/17 (64.7%)	12/15 (80.0%)	-15.3%, 95% C.I.: -52.0%, 21.4%
H. influenzae (ß-l. +)	9/17 (52.9%)	12/18 (66.7%)	-13.7%, 95% C.I.: -51.7%, 24.2%
M. catarrhalis	2/4 (50.0%)	1/2 (50.0%)	NA
M. catarrhalis (ß-l. -)	1/1 (100%)	0/0 (NA)	NA
M. catarrhalis (ß-l. +)	8/17 (47.1%)	10/14 (71.4%)	-24.4%, 95% C.I.: -64.4%, 15.7%
S. pneumoniae	53/70 (75.7%)	43/70 (61.4%)	14.3%, 95% C.I.: -2.3%, 30.9%
S. pyogenes	11/14 (78.6%)	10/15 (66.7%)	11.9%, 95% C.I.: -27.1%, 50.9%

TABLE 3.14: STUDY 0098B: BY PATHOGEN BACTERIAL ERADICATION RATES OF THE SUBJECTS OF THE MO SUB-POPULATION AT TEST OF CURE (FOR MOST COMMON ISOLATED BASELINE PATHOGENS)

Pathogen	Cefpodoxime	Cefixime	Cefpodoxime vs Cefixime by Eradication
H. influenzae	1/1 (100%)	4/6 (66.7%)	NA
H. influenzae (ß-l. -)	11/17 (64.7%)	12/14 (85.7%)	-21.0%, 95% C.I.: -56.7%, 14.7%
H. influenzae (ß-l. +)	8/14 (57.1%)	11/17 (64.7%)	-7.6%, 95% C.I.: -48.5%, 33.4%
M. catarrhalis	2/4 (50.0%)	1/2 (50.0%)	NA
M. catarrhalis (ß-l. -)	1/1 (100%)	0/0 (NA)	NA
M. catarrhalis (ß-l. +)	8/16 (50.0%)	10/13 (76.9%)	-26.9%, 95% C.I.: -67.4%, 13.6%
S. pneumoniae	48/63 (76.2%)	39/62 (62.9%)	13.3%, 95% C.I.: -4.3%, 30.9%
S. pyogenes	12/15 (80.0%)	10/15 (66.7%)	13.3%, 95% C.I.: -24.6%, 51.3%

Reviewer's Note: *The 95% confidence intervals for the difference in success rates of the overall clinical responses at Test of Cure between cefpodoxime and cefixime groups indicate the therapeutic equivalence of the two treatment groups as per the intent-to-treat subjects, the evaluable subjects, and the subjects of the Medical Officer sub-population, which are presented in Tables 3.15 3.16, and 3.17, respectively.*

TABLE 3.15: STUDY 0098B: OVERALL CLINICAL RESPONSE OF THE ITT SUBJECTS AT TEST OF CURE

Clinical Response	Cefpodoxime (N=256)	Cefixime (N=258)
Success Failure	110 (43.0%) 146 (57.0%)	102 (39.5%) 156 (60.5%)
Cefpodoxime vs Cefixime by Success	3.4%, 95% C.I.: -5.5%, 12.3%	

TABLE 3.16: STUDY 0098B: OVERALL CLINICAL RESPONSE OF THE EVALUABLE SUBJECTS AT TEST OF CURE

Clinical Response	Cefpodoxime (N=136)	Cefixime (N=140)
Success Failure	94 (69.1%) 42 (30.9%)	90 (64.3%) 50 (35.7%)
Cefpodoxime vs Cefixime by Success	4.8%, 95% C.I.: -7.0%, 16.7%	

TABLE 3.17: STUDY 0098B: OVERALL CLINICAL RESPONSE OF THE SUBJECTS OF THE MO SUB-POPULATION AT TEST OF CURE

Clinical Response	Cefpodoxime (N=126)	Cefixime (N=130)
Success Failure	89 (70.6%) 37 (29.4%)	85 (65.4%) 45 (34.6%)
Cefpodoxime vs Cefixime by Success	5.3%, 95% C.I.: -6.9%, 17.4%	

Reviewer's Note: *The overall bacteriologic responses at End of Therapy are shown for the intent-to-treat subjects, the evaluable subjects, and the subjects of the Medical Officer sub-population in Tables 3.18, 3.19, and 3.20, respectively. All comparisons (95% confidence intervals) of the difference between the two treatment groups illustrate the equivalence of cefpodoxime to cefixime.*

TABLE 3.18: STUDY 0098B: OVERALL BACTERIOLOGIC RESPONSE OF THE ITT SUBJECTS AT END OF THERAPY		
Bacteriological Response	Cefpodoxime (N=256)	Cefixime (N=258)
Cure Failure	136 (53.1%) 120 (46.9%)	134 (51.9%) 124 (48.1%)
Cefpodoxime vs Cefixime by Cure	1.2%, 95% C.I.: -7.8%, 10.2%	

TABLE 3.19: STUDY 0098B: OVERALL BACTERIOLOGIC RESPONSE OF THE EVALUABLE SUBJECTS AT END OF THERAPY		
Clinical Response	Cefpodoxime (N=136)	Cefixime (N=140)
Cure Failure	118 (86.8%) 18 (13.2%)	120 (85.7%) 20 (14.3%)
Cefpodoxime vs Cefixime by Cure	1.1%, 95% C.I.: -7.8%, 9.9%	

TABLE 3.20: STUDY 0098B: OVERALL BACTERIOLOGIC RESPONSE OF THE SUBJECTS OF THE MO SUB-POPULATION AT END OF THERAPY		
Bacteriological Response	Cefpodoxime (N=126)	Cefixime (N=130)
Cure Failure	89 (70.6%) 37 (29.4%)	85 (65.4%) 45 (34.6%)
Cefpodoxime vs Cefixime by Cure	5.3%, 95% C.I.: -6.9%, 17.4%	

Reviewer's Note: *The pathogen eradication rates for the most common isolated baseline pathogens at End of Therapy are summarized for the intent-to-treat subjects, the evaluable subjects, and the subjects of the Medical Officer sub-population in Tables 3.21, 3.22, and 3.23, respectively.*

TABLE 3.21: STUDY 0098B: BY PATHOGEN BACTERIAL ERADICATION RATES OF THE ITT SUBJECTS AT END OF THERAPY (FOR MOST COMMON ISOLATED BASELINE PATHOGENS)			
Pathogen	Cefpodoxime	Cefixime	Cefpodoxime vs Cefixime by Eradication
H. influenzae	2/2 (100%)	6/7 (85.7%)	NA
H. influenzae (ß-l. -)	15/17 (88.2%)	16/19 (84.2%)	4.0%, 95% C.I.: -24.0%, 32.0%
H. influenzae (ß-l. +)	20/22 (90.9%)	21/25 (84.0%)	6.9%, 95% C.I.: -16.1%, 29.9%
M. catarrhalis	2/4 (50.0%)	1/2 (50.0%)	NA
M. catarrhalis (ß-l. -)	1/1 (100%)	0/0 (NA)	NA
M. catarrhalis (ß-l. +)	15/20 (75.0%)	15/16 (93.8%)	-18.8%, 95% C.I.: -46.8%, 9.3%
S. pneumoniae	72/79 (91.1%)	64/77 (83.1%)	8.0%, 95% C.I.: -3.7%, 19.8%
S. pyogenes	14/16 (87.5%)	12/16 (75.0%)	12.5%, 95% C.I.: -20.4%, 45.4%

TABLE 3.22: STUDY 0098B: BY PATHOGEN BACTERIAL ERADICATION RATES OF THE EVALUABLE SUBJECTS AT END OF THERAPY (FOR MOST COMMON ISOLATED BASELINE PATHOGENS)			
Pathogen	Cefpodoxime	Cefixime	Cefpodoxime vs Cefixime by Eradication
H. influenzae	1/1 (100%)	5/6 (83.3%)	NA
H. influenzae (ß-l. -)	15/17 (88.2%)	13/15 (86.7%)	1.6%, 95% C.I.: -27.7%, 30.9%
H. influenzae (ß-l. +)	18/20 (90.0%)	18/21 (85.7%)	4.3%, 95% C.I.: -20.5%, 29.1%
M. catarrhalis	2/4 (50.0%)	1/2 (50.0%)	NA
M. catarrhalis (ß-l. -)	1/1 (100%)	0/0 (NA)	NA
M. catarrhalis (ß-l. +)	13/18 (72.2%)	14/15 (93.3%)	-21.1%, 95% C.I.: -51.5%, 9.2%
S. pneumoniae	66/72 (91.7%)	61/74 (82.4%)	9.2%, 95% C.I.: -2.9%, 21.4%
S. pyogenes	12/14 (85.7%)	12/16 (75.0%)	10.7%, 95% C.I.: -24.0%, 45.4%

TABLE 3.23: STUDY 0098B: BY PATHOGEN BACTERIAL ERADICATION RATES OF THE SUBJECTS OF THE MO SUB-POPULATION AT END OF THERAPY (FOR MOST COMMON ISOLATED BASELINE PATHOGENS)			
Pathogen	Cefpodoxime	Cefixime	Cefpodoxime vs Cefixime by Eradication
H. influenzae	1/1 (100%)	5/6 (83.3%)	NA
H. influenzae (ß-l. -)	15/17 (88.2%)	13/14 (92.9%)	-4.6%, 95% C.I.: -31.5%, 22.3%
H. influenzae (ß-l. +)	14/16 (87.5%)	16/19 (84.2%)	3.3%, 95% C.I.: -25.5%, 32.1%
M. catarrhalis	2/4 (50.0%)	½ (50.0%)	NA
M. catarrhalis (ß-l. -)	1/1 (100%)	0/0 (NA)	NA
M. catarrhalis (ß-l. +)	12/16 (75.0%)	14/14 (100%)	-25.0%, 95% C.I.: -52.9%, 2.9%
S. pneumoniae	58/64 (90.6%)	53/65 (81.5%)	9.1%, 95% C.I.: -4.3%, 22.5%
S. pyogenes	13/15 (86.7%)	12/16 (75.0%)	11.7%, 95% C.I.: -22.1%, 45.4%

Reviewer's Note: *Tables 3.24, 3.25, and 3.26 show clinical responses of the intent-to-treat subjects, the evaluable subjects, and the subjects of the Medical Officer sub-population at End of Therapy, respectively. Confidence interval results from these populations show that the two treatment groups were therapeutically equivalent with respect to the success rates at this time point.*

TABLE 3.24: STUDY 0098B: OVERALL CLINICAL RESPONSE OF THE ITT SUBJECTS AT END OF THERAPY		
Clinical Response	Cefpodoxime (N=256)	Cefixime (N=258)
Success	139 (54.3%)	136 (52.7%)
Failure	117 (45.7%)	122 (47.3%)
Cefpodoxime vs Cefixime by Success	1.6%, 95% C.I.: -7.4%, 10.6%	

TABLE 3.25: STUDY 0098B: OVERALL CLINICAL RESPONSE OF THE EVALUABLE SUBJECTS AT END OF THERAPY		
Clinical Response	Cefpodoxime (N=136)	Cefixime (N=140)
Success Failure	118 (86.8%) 18 (13.2%)	120 (85.7%) 20 (14.3%)
Cefpodoxime vs Cefixime by Success	1.1%, 95% C.I.: -7.8%, 9.9%	

TABLE 3.26: STUDY 0098B: OVERALL CLINICAL RESPONSE OF THE SUBJECTS OF THE MO SUB-POPULATION AT END OF THERAPY		
Clinical Response	Cefpodoxime (N=126)	Cefixime (N=130)
Success Failure	109 (86.5%) 17 (13.5%)	110 (84.6%) 20 (15.4%)
Cefpodoxime vs Cefixime by Success	1.9%, 95% C.I.: -7.5%, 11.3%	

Reviewer's Note: The following twelve tables (Tables 3.27 to 3.38) present other secondary efficacy data as per the evaluable subjects and the subjects of the Medical Officer sub-population, including overall bacteriologic and clinical responses at Visit 2, Visit 3, and Final Visit. Confidence interval results show that the two treatment groups were therapeutically equivalent with respect to the overall bacteriological responses and the overall clinical responses only at Final Visit.

TABLE 3.27: STUDY 0098B: OVERALL BACTERIOLOGIC RESPONSE OF THE EVALUABLE SUBJECTS AT VISIT 2		
Bacteriological Response	Cefpodoxime (N=136)	Cefixime (N=140)
Cure Failure	118 (86.8%) 18 (13.2%)	129 (92.1%) 11 (7.9%)
Cefpodoxime vs Cefixime by Cure	-5.4%, 95% C.I.: -13.3%, 2.6%	

TABLE 3.28: STUDY 0098B: OVERALL BACTERIOLOGIC RESPONSE OF THE SUBJECTS OF THE MO SUB-POPULATION AT VISIT 2		
Bacteriological Response	Cefpodoxime (N=126)	Cefixime (N=130)
Cure Failure	109 (86.5%) 17 (13.5%)	119 (91.5%) 11 (8.5%)
Cefpodoxime vs Cefixime by Cure	-5.0%, 95% C.I.: -13.5%, 3.4%	

TABLE 3.29: STUDY 0098B: OVERALL BACTERIOLOGIC RESPONSE OF THE EVALUABLE SUBJECTS AT VISIT 3		
Bacteriological Response	Cefpodoxime (N=136)	Cefixime (N=140)
Cure	104 (76.5%)	120 (85.7%)
Failure	32 (23.5%)	20 (14.3%)
Cefpodoxime vs Cefixime by Cure	-9.2%, 95% C.I.: -19.2%, 0.7%	

TABLE 3.30: STUDY 0098B: OVERALL BACTERIOLOGIC RESPONSE OF THE SUBJECTS OF THE MO SUB-POPULATION AT VISIT 3		
Bacteriological Response	Cefpodoxime (N=126)	Cefixime (N=130)
Cure	97 (77.0%)	110 (84.6%)
Failure	29 (23.0%)	20 (15.4%)
Cefpodoxime vs Cefixime by Cure	-7.6%, 95% C.I.: -18.0%, 2.8%	

TABLE 3.31: STUDY 0098B: OVERALL BACTERIOLOGIC RESPONSE OF THE EVALUABLE SUBJECTS AT FINAL VISIT		
Bacteriological Response	Cefpodoxime (N=136)	Cefixime (N=140)
Cure	89 (65.4%)	91 (65.0%)
Failure	47 (34.6%)	49 (35.0%)
Cefpodoxime vs Cefixime by Cure	0.4%, 95% C.I.: -11.5%, 12.4%	

TABLE 3.32: STUDY 0098A: OVERALL BACTERIOLOGIC RESPONSE OF THE SUBJECTS OF THE MO SUB-POPULATION AT FINAL VISIT		
Bacteriological Response	Cefpodoxime (N=126)	Cefixime (N=130)
Cure	84 (66.7%)	85 (65.4%)
Failure	42 (33.3%)	45 (34.6%)
Cefpodoxime vs Cefixime by Cure	1.3%, 95% C.I.: -11.1%, 13.7%	

TABLE 3.33: STUDY 0098B: OVERALL CLINICAL RESPONSE OF THE EVALUABLE SUBJECTS AT VISIT 2		
Clinical Response	Cefpodoxime (N=136)	Cefixime (N=140)
Success Failure	118 (86.8%) 18 (13.2%)	136 (92.1%) 11 (7.9%)
Cefpodoxime vs Cefixime by Success	-10.4%, 95% C.I.: -17.4%, -3.3%	

TABLE 3.34: STUDY 0098B: OVERALL CLINICAL RESPONSE OF THE SUBJECTS OF THE MO SUB-POPULATION AT VISIT 2		
Clinical Response	Cefpodoxime (N=126)	Cefixime (N=130)
Success Failure	109 (86.5%) 17 (13.5%)	119 (91.5%) 11 (8.5%)
Cefpodoxime vs Cefixime by Success	-5.0%, 95% C.I.: -13.5%, 3.4%	

TABLE 3.35: STUDY 0098B: OVERALL CLINICAL RESPONSE OF THE EVALUABLE SUBJECTS AT VISIT 3		
Clinical Response	Cefpodoxime (N=136)	Cefixime (N=140)
Success Failure	104 (76.5%) 32 (23.5%)	120 (85.7%) 20 (14.3%)
Cefpodoxime vs Cefixime by Success	-9.2%, 95% C.I.: -19.2%, 0.7%	

TABLE 3.36: STUDY 0098B: OVERALL CLINICAL RESPONSE OF THE SUBJECTS OF THE MO SUB-POPULATION AT VISIT 3		
Clinical Response	Cefpodoxime (N=126)	Cefixime (N=130)
Success Failure	97 (77.0%) 29 (23.0%)	110 (84.6%) 20 (15.4%)
Cefpodoxime vs Cefixime by Success	-7.6%, 95% C.I.: -18.0%, 2.8%	

TABLE 3.37: STUDY 0098B: OVERALL CLINICAL RESPONSE OF THE EVALUABLE SUBJECTS AT FINAL VISIT		
Clinical Response	Cefpodoxime (N=136)	Cefixime (N=140)
Success Failure	89 (65.4%) 47 (34.6%)	91 (65.0%) 49 (35.0%)
Cefpodoxime vs Cefixime by Success	0.4%, 95% C.I.: -11.5%, 12.4%	

TABLE 3.38: STUDY 0098B: OVERALL CLINICAL RESPONSE OF THE SUBJECTS OF THE MO SUB-POPULATION AT FINAL VISIT		
Clinical Response	Cefpodoxime (N=126)	Cefixime (N=130)
Success Failure	84 (66.7%) 42 (33.3%)	85 (65.4%) 45 (34.6%)
Cefpodoxime vs Cefixime by Success	1.3%, 95% C.I.: -11.1%, 13.7%	

Reviewer's Note: *For all subjects who were randomized to treatment and received at least one dose of study medication, the rates of at least one adverse event, the rates of at least one treatment related adverse event, the rates of serious adverse events, and the rate of discontinued due to adverse events are presented in Table 3.39. No significant differences were detected regarding all these safety parameters between the two treatment groups.*

No deaths were reported during the study.

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TABLE 3.39: STUDY 0098B: MEDICAL EVENT RATES			
Safety Outcome	Cefpodoxime (N=256)	Cefixime (N=258)	Fisher's P-value
Subject with at Least AE	103 (40.2%)	119 (46.1%)	0.183
Body as a Whole	44 (17.2%)	44 (17.1%)	1.000
Cardiovascular	0 (0)	1 (0.4%)	1.000
Digestive	45 (17.6%)	50 (19.4%)	0.650
Hemic and Lymphatic	0 (0%)	2 (0.8%)	0.499
Metabolic and Nutritional	0 (0%)	2 (0.8%)	0.499
Nervous	5 (2.0%)	1 (0.4%)	0.122
Respiratory	36 (14.1%)	41 (15.9%)	0.621
Skin	11 (4.3%)	17 (6.6%)	0.331
Special Senses	9 (3.5%)	13 (5.0%)	0.514
Urogenital	1 (0.4%)	1 (0.4%)	1.000
Subject with Treatment Related AEs	35 (13.7%)	35 (13.6%)	1.000
Body as a Whole	1 (0.4%)	1 (0.4%)	1.000
Digestive	18 (7.0%)	19 (7.4%)	1.000
Nervous	1 (0.4%)	1 (0.4%)	1.000
Skin	5 (2.0%)	9 (3.5%)	0.417
Urogenital	0 (0)	1 (0.4%)	1.000
Subject with Serious AEs	0 (0)	1 (0.4%)	1.000
Subject Discontinued due to AEs	4 (1.6%)	5 (1.9%)	1.000

Reviewer's Summary and Conclusions: *See Section IV.*

IV. SUMMARY AND CONCLUSIONS
(Which May be Conveyed to the Sponsor)

ACUTE OTITIS MEDIA IN PEDIATRIC PATIENTS

This indication was supported by two controlled studies to demonstrate the efficacy and safety of cefpodoxime, and these two studies 0098-A and 0098-B were identical with respect to design, methods, study conduct, and analyses.

Statistical evaluation of efficacy was primarily based upon the two-sided 95% confidence interval of difference in overall bacteriological cure rates at Test of Cure between the treatment groups in the evaluable subjects.

Statistical evaluation of safety was based upon the comparison of adverse event rates between the treatment groups in all subjects receiving at least one dose of study medication by two-sided Fisher's exact test.

The following statements pertain to Study 0098-A:

1. The 95% confidence interval of the difference in overall bacteriologic cure rates of the evaluable subjects was $_{124, 132}$ (-7.5%, 18.1%) $_{82.1\%, 86.8\%}$, which demonstrated that cefpodoxime was therapeutically equivalent in efficacy to cefixime in the treatment of acute otitis media in pediatric patients.

2. No significant differences between the cefpodoxime and cefixime treatment groups were detected with respect to the rate of at least one adverse event, the rate of at least one treatment related adverse event, the rates of serious adverse events, and the rate of discontinued due to adverse events.

The following statements pertain to Study 0098-B:

1. The 95% confidence interval of the difference in overall bacteriologic cure rates of the evaluable subjects was $_{136, 140}$ (-7.0%, 16.7%) $_{80.1\%, 84.3\%}$, which demonstrated that cefpodoxime was therapeutically equivalent in efficacy to cefixime in the treatment of acute otitis media in pediatric patients.

2. No significant differences between the cefpodoxime and cefixime treatment groups were detected with respect to the rate of at least one adverse event, the rate of at least one treatment related adverse event, the rates of serious adverse events, and the rate of discontinued due to adverse events.

REVIEWER CONCLUSIONS: *For the studies 0098-A and 0098-B, the efficacy analyses of the evaluable subjects demonstrated that cefpodoxime proxetil (5 mg/kg b.i.d. for 5 days) was therapeutically equivalent in efficacy to cefixime (8 mg/kg q.d. for 10 days) in the treatment of acute otitis media in pediatric patients. Both Studies provided the evidence that cefpodoxime featured a similar safety profile to cefixime.*

RECOMMENDED REGULATORY ACTION: *Based on the above analyses, from a statistical standpoint, an approvable regulatory decision toward 5 days regimen of cefpodoxime proxetil administered twice daily at 10 mg/kg/day is recommended for the treatment of acute otitis media for pediatrics patients .*

/S/ 9/28/98

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cc:
Archival: NDA50675/S-014
HFD-520
HFD-520/Dr. Chikami
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HFD-520/Dr. Viraraghavan
HFD-520/Mr. DeBallas
HFD-725/Dr. Huque
HFD-725/Dr. Lin
HFD-725/Dr. Jiang
HFD-344/Dr. Thomas
HFD-725/Chron.
This review contains 34 pages and 79 tables.
Microsoft Word 7.0/NDA50675.doc/9/15/98.