U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Translational Sciences
Office of Biostatistics

STATISTICAL REVIEW AND EVALUATION

ADDENDUM

CLINICAL STUDIES

NDA #:	207986
Drug Name:	OTO-201 (6% ciprofloxacin otic suspension)
Indication(s):	Intra-operative treatment of middle ear effusion in pediatric subjects requiring tympanostomy tube placement
Applicant:	Otonomy, Inc.
Submission Date(s):	February 25, 2015
Review Priority:	Standard
PDUFA Date:	December 25, 2015
Biometrics Division:	Division of Biometrics IV
Statistical Reviewer:	Mushfiqur Rashid, Ph.D.
Concurring Reviewers:	Karen Higgins, Sc.D.
Medical Division:	Division of Anti-infective Products
Clinical Team:	Mark Needles, M.D. and Thomas Smith, M.D.
Project Manager:	Jane Dean
Keywords:	Sham-controlled, Confidence Interval, Cochran-Mantel-Haenszel test, Sensitivity Analyses

Addendum to the Statistical review:

In this submission, the applicant was seeking approval to market OTIPRIO (OTO-201), a 6% Ciprofloxacin otic suspension (OTO-201) for the treatment of middle ear effusion (MEE) in pediatric patients (aged 6 months to 17 years) with otitis media who are undergoing tympanostomy tube (TT) placement. The statistical review was posted in DARRTS on November 20, 2015. There were typos in row 5 Table 9 of the review. The corrected (with highlighted row 5) Table 9 is provided below:

Table 9: Components of Study Treatment Failure by Study, Treatment Group and Time point (Full Analysis Set)

	Study 201-201302		Study 201-201303	
	OTO-201 6 mg N = 179	Sham N = 87	OTO-201 6 mg N = 178	Sham N = 88
Cumulative proportion of Study Treatment Failures due to:				
Otorrhea-only				
Through Day 4	8 (4.5%)	7 (8.0%)	6 (3.4%)	17 (19.3%)
Through Day 8	11 (6.1%)	8 (9.2%)	9 (5.1%)	21 (23.9%)
Through Day 15	13 (7.3%)	10 (11.5%)	12 (6.7%)	24 (27.3%)
Through Day 29	15 (8.4%)	12 (13.8%)	22 (12.4%)	29 (33.0%)
Otic Antibiotics-only				
Through Day 4	2 (1.1%)	12 (13.8%)	1 (0.6%)	5 (5.7%)
Through Day 8	4 (2.2%)	15 (17.2%)	4 (2.2%)	5 (5.7%)
Through Day 15	10 (5.6%)	15 (17.2%)	9 (5.1%)	7 (8.0%)
Through Day 29	15 (8.4%)	17 (19.5%)	12 (6.7%)	9 (10.2%)
Systemic Antibiotics-only				
Through Day 4	1 (0.6%)	0	0	1 (1.1%)
Through Day 8	2 (1.1%)	1 (1.1%)	3 (1.7%)	3 (3.4%)
Through Day 15	3 (1.7%)	4 (4.6%)	6 (3.4%)	3 (3.4%)
Through Day 29	6 (3.4%)	6 (6.9%)	9 (5.1%)	6 (6.8%)
Lost-to-follow-up-only				
Through Day 4	1 (0.6%)	0	1 (0.6%)	0
Through Day 8	1 (0.6%)	0	1 (0.6%)	0
Through Day 15	1 (0.6%)	0	1 (0.6%)	0
Through Day 29	1 (0.6%)	0	1 (0.6%)	0
Missed Visits-only				
Through Day 4	4 (2.2%)	2 (2.3%)	1 (0.6%)	2 (2.3%)
Through Day 8	9 (5.0%)	7 (8.0%)	8 (4.5%)	3 (3.4%)
Through Day 15	17 (9.5%)	10 (11.5%)	10 (5.6%)	6 (6.8%)
Through Day 29	21 (11.7%)	13 (14.9%)	14 (7.9%)	7 (8.0%)

Source: Table 11-6, Clinical Study reports

Note: A patient was defined as a study treatment failure from the earliest time point of the 5 events as described in the statistical analysis plan and was considered a study treatment failure for the remainder of the study.

Note: A patient receiving otic antibiotic drops or systemic antibiotics on the same day as confirmation of otorrhea by the blinded assessor was considered a study treatment failure due to otorrhea if they had not yet been identified as a study treatment failure.

Note: After a patient is identified a study treatment failure due to one of the treatment failure components, subsequent events during the study from other treatment failure components are not included in this table

---

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

MUSHFIQUR M RASHID
11/25/2015

KAREN M HIGGINS
11/30/2015
I concur.