CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 18-936/S-054

STATISTICAL REVIEW

Statistical Report: Prozac; OCPB NDA 18-936 (S-054), Eli Lilly Follow-up

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Additional bioequivalence analysis is conducted upon request on the ratio of labeled vs. unlabeled concentrations for endpoints AUC and Cmax.

Definition of Bioequivalence

Bioequivalence of one dose (40mg or 60mg) vs. the 20mg dose at an endpoint is concluded if the 90% confidence interval for the (test/ref) ratio of the endpoint lies entirely in the interval (0.8, 1.25).

Statistical Analysis:

ANOVA of treatment differences was performed on log-transformed data, and the confidence intervals exponentially transformed back to the original scale to obtain confidence intervals for the (test/ref) ratio of the endpoints. Estimates of the ratio and corresponding 90% confidence interval (C.I.) for fluoxetine and norfluoxetine were listed below.

	Fluoxetine			
Dose	AUC Ratio	C.I.	Cmax Ratio	C.I.
40 mg	0.98	(0.90, 1.08)	0.95	(0.89, 1.01)
60 mg	0.93	(0.83, 1.05)	0.98	(0.86, 1.11)

	Norfluoxetine			
Dose	AUC Ratio	C.I.	Cmax Ratio	C.I.
40 mg	0.96	(0.68, 1.36)	0.83	(0.67, 1.01)
60 mg	1.19	(0.86, 1.64)	0.94	(0.84, 1.06)

Conclusion

Basing analyses on the ratio of the radio-labeled and the unlabeled concentrations, the Cmax of norfluoxetine in the 40mg dose group is not bioequivalent to that in the 20mg dose group. For all other cases, the bioequivalence criterion was met.