

**APPENDIX 1**  
**TECHNICAL NOTES**  
**SAS VERSION 8.2 MODELS**

MODEL 1: Fixed Effects Heterogeneity Model (patient is fixed, study is fixed)  
proc mixed data=ten\_mg(when=(timepoint response ne .));  
classes patient treatment study;  
model timepoint response = baseline patient(study) treatment study study\*treatment /  
ddfm=kr outp=predict; \*\*baseline is a continuous covariate;  
parms .2 .2 .2 .2 .2 .2 .2; \*this statement added for the change from baseline at 15 mins.  
post-dose analysis only;  
repeated / group=study;

MODEL 1: Fixed Effects Heterogeneity Model (patient is random, study is fixed)  
proc mixed data=ten\_mg(when=(timepoint response ne .));  
classes patient treatment study;  
model timepoint response= baseline study treatment study\*treatment / ddfm=kr  
outp=predict; \*\*baseline is baseline (a continuous covariate);  
random int/subject=patient(study) group=study;  
repeated / group=study;

MODEL 2 (patient is fixed, study is fixed):  
proc mixed data=ten\_mg(when=(timepoint response ne .));  
classes patient treatment study;  
model timepoint response = baseline patient(study) study treatment/ ddfm=kr  
outp=predict;  
parms .2 .2 .2 .2 .2 ; \*this statement added for the change from baseline at 180 and 240  
min. analyses only;  
parms .2 .2 .2 .2 .2 .2 .2; \*this statement added for the change from baseline at 30 min.  
post-dose analysis only;  
repeated / group=study;

MODEL 2 (patient is random, study is fixed):  
proc mixed data=ten\_mg(when=(timepoint response ne .));  
classes patient treatment study;  
model timepoint response=baseline study treatment / ddfm=kr outp=predict;  
\*\*\*baseline is a continuous covariate;  
repeated / subject=patient(study) group=study type=cs;

MODEL 3 (patient, study, and treatment-by-study interaction are random):  
proc mixed data=ten\_mg(when=(timepoint response ne .));  
classes patient treatment study;  
model timepoint response= baseline treatment / ddfm=kr outp=predict; \*\*\*\*baseline is  
a continuous covariate;  
random study study\*treatment;  
repeated / subject=patient(study) group=study type=cs r;

parms .2 .2 .2 .2 .2 .2 .2 .2 .2 .2 .2 .2; \*this statement used for all analyses  
for 15 to 120 minutes;  
parms .2 .2 .2 .2 .2 .2 .2 .2 .2 .2 .2 .2; \*this statement used for all 180 and 240 minute  
analyses;