

NONMEM code

\$SUBROUTINES ADVAN5

\$MODEL

COMP=(1);DOSE

COMP=(2);CENTRAL

COMP=(3);transit com1

COMP=(4);transit com2

COMP=(5);transit com3

COMP=(6);transit com4

COMP=(7);transit com5

COMP=(8);transit com6

COMP=(9);transit com7

COMP=(10);transit com8

COMP=(11);transit com9

COMP=(12);transit com10

COMP=(13);transit com11

COMP=(14);transit com12

\$PK

MTT= THETA(1)*EXP(ETA(1)) ; Mean transit time

IF(VISIT.EQ.2) MTT=THETA(2)*MTT

IF(VISIT.EQ.3) MTT=THETA(3)*MTT

CL= THETA(4)*EXP(ETA(2)+IOVCL) ; Drug elimination clearance

IF(CYP.EQ.2) CL=THETA(5)*CL

IF(CYP.EQ.3) CL=THETA(6)*CL

IF(LF.EQ.2) CL=THETA(7)*CL

V=THETA(8) ; Volume of the central compartment

VISIT1=0

IF(VISIT.EQ.1) VISIT1=1

VISIT2=0

IF(VISIT.EQ.2) VISIT2=1

VISIT3=0

IF(VISIT.EQ.3) VISIT3=1

IOVCL=VISIT1*ETA(3)+VISIT2*ETA(4)+VISIT3*ETA(5) ; Inter-occasion variability of CL

NT=12 ; Number of transit compartments
KTR=(NT+1)/MTT ; Transit rate constant

K13=KTR
K34=KTR
K45=KTR
K56=KTR
K67=KTR
K78=KTR
K89=KTR
K910=KTR
K10T11=KTR
K11T12=KTR
K12T13=KTR
K13T14=KTR
K14T2=KTR

K20=CL/V
S2 = V/1000

\$ERROR
DEL=0
IF (F.LE.0.0001) DEL=1
IPRE=F
W1= F
W2= 1
IRES= DV-IPRE
IWRE=IRES/(W1+W2)
Y = F + W1*ERR(1)