

```
1 $PROBLEM PROJECT multiple oral dose ;DATE 6-2-04 PROGRAMMER:XXXX
2 ;UNITS: Time=hour, Concentration=ug/ml
3 ;Dose=250 and 500mg, Clearance=L/hr, Volume :
4
5 $DATA multoralest_par.csv IGNORE=C
6
7 $INPUT ID TIME CONC=DV AMT II ADDL MDV
8 ;II = Interdose interval
9 ;ADDL = Additional doses
10
11 $SUBROUTINE ADVAN2 TRANS2
12
13 $PK
14 TVCL = THETA(1)
15 CL = TVCL*EXP(ETA(1)) ;Clearance in L/hr
16 TVV = THETA(2)
17 V = TVV*EXP(ETA(2)) ;Central Volume of distribution in L
18 TVKA = THETA(3)
19 KA = TVKA*EXP(ETA(3))
20 S2 = V
21 F1 = THETA(4)*EXP(ETA(4)) ;Bioavailability
22
23 $ERROR
24 IPRED=F
25 Y=F+F*ERR(1)+ERR(2)
26
27 $THETA (0.01,1) ;POPCL
28 $THETA (1,10) ;POPV
29 $THETA (0.01,0.25) ;POPKA
30 $THETA (0.01,0.5,1) ;POPF1
31
32 $OMEGA 0.09 ;BSVCL
33 $OMEGA 0.09 ;BSVV
34 $OMEGA 0.09 ;BSVKA
35 $OMEGA 0.09 ;BSVF1
36
37 $SIGMA 0.0025 ;ERRCV
38 $SIGMA 1 ;ERRSD
39
40 $ESTIMATION METHOD=0 MAXEVAL=9990 PRINT=10 POSTHOC
41 ;$COVARIANCE
42
43 $TABLE ID TIME DV IPRED
44 NOPRINT ONEHEADER FILE=multoralest_par.fit
```