

```
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
```