

```
1  $PROBLEM ONE COMPARTMENT ORAL MIXED ORDER ABSORPTION ;DATE = 6/2/04 PROGRAMMER=XXXX
2  ;Dose = 100mg or 250mg
3  ;Units: Time=hr,
4  ;Concentration=ug/ml,
5  ;CL/F = L/hr; V/F = L
6
7  $DATA KOKAEST_PAR.CSV IGNORE=C
8
9  $INPUT ID TIME CONC=DV AMT CMT RATE MDV
10 ;RATE = -2 in the data file means that the duration for zero order input
11 ;will be mentioned in the controlstream
12
13 $SUBROUTINE ADVAN2 TRANS2
14
15 $PK
16 CL = THETA(1)*EXP(ETA(1)) ;CL/F
17 V = THETA(2)*EXP(ETA(2)) ;V/F
18 KA = THETA(3)*EXP(ETA(3)) ;Absorption rate constant
19 D2 = THETA(4)*EXP(ETA(4)) ;Duration of zero order input
20 ALAG1 = THETA(5)*EXP(ETA(5)) ;Lag time after which zero order absorption starts
21 F1 = THETA(6)*EXP(ETA(6)) ;Fraction of dose absorbed by first order process
22
23 S2 = V ;Scaling factor
24
25
26 $ERROR
27 IPRED=F
28 Y=F+F*ERR(1)+ERR(2)
29 ;Additive and proportional residual error model
30
31 $THETA (0.01,1) ;POPCL/F
32 $THETA (0.1,10) ;POPV/F
33 $THETA (0.1,3) ;POPKA
34 $THETA (0.1,1) ;POPD2
35 $THETA (0.1,2) ;POPALAG2
36 $THETA (0.01,0.3,1) ;POPfka
37
38
39 $OMEGA 0.09 ;BSVCL/F
40 $OMEGA 0.09 ;BSVV/F
41 $OMEGA 0.00,fix ;BSVKA
42 $OMEGA 0.04 ;BSVD2
43 $OMEGA 0.04 ;BSVALAG2
44 $OMEGA 0.01 ;BSVFka
45
46 $SIGMA 0.002 ;ERRCV
47 $SIGMA 1 ;ERRSD
48
49 $ESTIMATION METHOD=0 MAXEVAL=9999 PRINT=5 POSTHOC
50 $COVARIANCE
51
52 $TABLE ID TIME DV IPRED
53 NOPRINT ONEHEADER FILE=KOKAEST_PAR.FIT
54
55
```