```
 1  $PROBLEM PKPD singledose i.v bolus-effect compartment model
 2                                     ;DATE 6-2-04 PROGRAMMER:XXX
 3                                     ;Dose=100mg or 250mg,
 4                                     ;UNITS: Time=hour,
 5                                     ;Concentration=ug/ml
 6                                   ;Effect = biomarker concentration,ng/ml
 7
 8  $DATA iv1pkpdest_ce.csv IGNORE=C
 9
10  $INPUT ID TIME AMT CMT EFF=DV CLI VI
11
12  $SUBROUTINE ADVAN3  TRANS1
13  ;NONMEM is tricked to consider the peripheral compartment as effect compartment
14
15  $PK
16     CL  = CLI                 ; Individual Clearance in L/hr
17     V1  = VI                  ; Individual Volume of distribution in L
18     K   = CL/V1               ; Elimination rate constant
19     K12 = 0.001*K             ; negligible loss from Central cmt
20     K21 = THETA(1)*EXP(ETA(1)) ; KEO
21     S2  = V1*K12/K21          ; maintains cp=ce (k1e*Vc = keo*Ve)
22
23  $ERROR
24    EMAX  = THETA(2)*EXP(ETA(2))
25    EC50  = THETA(3)*EXP(ETA(3))
26    CE    = F                  ; Effect compartment concentration
27    E     = EMAX*CE/(EC50+CE)
28    IPRED = E
29    Y     = E+ERR(1)
30
31
32  $THETA (0.01,0.5,2.5)              ;POPKEO
33  $THETA (0.01,100,500)             ;POPEMAX
34  $THETA (0.01,10,50)               ;POPEC50
35
36  $OMEGA 0.09            ;BSVKEO
37  $OMEGA 0.09            ;BSVEMAX
38  $OMEGA 0.09            ;BSVEC50
39
40  $SIGMA 0.1               ;ERRCV
41
42  $ESTIMATION METHOD=0  MAXEVAL=9990 PRINT=10 POSTHOC
43  $COVARIANCE
44
45  $TABLE ID TIME DV IPRED CE
46  NOPRINT ONEHEADER FILE=IV1PKPDEST_CE.FIT
47
```