

```
1 $PROBLEM PROJECT singledose ivbolus nonlinear elimination ;DATE 6-2-04 PROGRAMMER:XXXX
2 ;UNITS: Time=hour, Concentration=ug/ml
3 ;Vmax = ug/hr, Km = ug/ml, Volume = L
4 ;Dose = 10,100 or 1000mg
5
6 $DATA ivnonlinestcor_par.csv IGNORE=C
7
8 $INPUT ID TIME CONC=DV AMT DOSE MDV
9
10 $SUBROUTINE ADVAN6 TRANS1 TOL=3
11
12 $MODEL
13 COMP=CENTRAL
14
15 $PK
16 VMAX = THETA(1)*EXP(ETA(1)) ;maximum rate of elimination
17 KM = THETA(2)*EXP(ETA(2)) ;conc at 50% Vmax
18 V = THETA(3)*EXP(ETA(3)) ;Volume of distribution in L
19 S1=V
20
21 $DES
22 CP=A(1)/S1
23 DADT(1)=-VMAX*CP/(KM+CP) ;Units of Vmax = ug/hr
24
25 $ERROR
26 IPRED=F
27 Y=F+F*ERR(1)+ERR(2)
28
29 $THETA (0.01,10) ;POPVmax
30 $THETA (1,30) ;POPkm
31 $THETA (1,5) ;POPV
32
33 $OMEGA 0.04 ;BSVVMAX
34 $OMEGA 0.04 ;BSVKM
35 $OMEGA 0.09 ;BSVV
36
37 $SIGMA 0.02 ;ERRCV
38 $SIGMA 0.1 ;ERRSD
39
40 $ESTIMATION METHOD=0 MAXEVAL=9990 PRINT=10 POSTHOC
41 $COVARIANCE MATRIX=S
42
43 $TABLE ID TIME IPRED DOSE
44 NOPRINT ONEHEADER FILE=ivnonlinestcor_par.fit
45
```