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;; 1. Based on: run2
;; 2. Description: TMDD Prop error (A9) No PRD=999 No 200mg OMEGA BLOCK 3 SEX on V1
;; x1. Author: smartk1
;Project Name: CSF-1R
```

```
$PROB RUN#3 two comp iv infusion TMDD
$INPUT C ID TIME DOSE AMT DV LNDV MDV EVID PRD DAY CHT AGE SEX WT HT NOMT TAD RATE
PAC CYCLE PVNS
$DATA nmpk04FEB14_v3.csv IGNORE=C IGNORE=(TIME.LT.0) IGNORE=(PRD.EQ.999)
IGNORE=(DOSE.EQ.200)
```

```
$SUBROUTINES ADVAN13 TOL=10
$MODEL NCOMP=3
COMP=(CENTRAL,DEFDOSE,DEFOBS)
COMP=(PERIPH)
COMP=(AUC)
```

```
$PK
IF(SEX.EQ.0) THEN
GEND=1
ELSE
GEND=2
ENDIF
```

```
TVCL=THETA(1)
CL=TVCL*EXP(ETA(1))
TVV1=THETA(2)*(2-GEND)+THETA(7)*(GEND-1)
V1=TVV1*EXP(ETA(2))
TVVM=THETA(3)
VM=TVVM*EXP(ETA(3))
TVQ=THETA(4)
Q=TVQ*EXP(ETA(4))
TVV2=THETA(5)
V2=TVV2*EXP(ETA(5))
TVKM=THETA(6)
KM=TVKM*EXP(ETA(6))
```

```
S1=V1
S2=V2
K10=CL/V1
K12=Q/V1
K21=Q/V2
```

```
$DES
DCP=A(1)/S1
```

```
DADT(1) = -A(1)*(K10+K12)+A(2)*K21-DCP*VM/(KM+DCP)
DADT(2) = A(1)*K12-A(2)*K21
DADT(3) = DCP
```

```
$ERROR
TY=A(1)/S1
AUC=A(3)
```

```
DEL = 0
IF (F.LE.0) DEL=0.0001
IPRED=F+DEL
```

```
W1=THETA(8)
```

W=IPRED\*W1  
Y = IPRED + W\*ERR(1)

IRES=IPRED-DV  
IWRES = IRES/W

\$THETA  
(0,0.02) ;[CL] ;L/h  
(0,3) ;[V1] ;L  
(0,0.5) ;[VM] ;(ug/mL)/h  
(0,0.03) ;[Q] ;L/h  
(0,3) ;[V2] ;L  
(0,0.5) ;[KM] ;ug/mL  
(0,1) ;[V1SEX1]  
(0.1) ;[W1]

\$OMEGA  
0.2 ;[BSV CL]

\$OMEGA BLOCK (3)  
0.05 ;[BSV V1]  
0.07 0.4 ;[BSV VM]  
0.05 0.1 0.3 ;[BSV Q]

\$OMEGA  
0.3 ;[BSV V2]  
0.8 ;[BSV KM]

\$\$SIGMA  
1 FIX ;[P] PROPORTIONAL COMPONENT

\$EST MAXEVAL=9999 MSFO=run3.msf PRINT=5 METHOD=1 INTER POSTHOC NOABORT SIG=3  
NOOMEGABOUNDTEST NOTHETABOUNDTEST  
\$COVARIANCE MAT=S PRINT=E UNCONDITIONAL  
\$TABLE DOSE AMT ID TIME TAD MDV TY IPRED IWRES IRES CWRES AUC ONEHEADER NOPRINT  
FILE=sdtab3  
\$TABLE ID CL V2 Q V1 VM KM ETA1 ETA2 ETA3 ETA4 ETA5 ETA6 ONEHEADER NOAPPEND NOPRINT  
FILE=patab3  
\$TABLE DOSE ID SEX CHT PRD PAC CYCLE PVNS ONEHEADER NOAPPEND NOPRINT FILE=catab3  
\$TABLE ID HT WT AGE ONEHEADER NOAPPEND NOPRINT FILE=cotab3

; Problem no. 2  
\$PROBLEM Model simulations  
\$INPUT C ID TIME DOSE AMT DV LNDV MDV EVID PRD DAY CHT AGE SEX WT HT NOMT TAD RATE  
PAC CYCLE PVNS  
\$DATA nmpk04FEB14\_v3.csv IGNORE=C IGNORE=(TIME.LT.0) IGNORE=(PRD.EQ.999)  
IGNORE=(DOSE.EQ.200) REWIND  
\$MSFI run3.msf  
\$\$SIMULATION (20200520) ONLYSIM NSUB=200 TRUE=FINAL  
\$TABLE DOSE ID SEX CHT PRD PAC CYCLE HT WT AGE TAD TIME EVID MDV TY DV IPRED  
ONEHEADER NOPRINT FILE=simtab3