

PROBLEM NO.: 1
THEOPHYLLINE ORAL P:ROOT F:BASE

DATA CHECKOUT RUN: NO
DATA SET LOCATED ON UNIT NO.: 2
THIS UNIT TO BE REWOUND: NO
NO. OF DATA RECS IN DATA SET: 144
NO. OF DATA ITEMS IN DATA SET: 8
ID DATA ITEM IS DATA ITEM NO.: 1
DEP VARIABLE IS DATA ITEM NO.: 5
MDV DATA ITEM IS DATA ITEM NO.: 6

INDICES PASSED TO SUBROUTINE PRED:
8 4 2 0 0 0 0 0 0
0 0

LABELS FOR DATA ITEMS:
ID AMT DOSE TIME DV MDV BWT EVID

(NONBLANK) LABELS FOR PRED-DEFINED ITEMS:
CL V KA K IPRE IWRE G11 G21 G31
H11

FORMAT FOR DATA:
(7E6.0,1F2.0)

TOT. NO. OF OBS RECS: 132
TOT. NO. OF INDIVIDUALS: 12

LENGTH OF THETA: 5

DEFAULT THETA BOUNDARY TEST OMITTED: YES

OMEGA HAS BLOCK FORM:
1
1 1
1 1 1

DEFAULT OMEGA BOUNDARY TEST OMITTED: YES

SIGMA HAS SIMPLE DIAGONAL FORM WITH DIMENSION: 1

DEFAULT SIGMA BOUNDARY TEST OMITTED: YES

INITIAL ESTIMATE OF THETA:
LOWER BOUND INITIAL EST UPPER BOUND
0.0000E+00 0.1000E+00 0.1000E+07
0.0000E+00 0.1000E+01 0.1000E+07
0.0000E+00 0.1000E+02 0.1000E+07
0.0000E+00 0.1000E+01 0.1000E+07
0.0000E+00 0.5000E+00 0.1000E+07

INITIAL ESTIMATE OF OMEGA:
BLOCK SET NO. BLOCK FIXED
1 NO
0.2000E+00
0.1000E+00 0.2000E+00
0.1000E+00 0.1000E+00 0.2000E+00

INITIAL ESTIMATE OF SIGMA:
0.1000E+01

SIGMA CONSTRAINED TO BE THIS INITIAL ESTIMATE

ESTIMATION STEP OMITTED: NO
CONDITIONAL ESTIMATES USED: YES
CENTERED ETA: NO
EPS-ETA INTERACTION: YES
LAPLACIAN OBJ. FUNC.: NO
NO. OF FUNCT. EVALS. ALLOWED: 9999
NO. OF SIG. FIGURES REQUIRED: 3
INTERMEDIATE PRINTOUT: YES
ESTIMATE OUTPUT TO MSF: YES
ABORT WITH PRED EXIT CODE 1: NO
IND. OBJ. FUNC. VALUES SORTED: NO

COVARIANCE STEP OMITTED: NO

R MATRIX PRINTED: YES
S MATRIX PRINTED: YES
EIGENVLS. PRINTED: YES
SPECIAL COMPUTATION: NO
COMPRESSED FORMAT: NO

TABLES STEP OMITTED: NO
NO. OF TABLES: 6

-- TABLE 1 --
PRINTED: NO
HEADER: YES
FILE TO BE FORWARDED: NO

USER-CHOSEN ITEMS

IN THE ORDER THEY WILL APPEAR IN THE TABLE:

ID	TIME	MDV	IPRE	IWRE	G11	G21	G31	H11
----	------	-----	------	------	-----	-----	-----	-----

-- TABLE 2 --

4 COLUMNS APPENDED: NO
PRINTED: NO
HEADER: YES
FILE TO BE FORWARDED: NO

USER-CHOSEN ITEMS

IN THE ORDER THEY WILL APPEAR IN THE TABLE:

ID	V	CL	KA	K	ETA1	ETA2	ETA3
----	---	----	----	---	------	------	------

-- TABLE 3 --

4 COLUMNS APPENDED: NO
PRINTED: NO
HEADER: YES
FILE TO BE FORWARDED: NO

USER-CHOSEN ITEMS

IN THE ORDER THEY WILL APPEAR IN THE TABLE:

ID	BWT
----	-----

-- TABLE 4 --

4 COLUMNS APPENDED: NO
PRINTED: NO
HEADER: YES
FILE TO BE FORWARDED: NO

USER-CHOSEN ITEMS

IN THE ORDER THEY WILL APPEAR IN THE TABLE:

ID

-- TABLE 5 --

FIRST RECORDS ONLY: YES

4 COLUMNS APPENDED: NO
PRINTED: NO
HEADER: YES
FILE TO BE FORWARDED: NO

USER-CHOSEN ITEMS

IN THE ORDER THEY WILL APPEAR IN THE TABLE:

ID	BWT	ETA1	ETA2	ETA3
----	-----	------	------	------

-- TABLE 6 --

FIRST RECORDS ONLY: YES

4 COLUMNS APPENDED: NO
PRINTED: NO
HEADER: YES
FILE TO BE FORWARDED: NO

USER-CHOSEN ITEMS

IN THE ORDER THEY WILL APPEAR IN THE TABLE:

ID	CL	K	V	KA
----	----	---	---	----

DOUBLE PRECISION PREDPP VERSION V LEVEL 2.0

ONE COMPARTMENT MODEL WITH FIRST-ORDER ABSORPTION (ADVAN2)

MAXIMUM NO. OF BASIC PK PARAMETERS: 3

BASIC PK PARAMETERS (AFTER TRANSLATION):

ELIMINATION RATE (K) IS BASIC PK PARAMETER NO.: 1
ABSORPTION RATE (KA) IS BASIC PK PARAMETER NO.: 3

TRANSLATOR WILL CONVERT PARAMETERS

CLEARANCE (CL) AND VOLUME (V) TO K (TRANS2)

COMPARTMENT ATTRIBUTES

COMPT. NO.	FUNCTION	INITIAL STATUS	ON/OFF ALLOWED	DOSE ALLOWED	DEFAULT FOR DOSE	DEFAULT FOR OBS.
1	DEPOT	OFF	YES	YES	YES	NO
2	CENTRAL	ON	NO	YES	NO	YES
3	OUTPUT	OFF	YES	NO	NO	NO

ADDITIONAL PK PARAMETERS - ASSIGNMENT OF ROWS IN GG

COMPT. NO.	SCALE	BIOAVAIL. FRACTION	ZERO-ORDER RATE	ZERO-ORDER DURATION	ABSORB LAG
1	*	*	*	*	*
2	4	*	*	*	*
3	*	-	-	-	-

- PARAMETER IS NOT ALLOWED FOR THIS MODEL
* PARAMETER IS NOT SUPPLIED BY PK SUBROUTINE;
WILL DEFAULT TO ONE IF APPLICABLE

DATA ITEM INDICES USED BY PRED ARE:

EVENT ID DATA ITEM IS DATA ITEM NO.: 8
TIME DATA ITEM IS DATA ITEM NO.: 4
DOSE AMOUNT DATA ITEM IS DATA ITEM NO.: 2

PK SUBROUTINE CALLED WITH EVERY EVENT RECORD.

PK SUBROUTINE NOT CALLED AT NONEVENT (ADDITIONAL OR LAGGED) DOSE TIMES.

ERROR SUBROUTINE CALLED WITH EVERY EVENT RECORD.

MONITORING OF SEARCH:

ITERATION NO.: 0 OBJECTIVE VALUE: 0.11716E+04 NO. OF FUNC. EVALS.: 7
CUMULATIVE NO. OF FUNC. EVALS.: 7
PARAMETER: 0.1000E+00 0.1000E+00 0.1000E+00 0.1000E+00 0.1000E+00 0.1000E+00 0.1000E+00 0.1000E+00 0.1000E+00 0.1000E+00
0.1000E+00
GRADIENT: -0.2546E+03 -0.5245E+02 -0.2309E+01 0.2170E+02 -0.2264E+03 -0.5762E+03 -0.6262E+03 -0.2617E+02 -0.6178E+02 -0.4997E+00
-0.3231E-01
NUMSIGDIG: 0.0000E+00 0.0000E+00 0.0000E+00 0.0000E+00 0.0000E+00 0.0000E+00 0.0000E+00 0.0000E+00 0.0000E+00 0.0000E+00
0.0000E+00

ITERATION NO.: 5 OBJECTIVE VALUE: 0.30570E+03 NO. OF FUNC. EVALS.: 10
CUMULATIVE NO. OF FUNC. EVALS.: 51
PARAMETER: 0.1444E+01 0.5708E+00 -0.3166E+00 -0.8717E+00 0.5773E-01 0.1973E+01 0.2118E+01 -0.6763E+00 0.2080E+00 0.8985E-01
0.9005E-01
GRADIENT: -0.1533E+02 0.1095E+02 0.1473E+02 0.2083E+02 0.1253E+03 -0.2710E+02 0.2473E+02 0.2038E+02 0.6009E+01 0.2063E+01
-0.3844E+01
NUMSIGDIG: -0.1521E+01 -0.1377E+01 -0.1143E+01 -0.9149E+00 -0.1806E+01 -0.1650E+01 -0.7014E+00 -0.1148E+01 -0.9639E+00 -0.1259E+01
-0.1548E+01

ITERATION NO.: 10 OBJECTIVE VALUE: 0.25480E+03 NO. OF FUNC. EVALS.: 8
CUMULATIVE NO. OF FUNC. EVALS.: 94
PARAMETER: 0.3253E+01 0.3723E+01 -0.5266E+00 -0.1054E+01 -0.2619E+00 0.1732E+01 0.1184E+01 -0.1286E+01 -0.1821E+01 -0.1167E+00
0.1151E+01
GRADIENT: -0.5684E+02 0.6931E+02 0.1598E+02 0.1513E+02 0.1044E+03 -0.5436E+01 0.2423E+02 -0.3980E+00 0.4970E-01 -0.1349E+01
-0.5601E+01
NUMSIGDIG: 0.6527E-01 -0.1227E+00 -0.5265E+00 -0.8409E+00 0.4583E+00 0.6177E+00 0.8016E-01 0.1363E+01 -0.1628E+00 0.6163E+00
-0.5029E+00

ITERATION NO.: 15 OBJECTIVE VALUE: 0.15931E+03 NO. OF FUNC. EVALS.: 8
CUMULATIVE NO. OF FUNC. EVALS.: 137
PARAMETER: 0.3935E+01 0.3810E+01 -0.1775E+01 -0.1276E+01 -0.8842E+00 0.9476E+00 0.2569E+00 -0.5717E+00 -0.4085E+00 -0.1121E+01
0.1872E+00
GRADIENT: 0.1901E+02 0.1877E+02 0.8663E+01 0.4810E+01 0.4959E+02 0.1858E+02 -0.4277E+02 -0.1636E+02 0.1507E+02 -0.9892E+00
-0.2897E+01
NUMSIGDIG: 0.9527E+00 0.7783E+00 0.2090E+00 0.8978E+00 0.5691E+00 0.7194E+00 -0.4490E-01 0.1659E+00 -0.3729E+00 0.6628E+00
-0.4239E+00

ITERATION NO.: 20 OBJECTIVE VALUE: 0.12623E+03 NO. OF FUNC. EVALS.: 8
CUMULATIVE NO. OF FUNC. EVALS.: 179
PARAMETER: 0.3223E+01 0.3497E+01 -0.1820E+01 -0.1099E+01 -0.1272E+01 0.1087E+01 0.1924E+00 -0.7811E-01 -0.2603E+01 0.2105E+00

0.9973E+00
GRADIENT: 0.1226E+02 -0.1678E+02 0.1410E+00 -0.3031E+01 -0.6573E+01 0.2910E+02 -0.3933E+02 -0.3774E+01 -0.1376E+01 0.2015E+01
0.1320E+02
NUMSIGDIG: 0.1093E+01 0.1551E+01 0.1353E+01 0.1379E+01 0.1255E+01 0.1952E+01 0.1265E+01 -0.1836E+00 0.4664E+00 -0.7539E+00
-0.3636E+00

ITERATION NO.: 25 OBJECTIVE VALUE: 0.11274E+03 NO. OF FUNC. EVALS.:10
CUMULATIVE NO. OF FUNC. EVALS.: 224
PARAMETER: 0.3298E+01 0.3510E+01 -0.1872E+01 -0.1071E+01 -0.1263E+01 0.8405E+00 0.1859E+00 0.3486E+00 -0.1678E+01 0.4165E+00
0.3384E-01
GRADIENT: 0.9005E+01 -0.1562E+02 0.7189E+01 0.1386E+01 0.3224E+01 0.2162E+02 -0.8114E+01 0.3447E+01 0.4259E+00 -0.8391E+00
-0.1625E+00
NUMSIGDIG: 0.1544E+01 0.2382E+01 0.2355E+01 0.2795E+01 0.1898E+01 0.1062E+01 0.1007E+01 0.1319E+01 0.5984E+00 0.5316E+00
0.9974E-01

ITERATION NO.: 30 OBJECTIVE VALUE: 0.98442E+02 NO. OF FUNC. EVALS.: 8
CUMULATIVE NO. OF FUNC. EVALS.: 265
PARAMETER: 0.3489E+01 0.3568E+01 -0.1850E+01 -0.7274E+00 -0.1524E+01 -0.1064E+00 0.7151E-01 0.6274E-01 -0.2228E+01 0.3981E+00
0.4305E-01
GRADIENT: 0.3594E+02 -0.4106E+02 0.1230E+01 0.4437E+00 -0.6408E+01 0.9922E+01 0.1986E+02 -0.1116E+02 -0.2319E+01 0.3965E+01
0.1710E+01
NUMSIGDIG: 0.2513E+01 0.2383E+01 0.1456E+01 0.1464E+01 0.1318E+01 -0.3279E+00 0.6856E+00 0.8252E-01 0.8574E+00 0.8335E+00
0.8318E+00

ITERATION NO.: 35 OBJECTIVE VALUE: 0.93790E+02 NO. OF FUNC. EVALS.: 9
CUMULATIVE NO. OF FUNC. EVALS.: 306
PARAMETER: 0.3399E+01 0.3554E+01 -0.1878E+01 -0.9800E+00 -0.1297E+01 -0.3933E+00 0.6089E-01 0.8888E-01 -0.2008E+01 0.3785E+00
-0.1390E+00
GRADIENT: -0.2897E+01 0.6730E+01 -0.1368E+01 0.3905E+01 0.2252E+01 0.1668E+01 0.2126E+02 -0.5453E+01 -0.2711E+00 -0.6166E+01
-0.7195E+00
NUMSIGDIG: 0.3088E+01 0.4392E+01 0.1648E+01 0.6645E+00 0.9725E+00 0.1092E+01 0.2648E+01 0.6298E+00 0.1056E+01 0.1916E+01
0.5763E+00

ITERATION NO.: 40 OBJECTIVE VALUE: 0.93182E+02 NO. OF FUNC. EVALS.: 8
CUMULATIVE NO. OF FUNC. EVALS.: 346
PARAMETER: 0.3408E+01 0.3554E+01 -0.1879E+01 -0.1137E+01 -0.1242E+01 -0.4622E+00 0.5702E-01 0.9440E-01 -0.1863E+01 0.4361E+00
-0.2170E+00
GRADIENT: 0.9969E+00 -0.1574E+01 0.6634E-02 0.1234E+00 0.5947E+00 -0.2192E+00 0.2820E+01 0.3847E-01 -0.2601E+00 -0.1310E+00
-0.6119E-01
NUMSIGDIG: 0.4075E+01 0.3880E+01 0.2976E+01 0.2632E+01 0.2737E+01 0.2602E+01 0.2613E+01 0.1724E+01 0.1958E+01 0.2387E+01
0.1668E+01

ITERATION NO.: 45 OBJECTIVE VALUE: 0.92862E+02 NO. OF FUNC. EVALS.:13
CUMULATIVE NO. OF FUNC. EVALS.: 414
PARAMETER: 0.3446E+01 0.3579E+01 -0.1805E+01 -0.1133E+01 -0.1244E+01 -0.4705E+00 0.5600E-01 0.8769E-01 -0.1838E+01 0.4395E+00
-0.2054E+00
GRADIENT: 0.1279E+01 -0.1171E+01 -0.2422E-01 0.3515E-01 -0.1231E+00 -0.2251E+00 0.5691E+01 -0.8994E+00 -0.7296E-01 0.7424E-01
-0.9706E-01
NUMSIGDIG: 0.2866E+01 0.3245E+01 0.3323E+01 0.2100E+01 0.2564E+01 0.1650E+01 0.1797E+01 0.1179E+01 0.1727E+01 0.1932E+01
0.1644E+01

ITERATION NO.: 50 OBJECTIVE VALUE: 0.92833E+02 NO. OF FUNC. EVALS.:13
CUMULATIVE NO. OF FUNC. EVALS.: 482
PARAMETER: 0.3443E+01 0.3580E+01 -0.1800E+01 -0.1146E+01 -0.1242E+01 -0.4696E+00 0.5533E-01 0.8823E-01 -0.1729E+01 0.4060E+00
0.6727E-01
GRADIENT: -0.4029E+00 0.5767E+00 0.1020E+00 -0.2998E-02 0.1001E+00 0.2231E+00 -0.4178E+01 0.2014E+00 -0.1038E-01 0.3396E+00
0.4530E-01
NUMSIGDIG: 0.3827E+01 0.4215E+01 0.3267E+01 0.2931E+01 0.5732E+01 0.2161E+01 0.2715E+01 0.2157E+01 0.3043E+01 0.1897E+01
0.7644E+00

ITERATION NO.: 55 OBJECTIVE VALUE: 0.92831E+02 NO. OF FUNC. EVALS.:13
CUMULATIVE NO. OF FUNC. EVALS.: 549
PARAMETER: 0.3444E+01 0.3580E+01 -0.1803E+01 -0.1145E+01 -0.1243E+01 -0.4713E+00 0.5574E-01 0.8928E-01 -0.1730E+01 0.3993E+00
0.8402E-01
GRADIENT: 0.3004E-02 -0.9087E-02 0.9709E-03 0.3069E-03 0.1028E-02 -0.1124E-02 0.1177E-01 -0.1328E-02 -0.1388E-03 0.1311E-02
-0.3115E-03
NUMSIGDIG: 0.6464E+01 0.5608E+01 0.5300E+01 0.4516E+01 0.5566E+01 0.4164E+01 0.4699E+01 0.4924E+01 0.3677E+01 0.3490E+01
0.2513E+01

ITERATION NO.: 58 OBJECTIVE VALUE: 0.92831E+02 NO. OF FUNC. EVALS.:10
CUMULATIVE NO. OF FUNC. EVALS.: 585
PARAMETER: 0.3444E+01 0.3580E+01 -0.1803E+01 -0.1145E+01 -0.1243E+01 -0.4712E+00 0.5574E-01 0.8929E-01 -0.1729E+01 0.3992E+00
0.8445E-01
GRADIENT: 0.9893E-05 0.2714E-05 0.4942E-05 0.8275E-05 0.3945E-04 0.2272E-05 -0.9890E-04 0.1341E-04 0.3307E-04 -0.9278E-04
-0.3285E-04
NUMSIGDIG: 0.7558E+01 0.8077E+01 0.7615E+01 0.6765E+01 0.6745E+01 0.6834E+01 0.6376E+01 0.5781E+01 0.5513E+01 0.6502E+01
0.5384E+01

MINIMIZATION SUCCESSFUL
NO. OF FUNCTION EVALUATIONS USED: 585

NO. OF SIG. DIGITS IN FINAL EST.: 5.4

ETABAR IS THE ARITHMETIC MEAN OF THE ETA-ESTIMATES,
AND THE P-VALUE IS GIVEN FOR THE NULL HYPOTHESIS THAT THE TRUE MEAN IS 0.

ETABAR: -0.73E-03 -0.22E-02 -0.12E-01
SE: 0.70E-01 0.38E-01 0.18E+00

P VAL.: 0.99E+00 0.95E+00 0.95E+00

***** MINIMUM VALUE OF OBJECTIVE FUNCTION *****

***** 92.831 *****

***** FINAL PARAMETER ESTIMATE *****

THETA - VECTOR OF FIXED EFFECTS PARAMETERS *****

TH 1	TH 2	TH 3	TH 4	TH 5
2.83E+00	3.24E+01	1.49E+00	2.88E-01	1.31E-01

OMEGA - COV MATRIX FOR RANDOM EFFECTS - ETAS *****

ETA1	ETA2	ETA3
6.38E-02		
3.15E-02	1.94E-02	
5.04E-02	5.69E-02	4.35E-01

SIGMA - COV MATRIX FOR RANDOM EFFECTS - EPSILONS ****

EPS1
1.00E+00

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*****  
*****  
***** CORRELATION MATRIX OF ESTIMATE *****  
*****  
*****  
*****
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*****
*****
***** EIGENVALUES OF COR MATRIX OF ESTIMATE *****
*****
*****
*****

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1	2	3	4	5	6	7	8	9	10	11
2.30E-04	1.01E-03	1.84E-02	6.29E-02	1.73E-01	1.85E-01	5.96E-01	1.40E+00	1.67E+00	3.02E+00	3.87E+00

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***** R MATRIX *****
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	TH 1	TH 2	TH 3	TH 4	TH 5	OM11	OM12	OM13	OM22	OM23	OM33	SG11
TH 1	4.15E+01											
TH 2	-4.76E+00	1.20E+00										
TH 3	7.37E+00	-2.94E+00	1.93E+01									
TH 4	1.45E+00	-4.04E-01	-2.57E-01	3.05E+02								
TH 5	2.60E+01	-9.79E+00	2.99E+01	1.01E+03	6.29E+03							
OM11	-3.08E+01	4.90E+00	-6.29E+00	1.92E+02	8.76E+02	5.87E+03						
OM12	4.35E+01	-3.20E+00	-6.72E-01	-9.70E+02	-3.85E+03	-1.62E+04	6.20E+04					
OM13	2.05E+01	-4.85E+00	7.91E+00	9.41E+01	3.20E+02	1.19E+03	-5.72E+03	1.32E+03				
OM22	6.53E+01	-2.05E+01	4.00E+01	1.21E+03	4.70E+03	1.10E+04	-5.08E+04	4.90E+03	6.15E+04			
OM23	-6.92E+01	1.57E+01	-2.37E+01	-2.38E+02	-8.48E+02	-1.67E+03	8.74E+03	-1.90E+03	-1.26E+04	5.74E+03		
OM33	5.11E+00	-1.01E+00	2.14E-01	1.57E+01	5.20E+01	6.57E+01	-3.68E+02	1.08E+02	6.97E+02	-4.74E+02	7.02E+01	
SG11

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***** S MATRIX *****
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*****

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	TH 1	TH 2	TH 3	TH 4	TH 5	OM11	OM12	OM13	OM22	OM23	OM33	SG11
TH 1	4.06E+01											
TH 2	-4.60E+00	1.17E+00										
TH 3	7.09E+00	-2.87E+00	1.91E+01									
TH 4	-9.39E+01	2.12E+00	-1.74E+01	8.69E+02								
TH 5	3.14E+02	-7.33E+01	1.02E+02	1.78E+03	1.96E+04							
OM11	-4.94E+02	3.75E+01	-4.61E+01	2.50E+03	-4.42E+02	9.71E+03						
OM12	8.04E+02	-1.81E+01	2.73E+01	-6.22E+03	-5.58E+03	-2.07E+04	5.14E+04					
OM13	-2.37E+01	-3.37E+00	2.06E+01	1.82E+02	4.03E+02	6.87E+02	-1.65E+03	1.52E+02				
OM22	-3.36E+01	-1.85E+01	-2.82E+02	3.92E+03	1.11E+04	8.49E+03	-2.94E+04	3.13E+02	4.07E+04			
OM23	-4.95E+01	-1.45E+01	1.21E+02	-1.49E+02	-1.77E+03	3.47E+02	-4.86E+02	2.29E+02	-5.25E+03	2.06E+03		

SG11