

Mlfuns Sample Script

Parameter Table

June 8, 2011

Tim Bergsma

1 Purpose

This script picks up after model.Rnw to process bootstrap results and make a parameter table.

1.1 Package

Listing 1:

```
> getwd()

[1] "/Users/timb/project/metrum/inst/sample/script"
```

Listing 2:

```
> require(MIfuns)

MIfuns 4.3.4
```

2 Parameter Table

Listing 3:

```
> library(Hmisc)
> tab <- wkitab(1005, '../nonmem')
> tab$estimate <- as.character(signif(as.numeric(tab$estimate), 3))
> tab$estimate <- with(tab, paste(estimate, '$', justUnits(model), '$'))
> tab$name <- with(tab, nospace(noUnits(lhs(model))))
> tab$root <- signif(sqrt(exp(as.numeric(tab$estimate))-1), 3)*100
> needcv <- contains('OMEGA|SIGMA', tab$parameter)
> tab <- within(tab, estimate[needcv] <- paste(estimate[needcv], parens(glue('\\%CV=', root[needcv]))))
> tab$root <- NULL
> #offdiag <- contains('2.1', tab$parameter)
```

```
> #tab$estimate[offdiag] <- text2decimal(tab$estimate[offdiag])
> #omegablock <- text2decimal(tab$estimate[contains('Omega..(1|2)',tab$parameter)])
> #cor <- signif(half(cov2cor(as.matrix(as.halfmatrix(omegablock))))[[2]],3)
> #tab$estimate[offdiag] <- paste(sep=',',tab$estimate[offdiag], ' (COR=',cor,')')
> tab$model[is.na(tab$model)] <- ''
> boot <- read.csv(' ../nonmem/1005.boot/log.csv',as.is=TRUE)
> boot <- boot[boot$moment=='estimate',]
> boot <- data.frame(cast(boot,... ~ moment))
> boot[] <- lapply(boot,as.character)
> boot <- boot[contains('THETA|OMEGA|SIGMA',boot$parameter),c('parameter','estimate')]
> boot$estimate <- as.numeric(boot$estimate)
> boot <- data.frame(cast(boot,parameter ~ .,value='estimate',fun=function(x)list(lo=as.character(signif(quantile(x,
  probs=0.05),3)),hi=as.character(signif(quantile(x,probs=0.95),3)))))
> boot$CI <- with(boot, parens(glue(lo,',',hi)))
> tab <- stableMerge(tab,boot[,c('parameter','CI')])
> tab <- within(tab, se <- name <- run <- tool <- parameter <- NULL)
> tab$model <- wiki2latex(noUnits(tab$model))
> tab
```

| | description | model |
|----|--|-------|
| 1 | apparent oral clearance | |
| 2 | central volume of distribution | |
| 3 | absorption rate constant | |
| 4 | intercompartmental clearance | |
| 5 | peripheral volume of distribution | |
| 6 | male effect on clearance | |
| 7 | weight effect on clearance | |
| 8 | interindividual variability of clearance | |
| 9 | interindividual variability of central volume | |
| 10 | interindividual variability of Ka | |
| 11 | proportional error | |
| 1 | $\text{CL}/F \sim \theta_1 \cdot \theta_6^{\text{MALE}} \cdot (WT/70)^{\theta_7} \cdot e^{\eta_1}$ | |
| 2 | $V_c/F \sim \theta_2 \cdot (WT/70)^1 \cdot e^{\eta_2}$ | |

```

3
4
5
6
7
8
9
10
11

```

$$\begin{aligned} & \mathrm{K}_a \sim \theta_3 \cdot e^{\eta_3} \\ & \mathrm{Q}/F \sim \theta_4 \\ & \mathrm{V}_p/F \sim \theta_5 \\ & \mathrm{MALE}_{\mathrm{CL}/F} \sim \theta_6 \\ & \mathrm{WT}_{\mathrm{CL}/F} \sim \theta_7 \\ & \mathrm{IIV}_{\mathrm{CL}/F} \sim \Omega_{1.1} \\ & \mathrm{IIV}_{\mathrm{V}_c/F} \sim \Omega_{2.2} \\ & \mathrm{IIV}_{\mathrm{K}_a} \sim \Omega_{3.3} \\ & \mathrm{err}_{\mathrm{prop}} \sim \Sigma_{1.1} \end{aligned}$$

| | estimate | prse | CI |
|----|------------------------------|------|------------------|
| 1 | 8.58 \$ L/h \$ | 9.51 | (6.91, 9.85) |
| 2 | 21.6 \$ L \$ | 9.33 | (17.8, 25.5) |
| 3 | 0.0684 \$ h ⁻¹ \$ | 8.04 | (0.0586, 0.079) |
| 4 | 3.78 \$ L/h \$ | 13.5 | (2.96, 4.94) |
| 5 | 107 \$ L \$ | 15.7 | (86.2, 151) |
| 6 | 0.999 \$ \$ | 13.7 | (0.807, 1.35) |
| 7 | 1.67 \$ \$ | 21.9 | (1.05, 2.36) |
| 8 | 0.196 \$ \$ (\\%CV=NA) | 23.1 | (0.117, 0.257) |
| 9 | 0.129 \$ \$ (\\%CV=NA) | 30.4 | (0.0645, 0.186) |
| 10 | 0.107 \$ \$ (\\%CV=NA) | 25.2 | (0.0649, 0.152) |
| 11 | 0.0671 \$ \$ (\\%CV=NA) | 11.4 | (0.0563, 0.0811) |

Table 1: Parameter Estimates from Population Pharmacokinetic Model Run 1005

| description | model | estimate | prse | CI |
|---|--|-----------------|------|-----------------|
| apparent oral clearance | $CL/F \sim \theta_1 \cdot \theta_6^{MALE} \cdot (WT/70)^{\theta_7} \cdot e^{\eta_1}$ | 8.58 L/h | 9.51 | (6.91,9.85) |
| central volume of distribution | $V_c/F \sim \theta_2 \cdot (WT/70)^1 \cdot e^{\eta_2}$ | 21.6 L | 9.33 | (17.8,25.5) |
| absorption rate constant | $K_a \sim \theta_3 \cdot e^{\eta_3}$ | 0.0684 h^{-1} | 8.04 | (0.0586,0.079) |
| intercompartmental clearance | $Q/F \sim \theta_4$ | 3.78 L/h | 13.5 | (2.96,4.94) |
| peripheral volume of distribution | $V_p/F \sim \theta_5$ | 107 L | 15.7 | (86.2,151) |
| male effect on clearance | $MALE_{CL/F} \sim \theta_6$ | 0.999 | 13.7 | (0.807,1.35) |
| weight effect on clearance | $WT_{CL/F} \sim \theta_7$ | 1.67 | 21.9 | (1.05,2.36) |
| interindividual variability of clearance | $IIV_{CL/F} \sim \Omega_{1.1}$ | 0.196 (%CV=NA) | 23.1 | (0.117,0.257) |
| interindividual variability of central volume | $IIV_{V_c/F} \sim \Omega_{2.2}$ | 0.129 (%CV=NA) | 30.4 | (0.0645,0.186) |
| interindividual variability of Ka | $IIV_{K_a} \sim \Omega_{3.3}$ | 0.107 (%CV=NA) | 25.2 | (0.0649,0.152) |
| proportional error | $err_{prop} \sim \Sigma_{1.1}$ | 0.0671 (%CV=NA) | 11.4 | (0.0563,0.0811) |