

# Validation of Noncompartmental Analysis Performed by NonCompart R package

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## 1 Introduction

NonCompart R package (Bae 2018; Kim et al. 2018) can conduct a noncompartmental analysis as similar as possible to the most widely used commercial software for pharmacokinetic analysis, i.e. Phoenix<sup>®</sup> WinNonlin<sup>®</sup> (Certara USA 2018). This document provides validation of noncompartmental analysis performed by NonCompart R package version 0.4.2 as compared to the results from the commercial software, WinNonlin<sup>®</sup> version 6.3 and 7.0.

## 2 Results

A function, `Equal()` will return `TRUE` if there is no difference between results from NonCompart and WinNonlin.

```
# install.packages("NonCompart", repos="http://r.acr.kr")
library(NonCompart)
RptCfgr = read.csv("RptCfgr.csv", as.is=TRUE)

Equal = function(Wres, Rres, Tol=0.001)
{
```

```

Wres[, "ID"] = as.character(Wres[, "Subject"])
ColName0 = colnames(Rres)
rownames(RptCfg) = RptCfg[, "PPTTESTCD"]
colnames(Rres) = c(ColName0[1], RptCfg[ColName0[-1], "WNL"])
Inter = intersect(colnames(Wres), colnames(Rres))

IsSame = TRUE
for (i in 1:nrow(Wres)) {
  for (j in Inter) {
    R = as.numeric(Rres[i, j])
    W = as.numeric(Wres[i, j])
    if (W != 0) {
      if (abs((R - W)/W) > Tol) {
        print(Wres[i, j])
        print(Rres[i, j])
        IsSame = FALSE
      }
    }
  }
}
return(IsSame)
}

```

Eight comparison tests were performed using **Theoph** and **Indometh** default datasets. (Table 1) Detailed side-by-side comparison is in Appendix A.

Table 1: Description of settings for the noncompartmental analysis performed in WinNonlin and links to the raw data

| No. | Dataset        | Down   | Route                | Hyperlink |
|-----|----------------|--------|----------------------|-----------|
| 1   | Theoph (n=12)  | Linear | Extravascular        | CSV       |
| 2   | Theoph (n=12)  | Log    | Extravascular        | CSV       |
| 3   | Indometh (n=6) | Linear | IV Bolus             | CSV       |
| 4   | Indometh (n=6) | Log    | IV Bolus             | CSV       |
| 5   | Indometh (n=6) | Linear | IV Infusion (0.25hr) | CSV       |
| 6   | Indometh (n=6) | Log    | IV Infusion (0.25hr) | CSV       |
| 7   | Indometh (n=6) | Linear | Extravascular        | CSV       |
| 8   | Indometh (n=6) | Log    | Extravascular        | CSV       |

```

Theoph[, "Subject"] = as.numeric(as.character(Theoph[, "Subject"]))
Indometh[, "Subject"] = as.numeric(as.character(Indometh[, "Subject"]))

Wres1 = read.csv("Final_Parameters_Pivoted_Theoph_Linear.csv")
Rres1 = tblNCA(Theoph, "Subject", "Time", "conc", dose=320, concUnit="mg/L")
Equal(Wres1, Rres1)

## [1] TRUE

Wres2 = read.csv("Final_Parameters_Pivoted_Theoph_Log.csv")
Rres2 = tblNCA(Theoph, "Subject", "Time", "conc", dose=320, down="Log",
               concUnit="mg/L")
Equal(Wres2, Rres2)

## [1] TRUE

```

```

Wres3 = read.csv("Final_Parameters_Pivoted_Indometh_Linear.csv")
Rres3 = tblNCA(Indometh, "Subject", "time", "conc", dose=25, adm="Bolus",
               concUnit="mg/L", R2ADJ=0.8)
Equal(Wres3, Rres3)

```

```
## [1] TRUE
```

```

Wres4 = read.csv("Final_Parameters_Pivoted_Indometh_Log.csv")
Rres4 = tblNCA(Indometh, "Subject", "time", "conc", dose=25, adm="Bolus",
               down="Log", concUnit="mg/L", R2ADJ=0.8)
Equal(Wres4, Rres4)

```

```
## [1] TRUE
```

```

Wres5 = read.csv("Final_Parameters_Pivoted_Indometh_Linear_Infusion.csv")
Rres5 = tblNCA(Indometh, "Subject", "time", "conc", dose=25, adm="Infusion",
               dur=0.25, concUnit="mg/L", R2ADJ=0.8)
Equal(Wres5, Rres5)

```

```
## [1] TRUE
```

```

Wres6 = read.csv("Final_Parameters_Pivoted_Indometh_Log_Infusion.csv")
Rres6 = tblNCA(Indometh, "Subject", "time", "conc", dose=25, adm="Infusion",
               dur=0.25, down="Log", concUnit="mg/L", R2ADJ=0.8)
Equal(Wres6, Rres6)

```

```
## [1] TRUE
```

```

Wres7 = read.csv("Final_Parameters_Pivoted_Indometh_Linear_Wrong_Extravascular.csv")
Rres7 = tblNCA(Indometh, "Subject", "time", "conc", dose=25, concUnit="mg/L",
               R2ADJ=0.8)
Equal(Wres7, Rres7)

```

```
## [1] TRUE
```

```

Wres8 = read.csv("Final_Parameters_Pivoted_Indometh_Log_Wrong_Extravascular.csv")
Rres8 = tblNCA(Indometh, "Subject", "time", "conc", dose=25, down="Log",
               concUnit="mg/L", R2ADJ=0.8)
Equal(Wres8, Rres8)

```

```
## [1] TRUE
```

### 3 Conclusion

*There is no discrepancy* between results from NonCompart and WinNonlin. We also performed multiple analyses with the real clinical trial datasets and have found no differences (data not shown: confidential). Noncompartmental analysis performed by the open-source R package, NonCompart can be **qualified and validated** enough to acquire the identical results of the commercial software, WinNonlin.

*Please report issues regarding validation of the R package to <https://github.com/asancpt/NonCompart-tests/issues>.*

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## A Side-by-side comparison of results

```
library(dplyr)
library(tidyr)

table_wres_rres <- function(wres, rres, Caption){
  wres %>%
    gather(WNL, WinNonlin, -Subject) %>%
    left_join(RptCfg %>% select(PTESTCD, WNL), by = "WNL") %>%
    left_join(rres %>% as.data.frame() %>% gather(PTESTCD, NonCompart, -Subject),
              by = c("Subject", "PTESTCD")) %>%
    select(Subject, PTESTCD, WNL, NonCompart, WinNonlin) %>%
    mutate(NonCompart = as.numeric(NonCompart),
           WinNonlin = as.numeric(WinNonlin)) %>%
    mutate(Difference = ifelse(NonCompart - WinNonlin < 0.00001,
                              yes = 0, no = 'Larger than 0.00001')) %>%
    filter(!is.na(WinNonlin) & !is.na(NonCompart)) %>%
    knitr::kable(longtable = TRUE, booktabs = TRUE, #format = "latex",
                  caption = Caption) %>%
    add_header_above(c(" ", "Pharmacokinetic Parameters" = 2, "Values" = 2, " ")) %>%
    kable_styling(latex_options = c("repeat_header"))
}
```

### A.1 Test 1: Theoph (n=12), Linear, Extravascular

```
table_wres_rres(Wres1, Rres1,
                 Caption = 'Theoph (n=12), Linear, Extravascular')
```

Table 2: Theoph (n=12), Linear, Extravascular

| Subject | Pharmacokinetic Parameters |               | Values     |           | Difference |
|---------|----------------------------|---------------|------------|-----------|------------|
|         | PTESTCD                    | WNL           | NonCompart | WinNonlin |            |
| 1       | R2                         | Rsqr          | 0.9999997  | 0.9999997 | 0          |
| 2       | R2                         | Rsqr          | 0.9971954  | 0.9971954 | 0          |
| 3       | R2                         | Rsqr          | 0.9993250  | 0.9993250 | 0          |
| 4       | R2                         | Rsqr          | 0.9989241  | 0.9989241 | 0          |
| 5       | R2                         | Rsqr          | 0.9986472  | 0.9986472 | 0          |
| 6       | R2                         | Rsqr          | 0.9982413  | 0.9982413 | 0          |
| 7       | R2                         | Rsqr          | 0.9986702  | 0.9986702 | 0          |
| 8       | R2                         | Rsqr          | 0.9910124  | 0.9910124 | 0          |
| 9       | R2                         | Rsqr          | 0.9994437  | 0.9994437 | 0          |
| 10      | R2                         | Rsqr          | 0.9995087  | 0.9995087 | 0          |
| 11      | R2                         | Rsqr          | 0.9999983  | 0.9999983 | 0          |
| 12      | R2                         | Rsqr          | 0.9993968  | 0.9993968 | 0          |
| 1       | R2ADJ                      | Rsqr_adjusted | 0.9999995  | 0.9999995 | 0          |
| 2       | R2ADJ                      | Rsqr_adjusted | 0.9957931  | 0.9957931 | 0          |
| 3       | R2ADJ                      | Rsqr_adjusted | 0.9986499  | 0.9986499 | 0          |
| 4       | R2ADJ                      | Rsqr_adjusted | 0.9978483  | 0.9978483 | 0          |
| 5       | R2ADJ                      | Rsqr_adjusted | 0.9979708  | 0.9979708 | 0          |

Table 2: Theoph (n=12), Linear, Extravascular (*continued*)

| Subject | Pharmacokinetic Parameters |                    | Values     |            | Difference |
|---------|----------------------------|--------------------|------------|------------|------------|
|         | PPTTESTCD                  | WNL                | NonCompart | WinNonlin  |            |
| 6       | R2ADJ                      | Rsqr_adjusted      | 0.9978896  | 0.9978896  | 0          |
| 7       | R2ADJ                      | Rsqr_adjusted      | 0.9980053  | 0.9980053  | 0          |
| 8       | R2ADJ                      | Rsqr_adjusted      | 0.9887655  | 0.9887655  | 0          |
| 9       | R2ADJ                      | Rsqr_adjusted      | 0.9988873  | 0.9988873  | 0          |
| 10      | R2ADJ                      | Rsqr_adjusted      | 0.9990174  | 0.9990174  | 0          |
| 11      | R2ADJ                      | Rsqr_adjusted      | 0.9999965  | 0.9999965  | 0          |
| 12      | R2ADJ                      | Rsqr_adjusted      | 0.9987936  | 0.9987936  | 0          |
| 1       | CORRXY                     | Corr_XY            | -0.9999999 | -0.9999999 | 0          |
| 2       | CORRXY                     | Corr_XY            | -0.9985967 | -0.9985967 | 0          |
| 3       | CORRXY                     | Corr_XY            | -0.9996624 | -0.9996624 | 0          |
| 4       | CORRXY                     | Corr_XY            | -0.9994619 | -0.9994619 | 0          |
| 5       | CORRXY                     | Corr_XY            | -0.9993234 | -0.9993234 | 0          |
| 6       | CORRXY                     | Corr_XY            | -0.9991203 | -0.9991203 | 0          |
| 7       | CORRXY                     | Corr_XY            | -0.9993349 | -0.9993349 | 0          |
| 8       | CORRXY                     | Corr_XY            | -0.9954961 | -0.9954961 | 0          |
| 9       | CORRXY                     | Corr_XY            | -0.9997218 | -0.9997218 | 0          |
| 10      | CORRXY                     | Corr_XY            | -0.9997543 | -0.9997543 | 0          |
| 11      | CORRXY                     | Corr_XY            | -0.9999991 | -0.9999991 | 0          |
| 12      | CORRXY                     | Corr_XY            | -0.9996984 | -0.9996984 | 0          |
| 1       | LAMZNPT                    | No_points_lambda_z | 3.0000000  | 3.0000000  | 0          |
| 2       | LAMZNPT                    | No_points_lambda_z | 4.0000000  | 4.0000000  | 0          |
| 3       | LAMZNPT                    | No_points_lambda_z | 3.0000000  | 3.0000000  | 0          |
| 4       | LAMZNPT                    | No_points_lambda_z | 3.0000000  | 3.0000000  | 0          |
| 5       | LAMZNPT                    | No_points_lambda_z | 4.0000000  | 4.0000000  | 0          |
| 6       | LAMZNPT                    | No_points_lambda_z | 7.0000000  | 7.0000000  | 0          |
| 7       | LAMZNPT                    | No_points_lambda_z | 4.0000000  | 4.0000000  | 0          |
| 8       | LAMZNPT                    | No_points_lambda_z | 6.0000000  | 6.0000000  | 0          |
| 9       | LAMZNPT                    | No_points_lambda_z | 3.0000000  | 3.0000000  | 0          |
| 10      | LAMZNPT                    | No_points_lambda_z | 3.0000000  | 3.0000000  | 0          |
| 11      | LAMZNPT                    | No_points_lambda_z | 3.0000000  | 3.0000000  | 0          |
| 12      | LAMZNPT                    | No_points_lambda_z | 3.0000000  | 3.0000000  | 0          |
| 1       | LAMZ                       | Lambda_z           | 0.0484570  | 0.0484570  | 0          |
| 2       | LAMZ                       | Lambda_z           | 0.1040864  | 0.1040864  | 0          |
| 3       | LAMZ                       | Lambda_z           | 0.1024443  | 0.1024443  | 0          |
| 4       | LAMZ                       | Lambda_z           | 0.0992870  | 0.0992870  | 0          |
| 5       | LAMZ                       | Lambda_z           | 0.0866189  | 0.0866189  | 0          |
| 6       | LAMZ                       | Lambda_z           | 0.0877957  | 0.0877957  | 0          |
| 7       | LAMZ                       | Lambda_z           | 0.0883365  | 0.0883365  | 0          |
| 8       | LAMZ                       | Lambda_z           | 0.0814505  | 0.0814505  | 0          |
| 9       | LAMZ                       | Lambda_z           | 0.0824586  | 0.0824586  | 0          |
| 10      | LAMZ                       | Lambda_z           | 0.0749598  | 0.0749598  | 0          |
| 11      | LAMZ                       | Lambda_z           | 0.0954586  | 0.0954586  | 0          |
| 12      | LAMZ                       | Lambda_z           | 0.1102595  | 0.1102595  | 0          |
| 1       | LAMZLL                     | Lambda_z_lower     | 9.0500000  | 9.0500000  | 0          |
| 2       | LAMZLL                     | Lambda_z_lower     | 7.0300000  | 7.0300000  | 0          |

Table 2: Theoph (n=12), Linear, Extravascular (*continued*)

| Subject | Pharmacokinetic Parameters |                | Values     |            | Difference |
|---------|----------------------------|----------------|------------|------------|------------|
|         | PPTSTCD                    | WNL            | NonCompart | WinNonlin  |            |
| 3       | LAMZLL                     | Lambda_z_lower | 9.0000000  | 9.0000000  | 0          |
| 4       | LAMZLL                     | Lambda_z_lower | 9.0200000  | 9.0200000  | 0          |
| 5       | LAMZLL                     | Lambda_z_lower | 7.0200000  | 7.0200000  | 0          |
| 6       | LAMZLL                     | Lambda_z_lower | 2.0300000  | 2.0300000  | 0          |
| 7       | LAMZLL                     | Lambda_z_lower | 6.9800000  | 6.9800000  | 0          |
| 8       | LAMZLL                     | Lambda_z_lower | 3.5300000  | 3.5300000  | 0          |
| 9       | LAMZLL                     | Lambda_z_lower | 8.8000000  | 8.8000000  | 0          |
| 10      | LAMZLL                     | Lambda_z_lower | 9.3800000  | 9.3800000  | 0          |
| 11      | LAMZLL                     | Lambda_z_lower | 9.0300000  | 9.0300000  | 0          |
| 12      | LAMZLL                     | Lambda_z_lower | 9.0300000  | 9.0300000  | 0          |
| 1       | LAMZUL                     | Lambda_z_upper | 24.3700000 | 24.3700000 | 0          |
| 2       | LAMZUL                     | Lambda_z_upper | 24.3000000 | 24.3000000 | 0          |
| 3       | LAMZUL                     | Lambda_z_upper | 24.1700000 | 24.1700000 | 0          |
| 4       | LAMZUL                     | Lambda_z_upper | 24.6500000 | 24.6500000 | 0          |
| 5       | LAMZUL                     | Lambda_z_upper | 24.3500000 | 24.3500000 | 0          |
| 6       | LAMZUL                     | Lambda_z_upper | 23.8500000 | 23.8500000 | 0          |
| 7       | LAMZUL                     | Lambda_z_upper | 24.2200000 | 24.2200000 | 0          |
| 8       | LAMZUL                     | Lambda_z_upper | 24.1200000 | 24.1200000 | 0          |
| 9       | LAMZUL                     | Lambda_z_upper | 24.4300000 | 24.4300000 | 0          |
| 10      | LAMZUL                     | Lambda_z_upper | 23.7000000 | 23.7000000 | 0          |
| 11      | LAMZUL                     | Lambda_z_upper | 24.0800000 | 24.0800000 | 0          |
| 12      | LAMZUL                     | Lambda_z_upper | 24.1500000 | 24.1500000 | 0          |
| 1       | LAMZHL                     | HL_Lambda_z    | 14.3043776 | 14.3043776 | 0          |
| 2       | LAMZHL                     | HL_Lambda_z    | 6.6593416  | 6.6593416  | 0          |
| 3       | LAMZHL                     | HL_Lambda_z    | 6.7660874  | 6.7660874  | 0          |
| 4       | LAMZHL                     | HL_Lambda_z    | 6.9812467  | 6.9812467  | 0          |
| 5       | LAMZHL                     | HL_Lambda_z    | 8.0022640  | 8.0022640  | 0          |
| 6       | LAMZHL                     | HL_Lambda_z    | 7.8949979  | 7.8949979  | 0          |
| 7       | LAMZHL                     | HL_Lambda_z    | 7.8466683  | 7.8466683  | 0          |
| 8       | LAMZHL                     | HL_Lambda_z    | 8.5100379  | 8.5100379  | 0          |
| 9       | LAMZHL                     | HL_Lambda_z    | 8.4059988  | 8.4059988  | 0          |
| 10      | LAMZHL                     | HL_Lambda_z    | 9.2469158  | 9.2469158  | 0          |
| 11      | LAMZHL                     | HL_Lambda_z    | 7.2612365  | 7.2612365  | 0          |
| 12      | LAMZHL                     | HL_Lambda_z    | 6.2865082  | 6.2865082  | 0          |
| 1       | TLAG                       | Tlag           | 0.0000000  | 0.0000000  | 0          |
| 2       | TLAG                       | Tlag           | 0.0000000  | 0.0000000  | 0          |
| 3       | TLAG                       | Tlag           | 0.0000000  | 0.0000000  | 0          |
| 4       | TLAG                       | Tlag           | 0.0000000  | 0.0000000  | 0          |
| 5       | TLAG                       | Tlag           | 0.0000000  | 0.0000000  | 0          |
| 6       | TLAG                       | Tlag           | 0.0000000  | 0.0000000  | 0          |
| 7       | TLAG                       | Tlag           | 0.0000000  | 0.0000000  | 0          |
| 8       | TLAG                       | Tlag           | 0.0000000  | 0.0000000  | 0          |
| 9       | TLAG                       | Tlag           | 0.0000000  | 0.0000000  | 0          |
| 10      | TLAG                       | Tlag           | 0.0000000  | 0.0000000  | 0          |
| 11      | TLAG                       | Tlag           | 0.0000000  | 0.0000000  | 0          |

Table 2: Theoph (n=12), Linear, Extravascular (*continued*)

| Subject | Pharmacokinetic Parameters |        | Values     |            | Difference |
|---------|----------------------------|--------|------------|------------|------------|
|         | PPTSTCD                    | WNL    | NonCompart | WinNonlin  |            |
| 12      | TLAG                       | Tlag   | 0.0000000  | 0.0000000  | 0          |
| 1       | TMAX                       | Tmax   | 1.1200000  | 1.1200000  | 0          |
| 2       | TMAX                       | Tmax   | 1.9200000  | 1.9200000  | 0          |
| 3       | TMAX                       | Tmax   | 1.0200000  | 1.0200000  | 0          |
| 4       | TMAX                       | Tmax   | 1.0700000  | 1.0700000  | 0          |
| 5       | TMAX                       | Tmax   | 1.0000000  | 1.0000000  | 0          |
| 6       | TMAX                       | Tmax   | 1.1500000  | 1.1500000  | 0          |
| 7       | TMAX                       | Tmax   | 3.4800000  | 3.4800000  | 0          |
| 8       | TMAX                       | Tmax   | 2.0200000  | 2.0200000  | 0          |
| 9       | TMAX                       | Tmax   | 0.6300000  | 0.6300000  | 0          |
| 10      | TMAX                       | Tmax   | 3.5500000  | 3.5500000  | 0          |
| 11      | TMAX                       | Tmax   | 0.9800000  | 0.9800000  | 0          |
| 12      | TMAX                       | Tmax   | 3.5200000  | 3.5200000  | 0          |
| 1       | CMAX                       | Cmax   | 10.5000000 | 10.5000000 | 0          |
| 2       | CMAX                       | Cmax   | 8.3300000  | 8.3300000  | 0          |
| 3       | CMAX                       | Cmax   | 8.2000000  | 8.2000000  | 0          |
| 4       | CMAX                       | Cmax   | 8.6000000  | 8.6000000  | 0          |
| 5       | CMAX                       | Cmax   | 11.4000000 | 11.4000000 | 0          |
| 6       | CMAX                       | Cmax   | 6.4400000  | 6.4400000  | 0          |
| 7       | CMAX                       | Cmax   | 7.0900000  | 7.0900000  | 0          |
| 8       | CMAX                       | Cmax   | 7.5600000  | 7.5600000  | 0          |
| 9       | CMAX                       | Cmax   | 9.0300000  | 9.0300000  | 0          |
| 10      | CMAX                       | Cmax   | 10.2100000 | 10.2100000 | 0          |
| 11      | CMAX                       | Cmax   | 8.0000000  | 8.0000000  | 0          |
| 12      | CMAX                       | Cmax   | 9.7500000  | 9.7500000  | 0          |
| 1       | CMAXD                      | Cmax_D | 0.0328125  | 0.0328125  | 0          |
| 2       | CMAXD                      | Cmax_D | 0.0260312  | 0.0260312  | 0          |
| 3       | CMAXD                      | Cmax_D | 0.0256250  | 0.0256250  | 0          |
| 4       | CMAXD                      | Cmax_D | 0.0268750  | 0.0268750  | 0          |
| 5       | CMAXD                      | Cmax_D | 0.0356250  | 0.0356250  | 0          |
| 6       | CMAXD                      | Cmax_D | 0.0201250  | 0.0201250  | 0          |
| 7       | CMAXD                      | Cmax_D | 0.0221562  | 0.0221562  | 0          |
| 8       | CMAXD                      | Cmax_D | 0.0236250  | 0.0236250  | 0          |
| 9       | CMAXD                      | Cmax_D | 0.0282188  | 0.0282188  | 0          |
| 10      | CMAXD                      | Cmax_D | 0.0319063  | 0.0319062  | 0          |
| 11      | CMAXD                      | Cmax_D | 0.0250000  | 0.0250000  | 0          |
| 12      | CMAXD                      | Cmax_D | 0.0304688  | 0.0304688  | 0          |
| 1       | TLST                       | Tlast  | 24.3700000 | 24.3700000 | 0          |
| 2       | TLST                       | Tlast  | 24.3000000 | 24.3000000 | 0          |
| 3       | TLST                       | Tlast  | 24.1700000 | 24.1700000 | 0          |
| 4       | TLST                       | Tlast  | 24.6500000 | 24.6500000 | 0          |
| 5       | TLST                       | Tlast  | 24.3500000 | 24.3500000 | 0          |
| 6       | TLST                       | Tlast  | 23.8500000 | 23.8500000 | 0          |
| 7       | TLST                       | Tlast  | 24.2200000 | 24.2200000 | 0          |
| 8       | TLST                       | Tlast  | 24.1200000 | 24.1200000 | 0          |



Table 2: Theoph (n=12), Linear, Extravascular (*continued*)

| Subject | Pharmacokinetic Parameters |            | Values      |             | Difference |
|---------|----------------------------|------------|-------------|-------------|------------|
|         | PPTSTCD                    | WNL        | NonCompart  | WinNonlin   |            |
| 9       | TLST                       | Tlast      | 24.4300000  | 24.4300000  | 0          |
| 10      | TLST                       | Tlast      | 23.7000000  | 23.7000000  | 0          |
| 11      | TLST                       | Tlast      | 24.0800000  | 24.0800000  | 0          |
| 12      | TLST                       | Tlast      | 24.1500000  | 24.1500000  | 0          |
| 1       | CLST                       | Clast      | 3.2800000   | 3.2800000   | 0          |
| 2       | CLST                       | Clast      | 0.9000000   | 0.9000000   | 0          |
| 3       | CLST                       | Clast      | 1.0500000   | 1.0500000   | 0          |
| 4       | CLST                       | Clast      | 1.1500000   | 1.1500000   | 0          |
| 5       | CLST                       | Clast      | 1.5700000   | 1.5700000   | 0          |
| 6       | CLST                       | Clast      | 0.9200000   | 0.9200000   | 0          |
| 7       | CLST                       | Clast      | 1.1500000   | 1.1500000   | 0          |
| 8       | CLST                       | Clast      | 1.2500000   | 1.2500000   | 0          |
| 9       | CLST                       | Clast      | 1.1200000   | 1.1200000   | 0          |
| 10      | CLST                       | Clast      | 2.4200000   | 2.4200000   | 0          |
| 11      | CLST                       | Clast      | 0.8600000   | 0.8600000   | 0          |
| 12      | CLST                       | Clast      | 1.1700000   | 1.1700000   | 0          |
| 1       | AUCLST                     | AUClast    | 148.9230500 | 148.9230500 | 0          |
| 2       | AUCLST                     | AUClast    | 91.5268000  | 91.5268000  | 0          |
| 3       | AUCLST                     | AUClast    | 99.2865000  | 99.2865000  | 0          |
| 4       | AUCLST                     | AUClast    | 106.7963000 | 106.7963000 | 0          |
| 5       | AUCLST                     | AUClast    | 121.2944000 | 121.2944000 | 0          |
| 6       | AUCLST                     | AUClast    | 73.7755500  | 73.7755500  | 0          |
| 7       | AUCLST                     | AUClast    | 90.7534000  | 90.7534000  | 0          |
| 8       | AUCLST                     | AUClast    | 88.5599500  | 88.5599500  | 0          |
| 9       | AUCLST                     | AUClast    | 86.3261500  | 86.3261500  | 0          |
| 10      | AUCLST                     | AUClast    | 138.3681000 | 138.3681000 | 0          |
| 11      | AUCLST                     | AUClast    | 80.0936000  | 80.0936000  | 0          |
| 12      | AUCLST                     | AUClast    | 119.9775000 | 119.9775000 | 0          |
| 1       | AUCALL                     | AUCall     | 148.9230500 | 148.9230500 | 0          |
| 2       | AUCALL                     | AUCall     | 91.5268000  | 91.5268000  | 0          |
| 3       | AUCALL                     | AUCall     | 99.2865000  | 99.2865000  | 0          |
| 4       | AUCALL                     | AUCall     | 106.7963000 | 106.7963000 | 0          |
| 5       | AUCALL                     | AUCall     | 121.2944000 | 121.2944000 | 0          |
| 6       | AUCALL                     | AUCall     | 73.7755500  | 73.7755500  | 0          |
| 7       | AUCALL                     | AUCall     | 90.7534000  | 90.7534000  | 0          |
| 8       | AUCALL                     | AUCall     | 88.5599500  | 88.5599500  | 0          |
| 9       | AUCALL                     | AUCall     | 86.3261500  | 86.3261500  | 0          |
| 10      | AUCALL                     | AUCall     | 138.3681000 | 138.3681000 | 0          |
| 11      | AUCALL                     | AUCall     | 80.0936000  | 80.0936000  | 0          |
| 12      | AUCALL                     | AUCall     | 119.9775000 | 119.9775000 | 0          |
| 1       | AUCIFO                     | AUCINF_obs | 216.6119330 | 216.6119330 | 0          |
| 2       | AUCIFO                     | AUCINF_obs | 100.1734591 | 100.1734591 | 0          |
| 3       | AUCIFO                     | AUCINF_obs | 109.5359707 | 109.5359707 | 0          |
| 4       | AUCIFO                     | AUCINF_obs | 118.3788814 | 118.3788814 | 0          |
| 5       | AUCIFO                     | AUCINF_obs | 139.4197778 | 139.4197778 | 0          |

Table 2: Theoph (n=12), Linear, Extravascular (*continued*)

| Subject | Pharmacokinetic Parameters |                 | Values      |             | Difference |
|---------|----------------------------|-----------------|-------------|-------------|------------|
|         | PPTSTCD                    | WNL             | NonCompart  | WinNonlin   |            |
| 6       | AUCIFO                     | AUCINF_obs      | 84.2544183  | 84.2544183  | 0          |
| 7       | AUCIFO                     | AUCINF_obs      | 103.7718018 | 103.7718018 | 0          |
| 8       | AUCIFO                     | AUCINF_obs      | 103.9066868 | 103.9066868 | 0          |
| 9       | AUCIFO                     | AUCINF_obs      | 99.9087179  | 99.9087179  | 0          |
| 10      | AUCIFO                     | AUCINF_obs      | 170.6520606 | 170.6520606 | 0          |
| 11      | AUCIFO                     | AUCINF_obs      | 89.1027449  | 89.1027449  | 0          |
| 12      | AUCIFO                     | AUCINF_obs      | 130.5888316 | 130.5888316 | 0          |
| 1       | AUCIFOD                    | AUCINF_D_obs    | 0.6769123   | 0.6769123   | 0          |
| 2       | AUCIFOD                    | AUCINF_D_obs    | 0.3130421   | 0.3130421   | 0          |
| 3       | AUCIFOD                    | AUCINF_D_obs    | 0.3422999   | 0.3422999   | 0          |
| 4       | AUCIFOD                    | AUCINF_D_obs    | 0.3699340   | 0.3699340   | 0          |
| 5       | AUCIFOD                    | AUCINF_D_obs    | 0.4356868   | 0.4356868   | 0          |
| 6       | AUCIFOD                    | AUCINF_D_obs    | 0.2632951   | 0.2632951   | 0          |
| 7       | AUCIFOD                    | AUCINF_D_obs    | 0.3242869   | 0.3242869   | 0          |
| 8       | AUCIFOD                    | AUCINF_D_obs    | 0.3247084   | 0.3247084   | 0          |
| 9       | AUCIFOD                    | AUCINF_D_obs    | 0.3122147   | 0.3122147   | 0          |
| 10      | AUCIFOD                    | AUCINF_D_obs    | 0.5332877   | 0.5332877   | 0          |
| 11      | AUCIFOD                    | AUCINF_D_obs    | 0.2784461   | 0.2784461   | 0          |
| 12      | AUCIFOD                    | AUCINF_D_obs    | 0.4080901   | 0.4080901   | 0          |
| 1       | AUCPEO                     | AUC_.Extrap_obs | 31.2489169  | 31.2489169  | 0          |
| 2       | AUCPEO                     | AUC_.Extrap_obs | 8.6316867   | 8.6316867   | 0          |
| 3       | AUCPEO                     | AUC_.Extrap_obs | 9.3571734   | 9.3571734   | 0          |
| 4       | AUCPEO                     | AUC_.Extrap_obs | 9.7843309   | 9.7843309   | 0          |
| 5       | AUCPEO                     | AUC_.Extrap_obs | 13.0005786  | 13.0005786  | 0          |
| 6       | AUCPEO                     | AUC_.Extrap_obs | 12.4371737  | 12.4371737  | 0          |
| 7       | AUCPEO                     | AUC_.Extrap_obs | 12.5452209  | 12.5452209  | 0          |
| 8       | AUCPEO                     | AUC_.Extrap_obs | 14.7697297  | 14.7697297  | 0          |
| 9       | AUCPEO                     | AUC_.Extrap_obs | 13.5949777  | 13.5949777  | 0          |
| 10      | AUCPEO                     | AUC_.Extrap_obs | 18.9180022  | 18.9180022  | 0          |
| 11      | AUCPEO                     | AUC_.Extrap_obs | 10.1109623  | 10.1109623  | 0          |
| 12      | AUCPEO                     | AUC_.Extrap_obs | 8.1257573   | 8.1257573   | 0          |
| 1       | VZFO                       | Vz_F_obs        | 30.4867482  | 30.4867482  | 0          |
| 2       | VZFO                       | Vz_F_obs        | 30.6904416  | 30.6904416  | 0          |
| 3       | VZFO                       | Vz_F_obs        | 28.5170999  | 28.5170999  | 0          |
| 4       | VZFO                       | Vz_F_obs        | 27.2259641  | 27.2259641  | 0          |
| 5       | VZFO                       | Vz_F_obs        | 26.4979947  | 26.4979946  | 0          |
| 6       | VZFO                       | Vz_F_obs        | 43.2597345  | 43.2597345  | 0          |
| 7       | VZFO                       | Vz_F_obs        | 34.9084408  | 34.9084408  | 0          |
| 8       | VZFO                       | Vz_F_obs        | 37.8105081  | 37.8105081  | 0          |
| 9       | VZFO                       | Vz_F_obs        | 38.8427934  | 38.8427934  | 0          |
| 10      | VZFO                       | Vz_F_obs        | 25.0155401  | 25.0155401  | 0          |
| 11      | VZFO                       | Vz_F_obs        | 37.6221852  | 37.6221852  | 0          |
| 12      | VZFO                       | Vz_F_obs        | 22.2242936  | 22.2242936  | 0          |
| 1       | CLFO                       | Cl_F_obs        | 1.4772963   | 1.4772963   | 0          |
| 2       | CLFO                       | Cl_F_obs        | 3.1944589   | 3.1944589   | 0          |

Table 2: Theoph (n=12), Linear, Extravascular (*continued*)

| Subject | Pharmacokinetic Parameters |                  | Values      |             | Difference |
|---------|----------------------------|------------------|-------------|-------------|------------|
|         | PPTTESTCD                  | WNL              | NonCompart  | WinNonlin   |            |
| 3       | CLFO                       | Cl_F_obs         | 2.9214147   | 2.9214147   | 0          |
| 4       | CLFO                       | Cl_F_obs         | 2.7031849   | 2.7031849   | 0          |
| 5       | CLFO                       | Cl_F_obs         | 2.2952267   | 2.2952267   | 0          |
| 6       | CLFO                       | Cl_F_obs         | 3.7980204   | 3.7980204   | 0          |
| 7       | CLFO                       | Cl_F_obs         | 3.0836893   | 3.0836894   | 0          |
| 8       | CLFO                       | Cl_F_obs         | 3.0796863   | 3.0796863   | 0          |
| 9       | CLFO                       | Cl_F_obs         | 3.2029237   | 3.2029237   | 0          |
| 10      | CLFO                       | Cl_F_obs         | 1.8751605   | 1.8751605   | 0          |
| 11      | CLFO                       | Cl_F_obs         | 3.5913596   | 3.5913596   | 0          |
| 12      | CLFO                       | Cl_F_obs         | 2.4504393   | 2.4504393   | 0          |
| 1       | AUCIFP                     | AUCINF_pred      | 216.6149558 | 216.6149558 | 0          |
| 2       | AUCIFP                     | AUCINF_pred      | 100.0643176 | 100.0643176 | 0          |
| 3       | AUCIFP                     | AUCINF_pred      | 109.5857218 | 109.5857218 | 0          |
| 4       | AUCIFP                     | AUCINF_pred      | 118.4435586 | 118.4435586 | 0          |
| 5       | AUCIFP                     | AUCINF_pred      | 139.2546304 | 139.2546304 | 0          |
| 6       | AUCIFP                     | AUCINF_pred      | 84.4966986  | 84.4966986  | 0          |
| 7       | AUCIFP                     | AUCINF_pred      | 103.8931470 | 103.8931470 | 0          |
| 8       | AUCIFP                     | AUCINF_pred      | 103.6430515 | 103.6430515 | 0          |
| 9       | AUCIFP                     | AUCINF_pred      | 99.8660677  | 99.8660677  | 0          |
| 10      | AUCIFP                     | AUCINF_pred      | 170.5679125 | 170.5679125 | 0          |
| 11      | AUCIFP                     | AUCINF_pred      | 89.1007190  | 89.1007190  | 0          |
| 12      | AUCIFP                     | AUCINF_pred      | 130.6390680 | 130.6390680 | 0          |
| 1       | AUCIFPD                    | AUCINF_D_pred    | 0.6769217   | 0.6769217   | 0          |
| 2       | AUCIFPD                    | AUCINF_D_pred    | 0.3127010   | 0.3127010   | 0          |
| 3       | AUCIFPD                    | AUCINF_D_pred    | 0.3424554   | 0.3424554   | 0          |
| 4       | AUCIFPD                    | AUCINF_D_pred    | 0.3701361   | 0.3701361   | 0          |
| 5       | AUCIFPD                    | AUCINF_D_pred    | 0.4351707   | 0.4351707   | 0          |
| 6       | AUCIFPD                    | AUCINF_D_pred    | 0.2640522   | 0.2640522   | 0          |
| 7       | AUCIFPD                    | AUCINF_D_pred    | 0.3246661   | 0.3246661   | 0          |
| 8       | AUCIFPD                    | AUCINF_D_pred    | 0.3238845   | 0.3238845   | 0          |
| 9       | AUCIFPD                    | AUCINF_D_pred    | 0.3120815   | 0.3120815   | 0          |
| 10      | AUCIFPD                    | AUCINF_D_pred    | 0.5330247   | 0.5330247   | 0          |
| 11      | AUCIFPD                    | AUCINF_D_pred    | 0.2784397   | 0.2784397   | 0          |
| 12      | AUCIFPD                    | AUCINF_D_pred    | 0.4082471   | 0.4082471   | 0          |
| 1       | AUCPEP                     | AUC_.Extrap_pred | 31.2498763  | 31.2498763  | 0          |
| 2       | AUCPEP                     | AUC_.Extrap_pred | 8.5320300   | 8.5320300   | 0          |
| 3       | AUCPEP                     | AUC_.Extrap_pred | 9.3983245   | 9.3983245   | 0          |
| 4       | AUCPEP                     | AUC_.Extrap_pred | 9.8335939   | 9.8335939   | 0          |
| 5       | AUCPEP                     | AUC_.Extrap_pred | 12.8974027  | 12.8974027  | 0          |
| 6       | AUCPEP                     | AUC_.Extrap_pred | 12.6882455  | 12.6882455  | 0          |
| 7       | AUCPEP                     | AUC_.Extrap_pred | 12.6473665  | 12.6473664  | 0          |
| 8       | AUCPEP                     | AUC_.Extrap_pred | 14.5529307  | 14.5529307  | 0          |
| 9       | AUCPEP                     | AUC_.Extrap_pred | 13.5580763  | 13.5580763  | 0          |
| 10      | AUCPEP                     | AUC_.Extrap_pred | 18.8780012  | 18.8780012  | 0          |
| 11      | AUCPEP                     | AUC_.Extrap_pred | 10.1089184  | 10.1089184  | 0          |

Table 2: Theoph (n=12), Linear, Extravascular (*continued*)

| Subject | Pharmacokinetic Parameters |                  | Values       |              | Difference |
|---------|----------------------------|------------------|--------------|--------------|------------|
|         | PPTTESTCD                  | WNL              | NonCompart   | WinNonlin    |            |
| 12      | AUCPEP                     | AUC_.Extrap_pred | 8.1610870    | 8.1610870    | 0          |
| 1       | VZFP                       | Vz_F_pred        | 30.4863228   | 30.4863228   | 0          |
| 2       | VZFP                       | Vz_F_pred        | 30.7239161   | 30.7239161   | 0          |
| 3       | VZFP                       | Vz_F_pred        | 28.5041534   | 28.5041534   | 0          |
| 4       | VZFP                       | Vz_F_pred        | 27.2110972   | 27.2110972   | 0          |
| 5       | VZFP                       | Vz_F_pred        | 26.5294196   | 26.5294196   | 0          |
| 6       | VZFP                       | Vz_F_pred        | 43.1356944   | 43.1356944   | 0          |
| 7       | VZFP                       | Vz_F_pred        | 34.8676684   | 34.8676684   | 0          |
| 8       | VZFP                       | Vz_F_pred        | 37.9066862   | 37.9066862   | 0          |
| 9       | VZFP                       | Vz_F_pred        | 38.8593822   | 38.8593822   | 0          |
| 10      | VZFP                       | Vz_F_pred        | 25.0278813   | 25.0278813   | 0          |
| 11      | VZFP                       | Vz_F_pred        | 37.6230406   | 37.6230406   | 0          |
| 12      | VZFP                       | Vz_F_pred        | 22.2157473   | 22.2157473   | 0          |
| 1       | CLFP                       | Cl_F_pred        | 1.4772757    | 1.4772757    | 0          |
| 2       | CLFP                       | Cl_F_pred        | 3.1979432    | 3.1979432    | 0          |
| 3       | CLFP                       | Cl_F_pred        | 2.9200884    | 2.9200884    | 0          |
| 4       | CLFP                       | Cl_F_pred        | 2.7017088    | 2.7017088    | 0          |
| 5       | CLFP                       | Cl_F_pred        | 2.2979487    | 2.2979487    | 0          |
| 6       | CLFP                       | Cl_F_pred        | 3.7871302    | 3.7871302    | 0          |
| 7       | CLFP                       | Cl_F_pred        | 3.0800877    | 3.0800877    | 0          |
| 8       | CLFP                       | Cl_F_pred        | 3.0875201    | 3.0875201    | 0          |
| 9       | CLFP                       | Cl_F_pred        | 3.2042916    | 3.2042916    | 0          |
| 10      | CLFP                       | Cl_F_pred        | 1.8760856    | 1.8760856    | 0          |
| 11      | CLFP                       | Cl_F_pred        | 3.5914413    | 3.5914413    | 0          |
| 12      | CLFP                       | Cl_F_pred        | 2.4494970    | 2.4494970    | 0          |
| 1       | AUMCLST                    | AUMClast         | 1459.0711035 | 1459.0711040 | 0          |
| 2       | AUMCLST                    | AUMClast         | 706.5865660  | 706.5865660  | 0          |
| 3       | AUMCLST                    | AUMClast         | 803.1858700  | 803.1858700  | 0          |
| 4       | AUMCLST                    | AUMClast         | 901.0842105  | 901.0842105  | 0          |
| 5       | AUMCLST                    | AUMClast         | 1017.1143165 | 1017.1143170 | 0          |
| 6       | AUMCLST                    | AUMClast         | 609.1523875  | 609.1523875  | 0          |
| 7       | AUMCLST                    | AUMClast         | 782.4198600  | 782.4198600  | 0          |
| 8       | AUMCLST                    | AUMClast         | 739.5345980  | 739.5345980  | 0          |
| 9       | AUMCLST                    | AUMClast         | 705.2296255  | 705.2296255  | 0          |
| 10      | AUMCLST                    | AUMClast         | 1278.1800420 | 1278.1800420 | 0          |
| 11      | AUMCLST                    | AUMClast         | 617.2422125  | 617.2422125  | 0          |
| 12      | AUMCLST                    | AUMClast         | 977.8807235  | 977.8807235  | 0          |
| 1       | AUMCIFO                    | AUMCINF_obs      | 4505.5348194 | 4505.5348190 | 0          |
| 2       | AUMCIFO                    | AUMCINF_obs      | 999.7722880  | 999.7722880  | 0          |
| 3       | AUMCIFO                    | AUMCINF_obs      | 1150.9647687 | 1150.9647690 | 0          |
| 4       | AUMCIFO                    | AUMCINF_obs      | 1303.2524014 | 1303.2524010 | 0          |
| 5       | AUMCIFO                    | AUMCINF_obs      | 1667.7216119 | 1667.7216120 | 0          |
| 6       | AUMCIFO                    | AUMCINF_obs      | 978.4284857  | 978.4284857  | 0          |
| 7       | AUMCIFO                    | AUMCINF_obs      | 1245.0984083 | 1245.0984080 | 0          |
| 8       | AUMCIFO                    | AUMCINF_obs      | 1298.1157547 | 1298.1157550 | 0          |

Table 2: Theoph (n=12), Linear, Extravascular (*continued*)

| Subject | Pharmacokinetic Parameters |                   | Values       |              | Difference |
|---------|----------------------------|-------------------|--------------|--------------|------------|
|         | PPTSTCD                    | WNL               | NonCompart   | WinNonlin    |            |
| 9       | AUMCIFO                    | AUMCINF_obs       | 1201.7715381 | 1201.7715380 | 0          |
| 10      | AUMCIFO                    | AUMCINF_obs       | 2473.9934274 | 2473.9934270 | 0          |
| 11      | AUMCIFO                    | AUMCINF_obs       | 928.5599714  | 928.5599714  | 0          |
| 12      | AUMCIFO                    | AUMCINF_obs       | 1330.3840024 | 1330.3840020 | 0          |
| 1       | AUMCPEO                    | AUMC_.Extrap_obs  | 67.6160287   | 67.6160287   | 0          |
| 2       | AUMCPEO                    | AUMC_.Extrap_obs  | 29.3252499   | 29.3252499   | 0          |
| 3       | AUMCPEO                    | AUMC_.Extrap_obs  | 30.2162940   | 30.2162940   | 0          |
| 4       | AUMCPEO                    | AUMC_.Extrap_obs  | 30.8588107   | 30.8588107   | 0          |
| 5       | AUMCPEO                    | AUMC_.Extrap_obs  | 39.0117446   | 39.0117446   | 0          |
| 6       | AUMCPEO                    | AUMC_.Extrap_obs  | 37.7417567   | 37.7417567   | 0          |
| 7       | AUMCPEO                    | AUMC_.Extrap_obs  | 37.1599984   | 37.1599984   | 0          |
| 8       | AUMCPEO                    | AUMC_.Extrap_obs  | 43.0301500   | 43.0301500   | 0          |
| 9       | AUMCPEO                    | AUMC_.Extrap_obs  | 41.3174965   | 41.3174965   | 0          |
| 10      | AUMCPEO                    | AUMC_.Extrap_obs  | 48.3353501   | 48.3353501   | 0          |
| 11      | AUMCPEO                    | AUMC_.Extrap_obs  | 33.5269416   | 33.5269415   | 0          |
| 12      | AUMCPEO                    | AUMC_.Extrap_obs  | 26.4963558   | 26.4963558   | 0          |
| 1       | AUMCIFP                    | AUMCINF_pred      | 4505.6708646 | 4505.6708650 | 0          |
| 2       | AUMCIFP                    | AUMCINF_pred      | 996.0715835  | 996.0715835  | 0          |
| 3       | AUMCIFP                    | AUMCINF_pred      | 1152.6528903 | 1152.6528900 | 0          |
| 4       | AUMCIFP                    | AUMCINF_pred      | 1305.4981092 | 1305.4981090 | 0          |
| 5       | AUMCIFP                    | AUMCINF_pred      | 1661.7936744 | 1661.7936740 | 0          |
| 6       | AUMCIFP                    | AUMCINF_pred      | 986.9664597  | 986.9664597  | 0          |
| 7       | AUMCIFP                    | AUMCINF_pred      | 1249.4110601 | 1249.4110600 | 0          |
| 8       | AUMCIFP                    | AUMCINF_pred      | 1288.5201162 | 1288.5201160 | 0          |
| 9       | AUMCIFP                    | AUMCINF_pred      | 1200.2123597 | 1200.2123600 | 0          |
| 10      | AUMCIFP                    | AUMCINF_pred      | 2470.8765418 | 2470.8765420 | 0          |
| 11      | AUMCIFP                    | AUMCINF_pred      | 928.4899636  | 928.4899636  | 0          |
| 12      | AUMCIFP                    | AUMCINF_pred      | 1332.0528341 | 1332.0528340 | 0          |
| 1       | AUMCPEP                    | AUMC_.Extrap_pred | 67.6170065   | 67.6170065   | 0          |
| 2       | AUMCPEP                    | AUMC_.Extrap_pred | 29.0626720   | 29.0626720   | 0          |
| 3       | AUMCPEP                    | AUMC_.Extrap_pred | 30.3184960   | 30.3184960   | 0          |
| 4       | AUMCPEP                    | AUMC_.Extrap_pred | 30.9777468   | 30.9777468   | 0          |
| 5       | AUMCPEP                    | AUMC_.Extrap_pred | 38.7941877   | 38.7941877   | 0          |
| 6       | AUMCPEP                    | AUMC_.Extrap_pred | 38.2803355   | 38.2803355   | 0          |
| 7       | AUMCPEP                    | AUMC_.Extrap_pred | 37.3769062   | 37.3769062   | 0          |
| 8       | AUMCPEP                    | AUMC_.Extrap_pred | 42.6058943   | 42.6058943   | 0          |
| 9       | AUMCPEP                    | AUMC_.Extrap_pred | 41.2412629   | 41.2412629   | 0          |
| 10      | AUMCPEP                    | AUMC_.Extrap_pred | 48.2701778   | 48.2701778   | 0          |
| 11      | AUMCPEP                    | AUMC_.Extrap_pred | 33.5219295   | 33.5219295   | 0          |
| 12      | AUMCPEP                    | AUMC_.Extrap_pred | 26.5884432   | 26.5884432   | 0          |
| 1       | MRTEVLST                   | MRTlast           | 9.7974834    | 9.7974834    | 0          |
| 2       | MRTEVLST                   | MRTlast           | 7.7199964    | 7.7199964    | 0          |
| 3       | MRTEVLST                   | MRTlast           | 8.0895778    | 8.0895778    | 0          |
| 4       | MRTEVLST                   | MRTlast           | 8.4374104    | 8.4374104    | 0          |
| 5       | MRTEVLST                   | MRTlast           | 8.3855010    | 8.3855010    | 0          |

Table 2: Theoph (n=12), Linear, Extravascular (*continued*)

| Subject | Pharmacokinetic Parameters |             | Values     |            | Difference |
|---------|----------------------------|-------------|------------|------------|------------|
|         | PPTESTCD                   | WNL         | NonCompart | WinNonlin  |            |
| 6       | MRTEVLST                   | MRTlast     | 8.2568329  | 8.2568329  | 0          |
| 7       | MRTEVLST                   | MRTlast     | 8.6213834  | 8.6213834  | 0          |
| 8       | MRTEVLST                   | MRTlast     | 8.3506664  | 8.3506664  | 0          |
| 9       | MRTEVLST                   | MRTlast     | 8.1693626  | 8.1693627  | 0          |
| 10      | MRTEVLST                   | MRTlast     | 9.2375341  | 9.2375341  | 0          |
| 11      | MRTEVLST                   | MRTlast     | 7.7065110  | 7.7065110  | 0          |
| 12      | MRTEVLST                   | MRTlast     | 8.1505343  | 8.1505343  | 0          |
| 1       | MRTEVIFO                   | MRTINF_obs  | 20.8000305 | 20.8000305 | 0          |
| 2       | MRTEVIFO                   | MRTINF_obs  | 9.9804109  | 9.9804109  | 0          |
| 3       | MRTEVIFO                   | MRTINF_obs  | 10.5076420 | 10.5076420 | 0          |
| 4       | MRTEVIFO                   | MRTINF_obs  | 11.0091630 | 11.0091630 | 0          |
| 5       | MRTEVIFO                   | MRTINF_obs  | 11.9618725 | 11.9618725 | 0          |
| 6       | MRTEVIFO                   | MRTINF_obs  | 11.6127855 | 11.6127855 | 0          |
| 7       | MRTEVIFO                   | MRTINF_obs  | 11.9984272 | 11.9984272 | 0          |
| 8       | MRTEVIFO                   | MRTINF_obs  | 12.4930916 | 12.4930916 | 0          |
| 9       | MRTEVIFO                   | MRTINF_obs  | 12.0286954 | 12.0286954 | 0          |
| 10      | MRTEVIFO                   | MRTINF_obs  | 14.4972959 | 14.4972959 | 0          |
| 11      | MRTEVIFO                   | MRTINF_obs  | 10.4212275 | 10.4212274 | 0          |
| 12      | MRTEVIFO                   | MRTINF_obs  | 10.1875787 | 10.1875787 | 0          |
| 1       | MRTEVIFP                   | MRTINF_pred | 20.8003683 | 20.8003683 | 0          |
| 2       | MRTEVIFP                   | MRTINF_pred | 9.9543135  | 9.9543135  | 0          |
| 3       | MRTEVIFP                   | MRTINF_pred | 10.5182762 | 10.5182762 | 0          |
| 4       | MRTEVIFP                   | MRTINF_pred | 11.0221115 | 11.0221115 | 0          |
| 5       | MRTEVIFP                   | MRTINF_pred | 11.9334895 | 11.9334895 | 0          |
| 6       | MRTEVIFP                   | MRTINF_pred | 11.6805328 | 11.6805328 | 0          |
| 7       | MRTEVIFP                   | MRTINF_pred | 12.0259237 | 12.0259237 | 0          |
| 8       | MRTEVIFP                   | MRTINF_pred | 12.4322866 | 12.4322866 | 0          |
| 9       | MRTEVIFP                   | MRTINF_pred | 12.0182199 | 12.0182199 | 0          |
| 10      | MRTEVIFP                   | MRTINF_pred | 14.4861745 | 14.4861745 | 0          |
| 11      | MRTEVIFP                   | MRTINF_pred | 10.4206787 | 10.4206787 | 0          |
| 12      | MRTEVIFP                   | MRTINF_pred | 10.1964355 | 10.1964355 | 0          |

## A.2 Test 2: Theoph (n=12), Log, Extravascular

```
table_wres_rres(Wres2, Rres2,
  Caption = 'Theoph (n=12), Log, Extravascular')
```

Table 3: Theoph (n=12), Log, Extravascular

| Subject | Pharmacokinetic Parameters |     | Values     |           | Difference |
|---------|----------------------------|-----|------------|-----------|------------|
|         | PPTESTCD                   | WNL | NonCompart | WinNonlin |            |
| 1       | R2                         | Rsq | 0.9999997  | 0.9999997 | 0          |
| 2       | R2                         | Rsq | 0.9971954  | 0.9971954 | 0          |

Table 3: Theoph (n=12), Log, Extravascular (*continued*)

| Subject | Pharmacokinetic Parameters |                    | Values     |            | Difference |
|---------|----------------------------|--------------------|------------|------------|------------|
|         | PPTTESTCD                  | WNL                | NonCompart | WinNonlin  |            |
| 3       | R2                         | Rsqr               | 0.9993250  | 0.9993250  | 0          |
| 4       | R2                         | Rsqr               | 0.9989241  | 0.9989241  | 0          |
| 5       | R2                         | Rsqr               | 0.9986472  | 0.9986472  | 0          |
| 6       | R2                         | Rsqr               | 0.9982413  | 0.9982413  | 0          |
| 7       | R2                         | Rsqr               | 0.9986702  | 0.9986702  | 0          |
| 8       | R2                         | Rsqr               | 0.9910124  | 0.9910124  | 0          |
| 9       | R2                         | Rsqr               | 0.9994437  | 0.9994437  | 0          |
| 10      | R2                         | Rsqr               | 0.9995087  | 0.9995087  | 0          |
| 11      | R2                         | Rsqr               | 0.9999983  | 0.9999983  | 0          |
| 12      | R2                         | Rsqr               | 0.9993968  | 0.9993968  | 0          |
| 1       | R2ADJ                      | Rsqr_adjusted      | 0.9999995  | 0.9999995  | 0          |
| 2       | R2ADJ                      | Rsqr_adjusted      | 0.9957931  | 0.9957931  | 0          |
| 3       | R2ADJ                      | Rsqr_adjusted      | 0.9986499  | 0.9986499  | 0          |
| 4       | R2ADJ                      | Rsqr_adjusted      | 0.9978483  | 0.9978483  | 0          |
| 5       | R2ADJ                      | Rsqr_adjusted      | 0.9979708  | 0.9979708  | 0          |
| 6       | R2ADJ                      | Rsqr_adjusted      | 0.9978896  | 0.9978896  | 0          |
| 7       | R2ADJ                      | Rsqr_adjusted      | 0.9980053  | 0.9980053  | 0          |
| 8       | R2ADJ                      | Rsqr_adjusted      | 0.9887655  | 0.9887655  | 0          |
| 9       | R2ADJ                      | Rsqr_adjusted      | 0.9988873  | 0.9988873  | 0          |
| 10      | R2ADJ                      | Rsqr_adjusted      | 0.9990174  | 0.9990174  | 0          |
| 11      | R2ADJ                      | Rsqr_adjusted      | 0.9999965  | 0.9999965  | 0          |
| 12      | R2ADJ                      | Rsqr_adjusted      | 0.9987936  | 0.9987936  | 0          |
| 1       | CORRXY                     | Corr_XY            | -0.9999999 | -0.9999999 | 0          |
| 2       | CORRXY                     | Corr_XY            | -0.9985967 | -0.9985967 | 0          |
| 3       | CORRXY                     | Corr_XY            | -0.9996624 | -0.9996624 | 0          |
| 4       | CORRXY                     | Corr_XY            | -0.9994619 | -0.9994619 | 0          |
| 5       | CORRXY                     | Corr_XY            | -0.9993234 | -0.9993234 | 0          |
| 6       | CORRXY                     | Corr_XY            | -0.9991203 | -0.9991203 | 0          |
| 7       | CORRXY                     | Corr_XY            | -0.9993349 | -0.9993349 | 0          |
| 8       | CORRXY                     | Corr_XY            | -0.9954961 | -0.9954961 | 0          |
| 9       | CORRXY                     | Corr_XY            | -0.9997218 | -0.9997218 | 0          |
| 10      | CORRXY                     | Corr_XY            | -0.9997543 | -0.9997543 | 0          |
| 11      | CORRXY                     | Corr_XY            | -0.9999991 | -0.9999991 | 0          |
| 12      | CORRXY                     | Corr_XY            | -0.9996984 | -0.9996984 | 0          |
| 1       | LAMZNPT                    | No_points_lambda_z | 3.0000000  | 3.0000000  | 0          |
| 2       | LAMZNPT                    | No_points_lambda_z | 4.0000000  | 4.0000000  | 0          |
| 3       | LAMZNPT                    | No_points_lambda_z | 3.0000000  | 3.0000000  | 0          |
| 4       | LAMZNPT                    | No_points_lambda_z | 3.0000000  | 3.0000000  | 0          |
| 5       | LAMZNPT                    | No_points_lambda_z | 4.0000000  | 4.0000000  | 0          |
| 6       | LAMZNPT                    | No_points_lambda_z | 7.0000000  | 7.0000000  | 0          |
| 7       | LAMZNPT                    | No_points_lambda_z | 4.0000000  | 4.0000000  | 0          |
| 8       | LAMZNPT                    | No_points_lambda_z | 6.0000000  | 6.0000000  | 0          |
| 9       | LAMZNPT                    | No_points_lambda_z | 3.0000000  | 3.0000000  | 0          |
| 10      | LAMZNPT                    | No_points_lambda_z | 3.0000000  | 3.0000000  | 0          |
| 11      | LAMZNPT                    | No_points_lambda_z | 3.0000000  | 3.0000000  | 0          |

Table 3: Theoph (n=12), Log, Extravascular (*continued*)

| Subject | Pharmacokinetic Parameters |                    | Values     |            | Difference |
|---------|----------------------------|--------------------|------------|------------|------------|
|         | PPTTESTCD                  | WNL                | NonCompart | WinNonlin  |            |
| 12      | LAMZNPT                    | No_points_lambda_z | 3.0000000  | 3.0000000  | 0          |
| 1       | LAMZ                       | Lambda_z           | 0.0484570  | 0.0484570  | 0          |
| 2       | LAMZ                       | Lambda_z           | 0.1040864  | 0.1040864  | 0          |
| 3       | LAMZ                       | Lambda_z           | 0.1024443  | 0.1024443  | 0          |
| 4       | LAMZ                       | Lambda_z           | 0.0992870  | 0.0992870  | 0          |
| 5       | LAMZ                       | Lambda_z           | 0.0866189  | 0.0866189  | 0          |
| 6       | LAMZ                       | Lambda_z           | 0.0877957  | 0.0877957  | 0          |
| 7       | LAMZ                       | Lambda_z           | 0.0883365  | 0.0883365  | 0          |
| 8       | LAMZ                       | Lambda_z           | 0.0814505  | 0.0814505  | 0          |
| 9       | LAMZ                       | Lambda_z           | 0.0824586  | 0.0824586  | 0          |
| 10      | LAMZ                       | Lambda_z           | 0.0749598  | 0.0749598  | 0          |
| 11      | LAMZ                       | Lambda_z           | 0.0954586  | 0.0954586  | 0          |
| 12      | LAMZ                       | Lambda_z           | 0.1102595  | 0.1102595  | 0          |
| 1       | LAMZLL                     | Lambda_z_lower     | 9.0500000  | 9.0500000  | 0          |
| 2       | LAMZLL                     | Lambda_z_lower     | 7.0300000  | 7.0300000  | 0          |
| 3       | LAMZLL                     | Lambda_z_lower     | 9.0000000  | 9.0000000  | 0          |
| 4       | LAMZLL                     | Lambda_z_lower     | 9.0200000  | 9.0200000  | 0          |
| 5       | LAMZLL                     | Lambda_z_lower     | 7.0200000  | 7.0200000  | 0          |
| 6       | LAMZLL                     | Lambda_z_lower     | 2.0300000  | 2.0300000  | 0          |
| 7       | LAMZLL                     | Lambda_z_lower     | 6.9800000  | 6.9800000  | 0          |
| 8       | LAMZLL                     | Lambda_z_lower     | 3.5300000  | 3.5300000  | 0          |
| 9       | LAMZLL                     | Lambda_z_lower     | 8.8000000  | 8.8000000  | 0          |
| 10      | LAMZLL                     | Lambda_z_lower     | 9.3800000  | 9.3800000  | 0          |
| 11      | LAMZLL                     | Lambda_z_lower     | 9.0300000  | 9.0300000  | 0          |
| 12      | LAMZLL                     | Lambda_z_lower     | 9.0300000  | 9.0300000  | 0          |
| 1       | LAMZUL                     | Lambda_z_upper     | 24.3700000 | 24.3700000 | 0          |
| 2       | LAMZUL                     | Lambda_z_upper     | 24.3000000 | 24.3000000 | 0          |
| 3       | LAMZUL                     | Lambda_z_upper     | 24.1700000 | 24.1700000 | 0          |
| 4       | LAMZUL                     | Lambda_z_upper     | 24.6500000 | 24.6500000 | 0          |
| 5       | LAMZUL                     | Lambda_z_upper     | 24.3500000 | 24.3500000 | 0          |
| 6       | LAMZUL                     | Lambda_z_upper     | 23.8500000 | 23.8500000 | 0          |
| 7       | LAMZUL                     | Lambda_z_upper     | 24.2200000 | 24.2200000 | 0          |
| 8       | LAMZUL                     | Lambda_z_upper     | 24.1200000 | 24.1200000 | 0          |
| 9       | LAMZUL                     | Lambda_z_upper     | 24.4300000 | 24.4300000 | 0          |
| 10      | LAMZUL                     | Lambda_z_upper     | 23.7000000 | 23.7000000 | 0          |
| 11      | LAMZUL                     | Lambda_z_upper     | 24.0800000 | 24.0800000 | 0          |
| 12      | LAMZUL                     | Lambda_z_upper     | 24.1500000 | 24.1500000 | 0          |
| 1       | LAMZHL                     | HL_Lambda_z        | 14.3043776 | 14.3043776 | 0          |
| 2       | LAMZHL                     | HL_Lambda_z        | 6.6593416  | 6.6593416  | 0          |
| 3       | LAMZHL                     | HL_Lambda_z        | 6.7660874  | 6.7660874  | 0          |
| 4       | LAMZHL                     | HL_Lambda_z        | 6.9812467  | 6.9812467  | 0          |
| 5       | LAMZHL                     | HL_Lambda_z        | 8.0022640  | 8.0022640  | 0          |
| 6       | LAMZHL                     | HL_Lambda_z        | 7.8949979  | 7.8949979  | 0          |
| 7       | LAMZHL                     | HL_Lambda_z        | 7.8466683  | 7.8466683  | 0          |
| 8       | LAMZHL                     | HL_Lambda_z        | 8.5100379  | 8.5100379  | 0          |



Table 3: Theoph (n=12), Log, Extravascular (*continued*)

| Subject | Pharmacokinetic Parameters |             | Values     |            | Difference |
|---------|----------------------------|-------------|------------|------------|------------|
|         | PPTSTCD                    | WNL         | NonCompart | WinNonlin  |            |
| 9       | LAMZHL                     | HL_Lambda_z | 8.4059988  | 8.4059988  | 0          |
| 10      | LAMZHL                     | HL_Lambda_z | 9.2469158  | 9.2469158  | 0          |
| 11      | LAMZHL                     | HL_Lambda_z | 7.2612365  | 7.2612365  | 0          |
| 12      | LAMZHL                     | HL_Lambda_z | 6.2865082  | 6.2865082  | 0          |
| 1       | TLAG                       | Tlag        | 0.0000000  | 0.0000000  | 0          |
| 2       | TLAG                       | Tlag        | 0.0000000  | 0.0000000  | 0          |
| 3       | TLAG                       | Tlag        | 0.0000000  | 0.0000000  | 0          |
| 4       | TLAG                       | Tlag        | 0.0000000  | 0.0000000  | 0          |
| 5       | TLAG                       | Tlag        | 0.0000000  | 0.0000000  | 0          |
| 6       | TLAG                       | Tlag        | 0.0000000  | 0.0000000  | 0          |
| 7       | TLAG                       | Tlag        | 0.0000000  | 0.0000000  | 0          |
| 8       | TLAG                       | Tlag        | 0.0000000  | 0.0000000  | 0          |
| 9       | TLAG                       | Tlag        | 0.0000000  | 0.0000000  | 0          |
| 10      | TLAG                       | Tlag        | 0.0000000  | 0.0000000  | 0          |
| 11      | TLAG                       | Tlag        | 0.0000000  | 0.0000000  | 0          |
| 12      | TLAG                       | Tlag        | 0.0000000  | 0.0000000  | 0          |
| 1       | TMAX                       | Tmax        | 1.1200000  | 1.1200000  | 0          |
| 2       | TMAX                       | Tmax        | 1.9200000  | 1.9200000  | 0          |
| 3       | TMAX                       | Tmax        | 1.0200000  | 1.0200000  | 0          |
| 4       | TMAX                       | Tmax        | 1.0700000  | 1.0700000  | 0          |
| 5       | TMAX                       | Tmax        | 1.0000000  | 1.0000000  | 0          |
| 6       | TMAX                       | Tmax        | 1.1500000  | 1.1500000  | 0          |
| 7       | TMAX                       | Tmax        | 3.4800000  | 3.4800000  | 0          |
| 8       | TMAX                       | Tmax        | 2.0200000  | 2.0200000  | 0          |
| 9       | TMAX                       | Tmax        | 0.6300000  | 0.6300000  | 0          |
| 10      | TMAX                       | Tmax        | 3.5500000  | 3.5500000  | 0          |
| 11      | TMAX                       | Tmax        | 0.9800000  | 0.9800000  | 0          |
| 12      | TMAX                       | Tmax        | 3.5200000  | 3.5200000  | 0          |
| 1       | CMAX                       | Cmax        | 10.5000000 | 10.5000000 | 0          |
| 2       | CMAX                       | Cmax        | 8.3300000  | 8.3300000  | 0          |
| 3       | CMAX                       | Cmax        | 8.2000000  | 8.2000000  | 0          |
| 4       | CMAX                       | Cmax        | 8.6000000  | 8.6000000  | 0          |
| 5       | CMAX                       | Cmax        | 11.4000000 | 11.4000000 | 0          |
| 6       | CMAX                       | Cmax        | 6.4400000  | 6.4400000  | 0          |
| 7       | CMAX                       | Cmax        | 7.0900000  | 7.0900000  | 0          |
| 8       | CMAX                       | Cmax        | 7.5600000  | 7.5600000  | 0          |
| 9       | CMAX                       | Cmax        | 9.0300000  | 9.0300000  | 0          |
| 10      | CMAX                       | Cmax        | 10.2100000 | 10.2100000 | 0          |
| 11      | CMAX                       | Cmax        | 8.0000000  | 8.0000000  | 0          |
| 12      | CMAX                       | Cmax        | 9.7500000  | 9.7500000  | 0          |
| 1       | CMAXD                      | Cmax_D      | 0.0328125  | 0.0328125  | 0          |
| 2       | CMAXD                      | Cmax_D      | 0.0260312  | 0.0260312  | 0          |
| 3       | CMAXD                      | Cmax_D      | 0.0256250  | 0.0256250  | 0          |
| 4       | CMAXD                      | Cmax_D      | 0.0268750  | 0.0268750  | 0          |
| 5       | CMAXD                      | Cmax_D      | 0.0356250  | 0.0356250  | 0          |

Table 3: Theoph (n=12), Log, Extravascular (*continued*)

| Subject | Pharmacokinetic Parameters |         | Values      |             | Difference |
|---------|----------------------------|---------|-------------|-------------|------------|
|         | PPTSTCD                    | WNL     | NonCompart  | WinNonlin   |            |
| 6       | CMAXD                      | Cmax_D  | 0.0201250   | 0.0201250   | 0          |
| 7       | CMAXD                      | Cmax_D  | 0.0221562   | 0.0221562   | 0          |
| 8       | CMAXD                      | Cmax_D  | 0.0236250   | 0.0236250   | 0          |
| 9       | CMAXD                      | Cmax_D  | 0.0282188   | 0.0282188   | 0          |
| 10      | CMAXD                      | Cmax_D  | 0.0319063   | 0.0319062   | 0          |
| 11      | CMAXD                      | Cmax_D  | 0.0250000   | 0.0250000   | 0          |
| 12      | CMAXD                      | Cmax_D  | 0.0304688   | 0.0304688   | 0          |
| 1       | TLST                       | Tlast   | 24.3700000  | 24.3700000  | 0          |
| 2       | TLST                       | Tlast   | 24.3000000  | 24.3000000  | 0          |
| 3       | TLST                       | Tlast   | 24.1700000  | 24.1700000  | 0          |
| 4       | TLST                       | Tlast   | 24.6500000  | 24.6500000  | 0          |
| 5       | TLST                       | Tlast   | 24.3500000  | 24.3500000  | 0          |
| 6       | TLST                       | Tlast   | 23.8500000  | 23.8500000  | 0          |
| 7       | TLST                       | Tlast   | 24.2200000  | 24.2200000  | 0          |
| 8       | TLST                       | Tlast   | 24.1200000  | 24.1200000  | 0          |
| 9       | TLST                       | Tlast   | 24.4300000  | 24.4300000  | 0          |
| 10      | TLST                       | Tlast   | 23.7000000  | 23.7000000  | 0          |
| 11      | TLST                       | Tlast   | 24.0800000  | 24.0800000  | 0          |
| 12      | TLST                       | Tlast   | 24.1500000  | 24.1500000  | 0          |
| 1       | CLST                       | Clast   | 3.2800000   | 3.2800000   | 0          |
| 2       | CLST                       | Clast   | 0.9000000   | 0.9000000   | 0          |
| 3       | CLST                       | Clast   | 1.0500000   | 1.0500000   | 0          |
| 4       | CLST                       | Clast   | 1.1500000   | 1.1500000   | 0          |
| 5       | CLST                       | Clast   | 1.5700000   | 1.5700000   | 0          |
| 6       | CLST                       | Clast   | 0.9200000   | 0.9200000   | 0          |
| 7       | CLST                       | Clast   | 1.1500000   | 1.1500000   | 0          |
| 8       | CLST                       | Clast   | 1.2500000   | 1.2500000   | 0          |
| 9       | CLST                       | Clast   | 1.1200000   | 1.1200000   | 0          |
| 10      | CLST                       | Clast   | 2.4200000   | 2.4200000   | 0          |
| 11      | CLST                       | Clast   | 0.8600000   | 0.8600000   | 0          |
| 12      | CLST                       | Clast   | 1.1700000   | 1.1700000   | 0          |
| 1       | AUCLST                     | AUClast | 147.2347485 | 147.2347485 | 0          |
| 2       | AUCLST                     | AUClast | 88.7312755  | 88.7312755  | 0          |
| 3       | AUCLST                     | AUClast | 95.8781978  | 95.8781978  | 0          |
| 4       | AUCLST                     | AUClast | 102.6336232 | 102.6336232 | 0          |
| 5       | AUCLST                     | AUClast | 118.1793538 | 118.1793538 | 0          |
| 6       | AUCLST                     | AUClast | 71.6970150  | 71.6970150  | 0          |
| 7       | AUCLST                     | AUClast | 87.9692274  | 87.9692274  | 0          |
| 8       | AUCLST                     | AUClast | 86.8065635  | 86.8065635  | 0          |
| 9       | AUCLST                     | AUClast | 83.9374360  | 83.9374360  | 0          |
| 10      | AUCLST                     | AUClast | 135.5760701 | 135.5760701 | 0          |
| 11      | AUCLST                     | AUClast | 77.8934723  | 77.8934723  | 0          |
| 12      | AUCLST                     | AUClast | 115.2202082 | 115.2202082 | 0          |
| 1       | AUCALL                     | AUCall  | 147.2347485 | 147.2347485 | 0          |
| 2       | AUCALL                     | AUCall  | 88.7312755  | 88.7312755  | 0          |

Table 3: Theoph (n=12), Log, Extravascular (*continued*)

| Subject | Pharmacokinetic Parameters |                 | Values      |             | Difference |
|---------|----------------------------|-----------------|-------------|-------------|------------|
|         | PPTTESTCD                  | WNL             | NonCompart  | WinNonlin   |            |
| 3       | AUCALL                     | AUCall          | 95.8781978  | 95.8781978  | 0          |
| 4       | AUCALL                     | AUCall          | 102.6336232 | 102.6336232 | 0          |
| 5       | AUCALL                     | AUCall          | 118.1793538 | 118.1793538 | 0          |
| 6       | AUCALL                     | AUCall          | 71.6970150  | 71.6970150  | 0          |
| 7       | AUCALL                     | AUCall          | 87.9692274  | 87.9692274  | 0          |
| 8       | AUCALL                     | AUCall          | 86.8065635  | 86.8065635  | 0          |
| 9       | AUCALL                     | AUCall          | 83.9374360  | 83.9374360  | 0          |
| 10      | AUCALL                     | AUCall          | 135.5760701 | 135.5760701 | 0          |
| 11      | AUCALL                     | AUCall          | 77.8934723  | 77.8934723  | 0          |
| 12      | AUCALL                     | AUCall          | 115.2202082 | 115.2202082 | 0          |
| 1       | AUCIFO                     | AUCINF_obs      | 214.9236316 | 214.9236316 | 0          |
| 2       | AUCIFO                     | AUCINF_obs      | 97.3779346  | 97.3779346  | 0          |
| 3       | AUCIFO                     | AUCINF_obs      | 106.1276685 | 106.1276685 | 0          |
| 4       | AUCIFO                     | AUCINF_obs      | 114.2162046 | 114.2162046 | 0          |
| 5       | AUCIFO                     | AUCINF_obs      | 136.3047316 | 136.3047316 | 0          |
| 6       | AUCIFO                     | AUCINF_obs      | 82.1758833  | 82.1758833  | 0          |
| 7       | AUCIFO                     | AUCINF_obs      | 100.9876292 | 100.9876292 | 0          |
| 8       | AUCIFO                     | AUCINF_obs      | 102.1533003 | 102.1533003 | 0          |
| 9       | AUCIFO                     | AUCINF_obs      | 97.5200039  | 97.5200039  | 0          |
| 10      | AUCIFO                     | AUCINF_obs      | 167.8600307 | 167.8600307 | 0          |
| 11      | AUCIFO                     | AUCINF_obs      | 86.9026173  | 86.9026173  | 0          |
| 12      | AUCIFO                     | AUCINF_obs      | 125.8315397 | 125.8315397 | 0          |
| 1       | AUCIFOD                    | AUCINF_D_obs    | 0.6716363   | 0.6716363   | 0          |
| 2       | AUCIFOD                    | AUCINF_D_obs    | 0.3043060   | 0.3043060   | 0          |
| 3       | AUCIFOD                    | AUCINF_D_obs    | 0.3316490   | 0.3316490   | 0          |
| 4       | AUCIFOD                    | AUCINF_D_obs    | 0.3569256   | 0.3569256   | 0          |
| 5       | AUCIFOD                    | AUCINF_D_obs    | 0.4259523   | 0.4259523   | 0          |
| 6       | AUCIFOD                    | AUCINF_D_obs    | 0.2567996   | 0.2567996   | 0          |
| 7       | AUCIFOD                    | AUCINF_D_obs    | 0.3155863   | 0.3155863   | 0          |
| 8       | AUCIFOD                    | AUCINF_D_obs    | 0.3192291   | 0.3192291   | 0          |
| 9       | AUCIFOD                    | AUCINF_D_obs    | 0.3047500   | 0.3047500   | 0          |
| 10      | AUCIFOD                    | AUCINF_D_obs    | 0.5245626   | 0.5245626   | 0          |
| 11      | AUCIFOD                    | AUCINF_D_obs    | 0.2715707   | 0.2715707   | 0          |
| 12      | AUCIFOD                    | AUCINF_D_obs    | 0.3932236   | 0.3932236   | 0          |
| 1       | AUCPEO                     | AUC_.Extrap_obs | 31.4943883  | 31.4943883  | 0          |
| 2       | AUCPEO                     | AUC_.Extrap_obs | 8.8794850   | 8.8794850   | 0          |
| 3       | AUCPEO                     | AUC_.Extrap_obs | 9.6576801   | 9.6576801   | 0          |
| 4       | AUCPEO                     | AUC_.Extrap_obs | 10.1409266  | 10.1409266  | 0          |
| 5       | AUCPEO                     | AUC_.Extrap_obs | 13.2976879  | 13.2976879  | 0          |
| 6       | AUCPEO                     | AUC_.Extrap_obs | 12.7517562  | 12.7517562  | 0          |
| 7       | AUCPEO                     | AUC_.Extrap_obs | 12.8910857  | 12.8910857  | 0          |
| 8       | AUCPEO                     | AUC_.Extrap_obs | 15.0232413  | 15.0232413  | 0          |
| 9       | AUCPEO                     | AUC_.Extrap_obs | 13.9279813  | 13.9279813  | 0          |
| 10      | AUCPEO                     | AUC_.Extrap_obs | 19.2326669  | 19.2326669  | 0          |
| 11      | AUCPEO                     | AUC_.Extrap_obs | 10.3669431  | 10.3669432  | 0          |

Table 3: Theoph (n=12), Log, Extravascular (*continued*)

| Subject | Pharmacokinetic Parameters |                 | Values      |             | Difference |
|---------|----------------------------|-----------------|-------------|-------------|------------|
|         | PPTSTCD                    | WNL             | NonCompart  | WinNonlin   |            |
| 12      | AUCPEO                     | AUC_.Extrap_obs | 8.4329665   | 8.4329665   | 0          |
| 1       | VZFO                       | Vz_F_obs        | 30.7262325  | 30.7262325  | 0          |
| 2       | VZFO                       | Vz_F_obs        | 31.5715024  | 31.5715024  | 0          |
| 3       | VZFO                       | Vz_F_obs        | 29.4329299  | 29.4329299  | 0          |
| 4       | VZFO                       | Vz_F_obs        | 28.2182304  | 28.2182304  | 0          |
| 5       | VZFO                       | Vz_F_obs        | 27.1035678  | 27.1035677  | 0          |
| 6       | VZFO                       | Vz_F_obs        | 44.3539348  | 44.3539348  | 0          |
| 7       | VZFO                       | Vz_F_obs        | 35.8708471  | 35.8708471  | 0          |
| 8       | VZFO                       | Vz_F_obs        | 38.4594978  | 38.4594978  | 0          |
| 9       | VZFO                       | Vz_F_obs        | 39.7942323  | 39.7942323  | 0          |
| 10      | VZFO                       | Vz_F_obs        | 25.4316257  | 25.4316257  | 0          |
| 11      | VZFO                       | Vz_F_obs        | 38.5746722  | 38.5746722  | 0          |
| 12      | VZFO                       | Vz_F_obs        | 23.0645237  | 23.0645237  | 0          |
| 1       | CLFO                       | Cl_F_obs        | 1.4889010   | 1.4889010   | 0          |
| 2       | CLFO                       | Cl_F_obs        | 3.2861654   | 3.2861654   | 0          |
| 3       | CLFO                       | Cl_F_obs        | 3.0152363   | 3.0152363   | 0          |
| 4       | CLFO                       | Cl_F_obs        | 2.8017040   | 2.8017040   | 0          |
| 5       | CLFO                       | Cl_F_obs        | 2.3476808   | 2.3476808   | 0          |
| 6       | CLFO                       | Cl_F_obs        | 3.8940865   | 3.8940865   | 0          |
| 7       | CLFO                       | Cl_F_obs        | 3.1687049   | 3.1687049   | 0          |
| 8       | CLFO                       | Cl_F_obs        | 3.1325469   | 3.1325469   | 0          |
| 9       | CLFO                       | Cl_F_obs        | 3.2813780   | 3.2813780   | 0          |
| 10      | CLFO                       | Cl_F_obs        | 1.9063502   | 1.9063502   | 0          |
| 11      | CLFO                       | Cl_F_obs        | 3.6822827   | 3.6822827   | 0          |
| 12      | CLFO                       | Cl_F_obs        | 2.5430826   | 2.5430826   | 0          |
| 1       | AUCIFP                     | AUCINF_pred     | 214.9266543 | 214.9266543 | 0          |
| 2       | AUCIFP                     | AUCINF_pred     | 97.2687931  | 97.2687931  | 0          |
| 3       | AUCIFP                     | AUCINF_pred     | 106.1774195 | 106.1774195 | 0          |
| 4       | AUCIFP                     | AUCINF_pred     | 114.2808818 | 114.2808818 | 0          |
| 5       | AUCIFP                     | AUCINF_pred     | 136.1395842 | 136.1395842 | 0          |
| 6       | AUCIFP                     | AUCINF_pred     | 82.4181636  | 82.4181636  | 0          |
| 7       | AUCIFP                     | AUCINF_pred     | 101.1089745 | 101.1089745 | 0          |
| 8       | AUCIFP                     | AUCINF_pred     | 101.8896649 | 101.8896649 | 0          |
| 9       | AUCIFP                     | AUCINF_pred     | 97.4773537  | 97.4773537  | 0          |
| 10      | AUCIFP                     | AUCINF_pred     | 167.7758826 | 167.7758826 | 0          |
| 11      | AUCIFP                     | AUCINF_pred     | 86.9005913  | 86.9005913  | 0          |
| 12      | AUCIFP                     | AUCINF_pred     | 125.8817762 | 125.8817762 | 0          |
| 1       | AUCIFPD                    | AUCINF_D_pred   | 0.6716458   | 0.6716458   | 0          |
| 2       | AUCIFPD                    | AUCINF_D_pred   | 0.3039650   | 0.3039650   | 0          |
| 3       | AUCIFPD                    | AUCINF_D_pred   | 0.3318044   | 0.3318044   | 0          |
| 4       | AUCIFPD                    | AUCINF_D_pred   | 0.3571278   | 0.3571278   | 0          |
| 5       | AUCIFPD                    | AUCINF_D_pred   | 0.4254362   | 0.4254362   | 0          |
| 6       | AUCIFPD                    | AUCINF_D_pred   | 0.2575568   | 0.2575568   | 0          |
| 7       | AUCIFPD                    | AUCINF_D_pred   | 0.3159655   | 0.3159655   | 0          |
| 8       | AUCIFPD                    | AUCINF_D_pred   | 0.3184052   | 0.3184052   | 0          |

Table 3: Theoph (n=12), Log, Extravascular (*continued*)

| Subject | Pharmacokinetic Parameters |                  | Values       |              | Difference |
|---------|----------------------------|------------------|--------------|--------------|------------|
|         | PPTTESTCD                  | WNL              | NonCompart   | WinNonlin    |            |
| 9       | AUCIFPD                    | AUCINF_D_pred    | 0.3046167    | 0.3046167    | 0          |
| 10      | AUCIFPD                    | AUCINF_D_pred    | 0.5242996    | 0.5242996    | 0          |
| 11      | AUCIFPD                    | AUCINF_D_pred    | 0.2715643    | 0.2715643    | 0          |
| 12      | AUCIFPD                    | AUCINF_D_pred    | 0.3933806    | 0.3933806    | 0          |
| 1       | AUCPEP                     | AUC_.Extrap_pred | 31.4953518   | 31.4953518   | 0          |
| 2       | AUCPEP                     | AUC_.Extrap_pred | 8.7772423    | 8.7772423    | 0          |
| 3       | AUCPEP                     | AUC_.Extrap_pred | 9.7000114    | 9.7000114    | 0          |
| 4       | AUCPEP                     | AUC_.Extrap_pred | 10.1917822   | 10.1917822   | 0          |
| 5       | AUCPEP                     | AUC_.Extrap_pred | 13.1925116   | 13.1925116   | 0          |
| 6       | AUCPEP                     | AUC_.Extrap_pred | 13.0082352   | 13.0082352   | 0          |
| 7       | AUCPEP                     | AUC_.Extrap_pred | 12.9956288   | 12.9956288   | 0          |
| 8       | AUCPEP                     | AUC_.Extrap_pred | 14.8033674   | 14.8033674   | 0          |
| 9       | AUCPEP                     | AUC_.Extrap_pred | 13.8903213   | 13.8903213   | 0          |
| 10      | AUCPEP                     | AUC_.Extrap_pred | 19.1921580   | 19.1921580   | 0          |
| 11      | AUCPEP                     | AUC_.Extrap_pred | 10.3648535   | 10.3648535   | 0          |
| 12      | AUCPEP                     | AUC_.Extrap_pred | 8.4695087    | 8.4695087    | 0          |
| 1       | VZFP                       | Vz_F_pred        | 30.7258003   | 30.7258003   | 0          |
| 2       | VZFP                       | Vz_F_pred        | 31.6069275   | 31.6069275   | 0          |
| 3       | VZFP                       | Vz_F_pred        | 29.4191386   | 29.4191386   | 0          |
| 4       | VZFP                       | Vz_F_pred        | 28.2022603   | 28.2022603   | 0          |
| 5       | VZFP                       | Vz_F_pred        | 27.1364464   | 27.1364464   | 0          |
| 6       | VZFP                       | Vz_F_pred        | 44.2235499   | 44.2235499   | 0          |
| 7       | VZFP                       | Vz_F_pred        | 35.8277969   | 35.8277969   | 0          |
| 8       | VZFP                       | Vz_F_pred        | 38.5590101   | 38.5590101   | 0          |
| 9       | VZFP                       | Vz_F_pred        | 39.8116439   | 39.8116439   | 0          |
| 10      | VZFP                       | Vz_F_pred        | 25.4443810   | 25.4443809   | 0          |
| 11      | VZFP                       | Vz_F_pred        | 38.5755715   | 38.5755715   | 0          |
| 12      | VZFP                       | Vz_F_pred        | 23.0553192   | 23.0553192   | 0          |
| 1       | CLFP                       | Cl_F_pred        | 1.4888800    | 1.4888800    | 0          |
| 2       | CLFP                       | Cl_F_pred        | 3.2898527    | 3.2898527    | 0          |
| 3       | CLFP                       | Cl_F_pred        | 3.0138235    | 3.0138235    | 0          |
| 4       | CLFP                       | Cl_F_pred        | 2.8001184    | 2.8001184    | 0          |
| 5       | CLFP                       | Cl_F_pred        | 2.3505287    | 2.3505287    | 0          |
| 6       | CLFP                       | Cl_F_pred        | 3.8826393    | 3.8826393    | 0          |
| 7       | CLFP                       | Cl_F_pred        | 3.1649020    | 3.1649020    | 0          |
| 8       | CLFP                       | Cl_F_pred        | 3.1406522    | 3.1406522    | 0          |
| 9       | CLFP                       | Cl_F_pred        | 3.2828138    | 3.2828138    | 0          |
| 10      | CLFP                       | Cl_F_pred        | 1.9073063    | 1.9073063    | 0          |
| 11      | CLFP                       | Cl_F_pred        | 3.6823685    | 3.6823685    | 0          |
| 12      | CLFP                       | Cl_F_pred        | 2.5420677    | 2.5420677    | 0          |
| 1       | AUMCLST                    | AUMClast         | 1499.1290852 | 1499.1290850 | 0          |
| 2       | AUMCLST                    | AUMClast         | 716.2787279  | 716.2787279  | 0          |
| 3       | AUMCLST                    | AUMClast         | 810.8726830  | 810.8726830  | 0          |
| 4       | AUMCLST                    | AUMClast         | 911.7828093  | 911.7828093  | 0          |
| 5       | AUMCLST                    | AUMClast         | 1038.8799844 | 1038.8799840 | 0          |

Table 3: Theoph (n=12), Log, Extravascular (*continued*)

| Subject | Pharmacokinetic Parameters |                   | Values       |              | Difference |
|---------|----------------------------|-------------------|--------------|--------------|------------|
|         | PPTSTCD                    | WNL               | NonCompart   | WinNonlin    |            |
| 6       | AUMCLST                    | AUMClast          | 618.6659191  | 618.6659191  | 0          |
| 7       | AUMCLST                    | AUMClast          | 795.6267785  | 795.6267785  | 0          |
| 8       | AUMCLST                    | AUMClast          | 756.3619816  | 756.3619816  | 0          |
| 9       | AUMCLST                    | AUMClast          | 723.3794155  | 723.3794155  | 0          |
| 10      | AUMCLST                    | AUMClast          | 1306.7406149 | 1306.7406150 | 0          |
| 11      | AUMCLST                    | AUMClast          | 626.6357849  | 626.6357849  | 0          |
| 12      | AUMCLST                    | AUMClast          | 982.6343023  | 982.6343023  | 0          |
| 1       | AUMCIFO                    | AUMCINF_obs       | 4545.5928011 | 4545.5928010 | 0          |
| 2       | AUMCIFO                    | AUMCINF_obs       | 1009.4644499 | 1009.4644500 | 0          |
| 3       | AUMCIFO                    | AUMCINF_obs       | 1158.6515817 | 1158.6515820 | 0          |
| 4       | AUMCIFO                    | AUMCINF_obs       | 1313.9510002 | 1313.9510000 | 0          |
| 5       | AUMCIFO                    | AUMCINF_obs       | 1689.4872798 | 1689.4872800 | 0          |
| 6       | AUMCIFO                    | AUMCINF_obs       | 987.9420173  | 987.9420173  | 0          |
| 7       | AUMCIFO                    | AUMCINF_obs       | 1258.3053268 | 1258.3053270 | 0          |
| 8       | AUMCIFO                    | AUMCINF_obs       | 1314.9431383 | 1314.9431380 | 0          |
| 9       | AUMCIFO                    | AUMCINF_obs       | 1219.9213281 | 1219.9213280 | 0          |
| 10      | AUMCIFO                    | AUMCINF_obs       | 2502.5540002 | 2502.5540000 | 0          |
| 11      | AUMCIFO                    | AUMCINF_obs       | 937.9535438  | 937.9535438  | 0          |
| 12      | AUMCIFO                    | AUMCINF_obs       | 1335.1375811 | 1335.1375810 | 0          |
| 1       | AUMCPEO                    | AUMC_.Extrap_obs  | 67.0201632   | 67.0201632   | 0          |
| 2       | AUMCPEO                    | AUMC_.Extrap_obs  | 29.0436897   | 29.0436897   | 0          |
| 3       | AUMCPEO                    | AUMC_.Extrap_obs  | 30.0158308   | 30.0158308   | 0          |
| 4       | AUMCPEO                    | AUMC_.Extrap_obs  | 30.6075486   | 30.6075486   | 0          |
| 5       | AUMCPEO                    | AUMC_.Extrap_obs  | 38.5091562   | 38.5091562   | 0          |
| 6       | AUMCPEO                    | AUMC_.Extrap_obs  | 37.3783169   | 37.3783169   | 0          |
| 7       | AUMCPEO                    | AUMC_.Extrap_obs  | 36.7699745   | 36.7699745   | 0          |
| 8       | AUMCPEO                    | AUMC_.Extrap_obs  | 42.4794913   | 42.4794914   | 0          |
| 9       | AUMCPEO                    | AUMC_.Extrap_obs  | 40.7027815   | 40.7027815   | 0          |
| 10      | AUMCPEO                    | AUMC_.Extrap_obs  | 47.7837196   | 47.7837196   | 0          |
| 11      | AUMCPEO                    | AUMC_.Extrap_obs  | 33.1911704   | 33.1911704   | 0          |
| 12      | AUMCPEO                    | AUMC_.Extrap_obs  | 26.4020191   | 26.4020191   | 0          |
| 1       | AUMCIFP                    | AUMCINF_pred      | 4545.7288462 | 4545.7288460 | 0          |
| 2       | AUMCIFP                    | AUMCINF_pred      | 1005.7637454 | 1005.7637450 | 0          |
| 3       | AUMCIFP                    | AUMCINF_pred      | 1160.3397033 | 1160.3397030 | 0          |
| 4       | AUMCIFP                    | AUMCINF_pred      | 1316.1967080 | 1316.1967080 | 0          |
| 5       | AUMCIFP                    | AUMCINF_pred      | 1683.5593423 | 1683.5593420 | 0          |
| 6       | AUMCIFP                    | AUMCINF_pred      | 996.4799913  | 996.4799913  | 0          |
| 7       | AUMCIFP                    | AUMCINF_pred      | 1262.6179786 | 1262.6179790 | 0          |
| 8       | AUMCIFP                    | AUMCINF_pred      | 1305.3474998 | 1305.3475000 | 0          |
| 9       | AUMCIFP                    | AUMCINF_pred      | 1218.3621498 | 1218.3621500 | 0          |
| 10      | AUMCIFP                    | AUMCINF_pred      | 2499.4371146 | 2499.4371150 | 0          |
| 11      | AUMCIFP                    | AUMCINF_pred      | 937.8835360  | 937.8835360  | 0          |
| 12      | AUMCIFP                    | AUMCINF_pred      | 1336.8064129 | 1336.8064130 | 0          |
| 1       | AUMCPEP                    | AUMC_.Extrap_pred | 67.0211503   | 67.0211503   | 0          |
| 2       | AUMCPEP                    | AUMC_.Extrap_pred | 28.7826061   | 28.7826061   | 0          |

Table 3: Theoph (n=12), Log, Extravascular (*continued*)

| Subject | Pharmacokinetic Parameters |                   | Values     |            | Difference |
|---------|----------------------------|-------------------|------------|------------|------------|
|         | PPTSTCD                    | WNL               | NonCompart | WinNonlin  |            |
| 3       | AUMCPEP                    | AUMC_.Extrap_pred | 30.1176474 | 30.1176474 | 0          |
| 4       | AUMCPEP                    | AUMC_.Extrap_pred | 30.7259467 | 30.7259467 | 0          |
| 5       | AUMCPEP                    | AUMC_.Extrap_pred | 38.2926424 | 38.2926424 | 0          |
| 6       | AUMCPEP                    | AUMC_.Extrap_pred | 37.9148679 | 37.9148679 | 0          |
| 7       | AUMCPEP                    | AUMC_.Extrap_pred | 36.9859457 | 36.9859457 | 0          |
| 8       | AUMCPEP                    | AUMC_.Extrap_pred | 42.0566568 | 42.0566568 | 0          |
| 9       | AUMCPEP                    | AUMC_.Extrap_pred | 40.6268969 | 40.6268969 | 0          |
| 10      | AUMCPEP                    | AUMC_.Extrap_pred | 47.7186040 | 47.7186040 | 0          |
| 11      | AUMCPEP                    | AUMC_.Extrap_pred | 33.1861835 | 33.1861835 | 0          |
| 12      | AUMCPEP                    | AUMC_.Extrap_pred | 26.4938967 | 26.4938967 | 0          |
| 1       | MRTEVLST                   | MRTlast           | 10.1818973 | 10.1818973 | 0          |
| 2       | MRTEVLST                   | MRTlast           | 8.0724494  | 8.0724494  | 0          |
| 3       | MRTEVLST                   | MRTlast           | 8.4573209  | 8.4573209  | 0          |
| 4       | MRTEVLST                   | MRTlast           | 8.8838607  | 8.8838607  | 0          |
| 5       | MRTEVLST                   | MRTlast           | 8.7907063  | 8.7907063  | 0          |
| 6       | MRTEVLST                   | MRTlast           | 8.6288937  | 8.6288937  | 0          |
| 7       | MRTEVLST                   | MRTlast           | 9.0443761  | 9.0443761  | 0          |
| 8       | MRTEVLST                   | MRTlast           | 8.7131889  | 8.7131889  | 0          |
| 9       | MRTEVLST                   | MRTlast           | 8.6180785  | 8.6180785  | 0          |
| 10      | MRTEVLST                   | MRTlast           | 9.6384311  | 9.6384311  | 0          |
| 11      | MRTEVLST                   | MRTlast           | 8.0447792  | 8.0447792  | 0          |
| 12      | MRTEVLST                   | MRTlast           | 8.5283156  | 8.5283156  | 0          |
| 1       | MRTEVIFO                   | MRTINF_obs        | 21.1498046 | 21.1498045 | 0          |
| 2       | MRTEVIFO                   | MRTINF_obs        | 10.3664599 | 10.3664599 | 0          |
| 3       | MRTEVIFO                   | MRTINF_obs        | 10.9175260 | 10.9175260 | 0          |
| 4       | MRTEVIFO                   | MRTINF_obs        | 11.5040681 | 11.5040681 | 0          |
| 5       | MRTEVIFO                   | MRTINF_obs        | 12.3949276 | 12.3949276 | 0          |
| 6       | MRTEVIFO                   | MRTINF_obs        | 12.0222866 | 12.0222866 | 0          |
| 7       | MRTEVIFO                   | MRTINF_obs        | 12.4599947 | 12.4599947 | 0          |
| 8       | MRTEVIFO                   | MRTINF_obs        | 12.8722531 | 12.8722531 | 0          |
| 9       | MRTEVIFO                   | MRTINF_obs        | 12.5094471 | 12.5094471 | 0          |
| 10      | MRTEVIFO                   | MRTINF_obs        | 14.9085758 | 14.9085758 | 0          |
| 11      | MRTEVIFO                   | MRTINF_obs        | 10.7931564 | 10.7931564 | 0          |
| 12      | MRTEVIFO                   | MRTINF_obs        | 10.6105161 | 10.6105161 | 0          |
| 1       | MRTEVIFP                   | MRTINF_pred       | 21.1501401 | 21.1501401 | 0          |
| 2       | MRTEVIFP                   | MRTINF_pred       | 10.3400455 | 10.3400455 | 0          |
| 3       | MRTEVIFP                   | MRTINF_pred       | 10.9283095 | 10.9283095 | 0          |
| 4       | MRTEVIFP                   | MRTINF_pred       | 11.5172082 | 11.5172082 | 0          |
| 5       | MRTEVIFP                   | MRTINF_pred       | 12.3664205 | 12.3664205 | 0          |
| 6       | MRTEVIFP                   | MRTINF_pred       | 12.0905386 | 12.0905386 | 0          |
| 7       | MRTEVIFP                   | MRTINF_pred       | 12.4876944 | 12.4876944 | 0          |
| 8       | MRTEVIFP                   | MRTINF_pred       | 12.8113828 | 12.8113828 | 0          |
| 9       | MRTEVIFP                   | MRTINF_pred       | 12.4989252 | 12.4989252 | 0          |
| 10      | MRTEVIFP                   | MRTINF_pred       | 14.8974756 | 14.8974756 | 0          |
| 11      | MRTEVIFP                   | MRTINF_pred       | 10.7926025 | 10.7926025 | 0          |

Table 3: Theoph (n=12), Log, Extravascular (*continued*)

| Subject | Pharmacokinetic Parameters |             | Values     |            | Difference |
|---------|----------------------------|-------------|------------|------------|------------|
|         | PPTTESTCD                  | WNL         | NonCompart | WinNonlin  |            |
| 12      | MRTEVIFP                   | MRTINF_pred | 10.6195388 | 10.6195388 | 0          |

### A.3 Test 3: Indometh (n=6), Linear, IV Bolus

```
table_wres_rres(Wres3, Rres3,
  Caption = 'Indometh (n=6), Linear, IV Bolus')
```

Table 4: Indometh (n=6), Linear, IV Bolus

| Subject | Pharmacokinetic Parameters |                    | Values     |            | Difference |
|---------|----------------------------|--------------------|------------|------------|------------|
|         | PPTTESTCD                  | WNL                | NonCompart | WinNonlin  |            |
| 1       | R2                         | Rsqr               | 0.9970667  | 0.9970667  | 0          |
| 2       | R2                         | Rsqr               | 0.9476691  | 0.9476691  | 0          |
| 3       | R2                         | Rsqr               | 0.8758261  | 0.8758261  | 0          |
| 4       | R2                         | Rsqr               | 0.8728249  | 0.8728249  | 0          |
| 5       | R2                         | Rsqr               | 0.8752442  | 0.8752442  | 0          |
| 6       | R2                         | Rsqr               | 0.9039538  | 0.9039538  | 0          |
| 1       | R2ADJ                      | Rsqr_adjusted      | 0.9941335  | 0.9941335  | 0          |
| 2       | R2ADJ                      | Rsqr_adjusted      | 0.9401933  | 0.9401933  | 0          |
| 3       | R2ADJ                      | Rsqr_adjusted      | 0.8603043  | 0.8603043  | 0          |
| 4       | R2ADJ                      | Rsqr_adjusted      | 0.8586943  | 0.8586943  | 0          |
| 5       | R2ADJ                      | Rsqr_adjusted      | 0.8544516  | 0.8544516  | 0          |
| 6       | R2ADJ                      | Rsqr_adjusted      | 0.8902329  | 0.8902329  | 0          |
| 1       | CORRXY                     | Corr_XY            | -0.9985323 | -0.9985323 | 0          |
| 2       | CORRXY                     | Corr_XY            | -0.9734830 | -0.9734830 | 0          |
| 3       | CORRXY                     | Corr_XY            | -0.9358558 | -0.9358558 | 0          |
| 4       | CORRXY                     | Corr_XY            | -0.9342510 | -0.9342510 | 0          |
| 5       | CORRXY                     | Corr_XY            | -0.9355449 | -0.9355449 | 0          |
| 6       | CORRXY                     | Corr_XY            | -0.9507649 | -0.9507649 | 0          |
| 1       | LAMZNPT                    | No_points_lambda_z | 3.0000000  | 3.0000000  | 0          |
| 2       | LAMZNPT                    | No_points_lambda_z | 9.0000000  | 9.0000000  | 0          |
| 3       | LAMZNPT                    | No_points_lambda_z | 10.0000000 | 10.0000000 | 0          |
| 4       | LAMZNPT                    | No_points_lambda_z | 11.0000000 | 11.0000000 | 0          |
| 5       | LAMZNPT                    | No_points_lambda_z | 8.0000000  | 8.0000000  | 0          |
| 6       | LAMZNPT                    | No_points_lambda_z | 9.0000000  | 9.0000000  | 0          |
| 1       | LAMZ                       | Lambda_z           | 0.1583205  | 0.1583205  | 0          |
| 2       | LAMZ                       | Lambda_z           | 0.3022800  | 0.3022800  | 0          |
| 3       | LAMZ                       | Lambda_z           | 0.4218926  | 0.4218926  | 0          |
| 4       | LAMZ                       | Lambda_z           | 0.4554455  | 0.4554455  | 0          |
| 5       | LAMZ                       | Lambda_z           | 0.2527478  | 0.2527478  | 0          |
| 6       | LAMZ                       | Lambda_z           | 0.3535205  | 0.3535205  | 0          |
| 1       | LAMZLL                     | Lambda_z_lower     | 5.0000000  | 5.0000000  | 0          |
| 2       | LAMZLL                     | Lambda_z_lower     | 0.7500000  | 0.7500000  | 0          |



Table 4: Indometh (n=6), Linear, IV Bolus (*continued*)

| Subject | Pharmacokinetic Parameters |                | Values     |           | Difference |
|---------|----------------------------|----------------|------------|-----------|------------|
|         | PPTESTCD                   | WNL            | NonCompart | WinNonlin |            |
| 3       | LAMZLL                     | Lambda_z_lower | 0.5000000  | 0.5000000 | 0          |
| 4       | LAMZLL                     | Lambda_z_lower | 0.2500000  | 0.2500000 | 0          |
| 5       | LAMZLL                     | Lambda_z_lower | 1.0000000  | 1.0000000 | 0          |
| 6       | LAMZLL                     | Lambda_z_lower | 0.7500000  | 0.7500000 | 0          |
| 1       | LAMZUL                     | Lambda_z_upper | 8.0000000  | 8.0000000 | 0          |
| 2       | LAMZUL                     | Lambda_z_upper | 8.0000000  | 8.0000000 | 0          |
| 3       | LAMZUL                     | Lambda_z_upper | 8.0000000  | 8.0000000 | 0          |
| 4       | LAMZUL                     | Lambda_z_upper | 8.0000000  | 8.0000000 | 0          |
| 5       | LAMZUL                     | Lambda_z_upper | 8.0000000  | 8.0000000 | 0          |
| 6       | LAMZUL                     | Lambda_z_upper | 8.0000000  | 8.0000000 | 0          |
| 1       | LAMZHL                     | HL_Lambda_z    | 4.3781270  | 4.3781270 | 0          |
| 2       | LAMZHL                     | HL_Lambda_z    | 2.2930632  | 2.2930632 | 0          |
| 3       | LAMZHL                     | HL_Lambda_z    | 1.6429468  | 1.6429468 | 0          |
| 4       | LAMZHL                     | HL_Lambda_z    | 1.5219104  | 1.5219104 | 0          |
| 5       | LAMZHL                     | HL_Lambda_z    | 2.7424461  | 2.7424461 | 0          |
| 6       | LAMZHL                     | HL_Lambda_z    | 1.9606986  | 1.9606986 | 0          |
| 1       | TMAX                       | Tmax           | 0.2500000  | 0.2500000 | 0          |
| 2       | TMAX                       | Tmax           | 0.2500000  | 0.2500000 | 0          |
| 3       | TMAX                       | Tmax           | 0.2500000  | 0.2500000 | 0          |
| 4       | TMAX                       | Tmax           | 0.2500000  | 0.2500000 | 0          |
| 5       | TMAX                       | Tmax           | 0.2500000  | 0.2500000 | 0          |
| 6       | TMAX                       | Tmax           | 0.2500000  | 0.2500000 | 0          |
| 1       | CMAX                       | Cmax           | 1.5000000  | 1.5000000 | 0          |
| 2       | CMAX                       | Cmax           | 2.0300000  | 2.0300000 | 0          |
| 3       | CMAX                       | Cmax           | 2.7200000  | 2.7200000 | 0          |
| 4       | CMAX                       | Cmax           | 1.8500000  | 1.8500000 | 0          |
| 5       | CMAX                       | Cmax           | 2.0500000  | 2.0500000 | 0          |
| 6       | CMAX                       | Cmax           | 2.3100000  | 2.3100000 | 0          |
| 1       | CMAXD                      | Cmax_D         | 0.0600000  | 0.0600000 | 0          |
| 2       | CMAXD                      | Cmax_D         | 0.0812000  | 0.0812000 | 0          |
| 3       | CMAXD                      | Cmax_D         | 0.1088000  | 0.1088000 | 0          |
| 4       | CMAXD                      | Cmax_D         | 0.0740000  | 0.0740000 | 0          |
| 5       | CMAXD                      | Cmax_D         | 0.0820000  | 0.0820000 | 0          |
| 6       | CMAXD                      | Cmax_D         | 0.0924000  | 0.0924000 | 0          |
| 1       | C0                         | C0             | 2.3936170  | 2.3936170 | 0          |
| 2       | C0                         | C0             | 2.5281595  | 2.5281595 | 0          |
| 3       | C0                         | C0             | 4.9653691  | 4.9653691 | 0          |
| 4       | C0                         | C0             | 2.4622302  | 2.4622302 | 0          |
| 5       | C0                         | C0             | 4.0408654  | 4.0408654 | 0          |
| 6       | C0                         | C0             | 3.7056250  | 3.7056250 | 0          |
| 1       | TLST                       | Tlast          | 8.0000000  | 8.0000000 | 0          |
| 2       | TLST                       | Tlast          | 8.0000000  | 8.0000000 | 0          |
| 3       | TLST                       | Tlast          | 8.0000000  | 8.0000000 | 0          |
| 4       | TLST                       | Tlast          | 8.0000000  | 8.0000000 | 0          |
| 5       | TLST                       | Tlast          | 8.0000000  | 8.0000000 | 0          |

Table 4: Indometh (n=6), Linear, IV Bolus (*continued*)

| Subject | Pharmacokinetic Parameters |                   | Values     |            | Difference |
|---------|----------------------------|-------------------|------------|------------|------------|
|         | PPTESTCD                   | WNL               | NonCompart | WinNonlin  |            |
| 6       | TLST                       | Tlast             | 8.0000000  | 8.0000000  | 0          |
| 1       | CLST                       | Clast             | 0.0500000  | 0.0500000  | 0          |
| 2       | CLST                       | Clast             | 0.0800000  | 0.0800000  | 0          |
| 3       | CLST                       | Clast             | 0.0800000  | 0.0800000  | 0          |
| 4       | CLST                       | Clast             | 0.0700000  | 0.0700000  | 0          |
| 5       | CLST                       | Clast             | 0.0600000  | 0.0600000  | 0          |
| 6       | CLST                       | Clast             | 0.0900000  | 0.0900000  | 0          |
| 1       | AUCLST                     | AUClast           | 2.0404521  | 2.0404521  | 0          |
| 2       | AUCLST                     | AUClast           | 3.2485199  | 3.2485199  | 0          |
| 3       | AUCLST                     | AUClast           | 3.5544211  | 3.5544211  | 0          |
| 4       | AUCLST                     | AUClast           | 2.7852788  | 2.7852788  | 0          |
| 5       | AUCLST                     | AUClast           | 2.4588582  | 2.4588582  | 0          |
| 6       | AUCLST                     | AUClast           | 3.3357031  | 3.3357031  | 0          |
| 1       | AUCALL                     | AUCall            | 2.0404521  | 2.0404521  | 0          |
| 2       | AUCALL                     | AUCall            | 3.2485199  | 3.2485199  | 0          |
| 3       | AUCALL                     | AUCall            | 3.5544211  | 3.5544211  | 0          |
| 4       | AUCALL                     | AUCall            | 2.7852788  | 2.7852788  | 0          |
| 5       | AUCALL                     | AUCall            | 2.4588582  | 2.4588582  | 0          |
| 6       | AUCALL                     | AUCall            | 3.3357031  | 3.3357031  | 0          |
| 1       | AUCIFO                     | AUCINF_obs        | 2.3562672  | 2.3562672  | 0          |
| 2       | AUCIFO                     | AUCINF_obs        | 3.5131752  | 3.5131752  | 0          |
| 3       | AUCIFO                     | AUCINF_obs        | 3.7440428  | 3.7440428  | 0          |
| 4       | AUCIFO                     | AUCINF_obs        | 2.9389745  | 2.9389745  | 0          |
| 5       | AUCIFO                     | AUCINF_obs        | 2.6962490  | 2.6962490  | 0          |
| 6       | AUCIFO                     | AUCINF_obs        | 3.5902852  | 3.5902852  | 0          |
| 1       | AUCIFOD                    | AUCINF_D_obs      | 0.0942507  | 0.0942507  | 0          |
| 2       | AUCIFOD                    | AUCINF_D_obs      | 0.1405270  | 0.1405270  | 0          |
| 3       | AUCIFOD                    | AUCINF_D_obs      | 0.1497617  | 0.1497617  | 0          |
| 4       | AUCIFOD                    | AUCINF_D_obs      | 0.1175590  | 0.1175590  | 0          |
| 5       | AUCIFOD                    | AUCINF_D_obs      | 0.1078500  | 0.1078500  | 0          |
| 6       | AUCIFOD                    | AUCINF_D_obs      | 0.1436114  | 0.1436114  | 0          |
| 1       | AUCPEO                     | AUC_.Extrap_obs   | 13.4031956 | 13.4031956 | 0          |
| 2       | AUCPEO                     | AUC_.Extrap_obs   | 7.5332215  | 7.5332215  | 0          |
| 3       | AUCPEO                     | AUC_.Extrap_obs   | 5.0646241  | 5.0646241  | 0          |
| 4       | AUCPEO                     | AUC_.Extrap_obs   | 5.2295685  | 5.2295685  | 0          |
| 5       | AUCPEO                     | AUC_.Extrap_obs   | 8.8044838  | 8.8044838  | 0          |
| 6       | AUCPEO                     | AUC_.Extrap_obs   | 7.0908603  | 7.0908603  | 0          |
| 1       | AUCPBEO                    | AUC_.Back_Ext_obs | 20.6556421 | 20.6556421 | 0          |
| 2       | AUCPBEO                    | AUC_.Back_Ext_obs | 16.2180906 | 16.2180906 | 0          |
| 3       | AUCPBEO                    | AUC_.Back_Ext_obs | 25.6586578 | 25.6586578 | 0          |
| 4       | AUCPBEO                    | AUC_.Back_Ext_obs | 18.3407098 | 18.3407098 | 0          |
| 5       | AUCPBEO                    | AUC_.Back_Ext_obs | 28.2376805 | 28.2376805 | 0          |
| 6       | AUCPBEO                    | AUC_.Back_Ext_obs | 20.9441054 | 20.9441054 | 0          |
| 1       | VZO                        | Vz_obs            | 67.0159780 | 67.0159780 | 0          |
| 2       | VZO                        | Vz_obs            | 23.5413171 | 23.5413171 | 0          |

Table 4: Indometh (n=6), Linear, IV Bolus (*continued*)

| Subject | Pharmacokinetic Parameters |                    | Values     |            | Difference |
|---------|----------------------------|--------------------|------------|------------|------------|
|         | PPTESTCD                   | WNL                | NonCompart | WinNonlin  |            |
| 3       | VZO                        | Vz_obs             | 15.8269504 | 15.8269504 | 0          |
| 4       | VZO                        | Vz_obs             | 18.6770303 | 18.6770303 | 0          |
| 5       | VZO                        | Vz_obs             | 36.6853493 | 36.6853493 | 0          |
| 6       | VZO                        | Vz_obs             | 19.6968341 | 19.6968341 | 0          |
| 1       | CLO                        | Cl_obs             | 10.6100020 | 10.6100020 | 0          |
| 2       | CLO                        | Cl_obs             | 7.1160698  | 7.1160698  | 0          |
| 3       | CLO                        | Cl_obs             | 6.6772740  | 6.6772740  | 0          |
| 4       | CLO                        | Cl_obs             | 8.5063686  | 8.5063686  | 0          |
| 5       | CLO                        | Cl_obs             | 9.2721407  | 9.2721407  | 0          |
| 6       | CLO                        | Cl_obs             | 6.9632351  | 6.9632351  | 0          |
| 1       | AUCIFP                     | AUCINF_pred        | 2.3578369  | 2.3578369  | 0          |
| 2       | AUCIFP                     | AUCINF_pred        | 3.4958268  | 3.4958268  | 0          |
| 3       | AUCIFP                     | AUCINF_pred        | 3.6491670  | 3.6491670  | 0          |
| 4       | AUCIFP                     | AUCINF_pred        | 2.8554521  | 2.8554521  | 0          |
| 5       | AUCIFP                     | AUCINF_pred        | 2.6549884  | 2.6549884  | 0          |
| 6       | AUCIFP                     | AUCINF_pred        | 3.4947956  | 3.4947956  | 0          |
| 1       | AUCIFPD                    | AUCINF_D_pred      | 0.0943135  | 0.0943135  | 0          |
| 2       | AUCIFPD                    | AUCINF_D_pred      | 0.1398331  | 0.1398331  | 0          |
| 3       | AUCIFPD                    | AUCINF_D_pred      | 0.1459667  | 0.1459667  | 0          |
| 4       | AUCIFPD                    | AUCINF_D_pred      | 0.1142181  | 0.1142181  | 0          |
| 5       | AUCIFPD                    | AUCINF_D_pred      | 0.1061995  | 0.1061995  | 0          |
| 6       | AUCIFPD                    | AUCINF_D_pred      | 0.1397918  | 0.1397918  | 0          |
| 1       | AUCPEP                     | AUC_.Extrap_pred   | 13.4608442 | 13.4608442 | 0          |
| 2       | AUCPEP                     | AUC_.Extrap_pred   | 7.0743442  | 7.0743442  | 0          |
| 3       | AUCPEP                     | AUC_.Extrap_pred   | 2.5963692  | 2.5963692  | 0          |
| 4       | AUCPEP                     | AUC_.Extrap_pred   | 2.4575198  | 2.4575198  | 0          |
| 5       | AUCPEP                     | AUC_.Extrap_pred   | 7.3872362  | 7.3872362  | 0          |
| 6       | AUCPEP                     | AUC_.Extrap_pred   | 4.5522694  | 4.5522694  | 0          |
| 1       | AUCPBEP                    | AUC_.Back_Ext_pred | 20.6418914 | 20.6418914 | 0          |
| 2       | AUCPBEP                    | AUC_.Back_Ext_pred | 16.2985748 | 16.2985748 | 0          |
| 3       | AUCPBEP                    | AUC_.Back_Ext_pred | 26.3257654 | 26.3257654 | 0          |
| 4       | AUCPBEP                    | AUC_.Back_Ext_pred | 18.8771782 | 18.8771782 | 0          |
| 5       | AUCPBEP                    | AUC_.Back_Ext_pred | 28.6765156 | 28.6765156 | 0          |
| 6       | AUCPBEP                    | AUC_.Back_Ext_pred | 21.5163690 | 21.5163690 | 0          |
| 1       | VZP                        | Vz_pred            | 66.9713647 | 66.9713647 | 0          |
| 2       | VZP                        | Vz_pred            | 23.6581437 | 23.6581437 | 0          |
| 3       | VZP                        | Vz_pred            | 16.2384403 | 16.2384403 | 0          |
| 4       | VZP                        | Vz_pred            | 19.2233361 | 19.2233361 | 0          |
| 5       | VZP                        | Vz_pred            | 37.2554675 | 37.2554675 | 0          |
| 6       | VZP                        | Vz_pred            | 20.2350180 | 20.2350180 | 0          |
| 1       | CLP                        | Cl_pred            | 10.6029388 | 10.6029388 | 0          |
| 2       | CLP                        | Cl_pred            | 7.1513841  | 7.1513841  | 0          |
| 3       | CLP                        | Cl_pred            | 6.8508786  | 6.8508786  | 0          |
| 4       | CLP                        | Cl_pred            | 8.7551811  | 8.7551811  | 0          |
| 5       | CLP                        | Cl_pred            | 9.4162369  | 9.4162369  | 0          |

Table 4: Indometh (n=6), Linear, IV Bolus (*continued*)

| Subject | Pharmacokinetic Parameters |                   | Values     |            | Difference |
|---------|----------------------------|-------------------|------------|------------|------------|
|         | PPTESTCD                   | WNL               | NonCompart | WinNonlin  |            |
| 6       | CLP                        | Cl_pred           | 7.1534941  | 7.1534941  | 0          |
| 1       | AUMCLST                    | AUMClast          | 3.2712500  | 3.2712500  | 0          |
| 2       | AUMCLST                    | AUMClast          | 6.3987500  | 6.3987500  | 0          |
| 3       | AUMCLST                    | AUMClast          | 5.0062500  | 5.0062500  | 0          |
| 4       | AUMCLST                    | AUMClast          | 4.3818750  | 4.3818750  | 0          |
| 5       | AUMCLST                    | AUMClast          | 3.7075000  | 3.7075000  | 0          |
| 6       | AUMCLST                    | AUMClast          | 5.5325000  | 5.5325000  | 0          |
| 1       | AUMCIFO                    | AUMCINF_obs       | 7.7925545  | 7.7925545  | 0          |
| 2       | AUMCIFO                    | AUMCINF_obs       | 9.3915223  | 9.3915223  | 0          |
| 3       | AUMCIFO                    | AUMCINF_obs       | 6.9726784  | 6.9726784  | 0          |
| 4       | AUMCIFO                    | AUMCINF_obs       | 5.9489028  | 5.9489028  | 0          |
| 5       | AUMCIFO                    | AUMCINF_obs       | 6.5458663  | 6.5458663  | 0          |
| 6       | AUMCIFO                    | AUMCINF_obs       | 8.2892908  | 8.2892908  | 0          |
| 1       | AUMCPEO                    | AUMC_.Extrap_obs  | 58.0208261 | 58.0208261 | 0          |
| 2       | AUMCPEO                    | AUMC_.Extrap_obs  | 31.8667432 | 31.8667432 | 0          |
| 3       | AUMCPEO                    | AUMC_.Extrap_obs  | 28.2019090 | 28.2019090 | 0          |
| 4       | AUMCPEO                    | AUMC_.Extrap_obs  | 26.3414589 | 26.3414589 | 0          |
| 5       | AUMCPEO                    | AUMC_.Extrap_obs  | 43.3612023 | 43.3612023 | 0          |
| 6       | AUMCPEO                    | AUMC_.Extrap_obs  | 33.2572574 | 33.2572574 | 0          |
| 1       | AUMCIFP                    | AUMCINF_pred      | 7.8150259  | 7.8150259  | 0          |
| 2       | AUMCIFP                    | AUMCINF_pred      | 9.1953427  | 9.1953427  | 0          |
| 3       | AUMCIFP                    | AUMCINF_pred      | 5.9887901  | 5.9887901  | 0          |
| 4       | AUMCIFP                    | AUMCINF_pred      | 5.0973376  | 5.0973376  | 0          |
| 5       | AUMCIFP                    | AUMCINF_pred      | 6.0525342  | 6.0525342  | 0          |
| 6       | AUMCIFP                    | AUMCINF_pred      | 7.2552635  | 7.2552635  | 0          |
| 1       | AUMCPEP                    | AUMC_.Extrap_pred | 58.1415337 | 58.1415337 | 0          |
| 2       | AUMCPEP                    | AUMC_.Extrap_pred | 30.4131425 | 30.4131425 | 0          |
| 3       | AUMCPEP                    | AUMC_.Extrap_pred | 16.4063210 | 16.4063210 | 0          |
| 4       | AUMCPEP                    | AUMC_.Extrap_pred | 14.0360055 | 14.0360055 | 0          |
| 5       | AUMCPEP                    | AUMC_.Extrap_pred | 38.7446663 | 38.7446663 | 0          |
| 6       | AUMCPEP                    | AUMC_.Extrap_pred | 23.7450164 | 23.7450164 | 0          |
| 1       | MRTIVLST                   | MRTlast           | 1.6031986  | 1.6031986  | 0          |
| 2       | MRTIVLST                   | MRTlast           | 1.9697432  | 1.9697432  | 0          |
| 3       | MRTIVLST                   | MRTlast           | 1.4084572  | 1.4084572  | 0          |
| 4       | MRTIVLST                   | MRTlast           | 1.5732267  | 1.5732267  | 0          |
| 5       | MRTIVLST                   | MRTlast           | 1.5078137  | 1.5078137  | 0          |
| 6       | MRTIVLST                   | MRTlast           | 1.6585709  | 1.6585709  | 0          |
| 1       | MRTIVIFO                   | MRTINF_obs        | 3.3071607  | 3.3071607  | 0          |
| 2       | MRTIVIFO                   | MRTINF_obs        | 2.6732291  | 2.6732291  | 0          |
| 3       | MRTIVIFO                   | MRTINF_obs        | 1.8623394  | 1.8623394  | 0          |
| 4       | MRTIVIFO                   | MRTINF_obs        | 2.0241424  | 2.0241424  | 0          |
| 5       | MRTIVIFO                   | MRTINF_obs        | 2.4277678  | 2.4277678  | 0          |
| 6       | MRTIVIFO                   | MRTINF_obs        | 2.3088112  | 2.3088112  | 0          |
| 1       | MRTIVIFP                   | MRTINF_pred       | 3.3144897  | 3.3144897  | 0          |
| 2       | MRTIVIFP                   | MRTINF_pred       | 2.6303771  | 2.6303771  | 0          |

Table 4: Indometh (n=6), Linear, IV Bolus (*continued*)

| Subject | Pharmacokinetic Parameters |             | Values     |            | Difference |
|---------|----------------------------|-------------|------------|------------|------------|
|         | PPTESTCD                   | WNL         | NonCompart | WinNonlin  |            |
| 3       | MRTIVIFP                   | MRTINF_pred | 1.6411390  | 1.6411390  | 0          |
| 4       | MRTIVIFP                   | MRTINF_pred | 1.7851245  | 1.7851245  | 0          |
| 5       | MRTIVIFP                   | MRTINF_pred | 2.2796838  | 2.2796838  | 0          |
| 6       | MRTIVIFP                   | MRTINF_pred | 2.0760194  | 2.0760194  | 0          |
| 1       | VSSO                       | Vss_obs     | 35.0889819 | 35.0889819 | 0          |
| 2       | VSSO                       | Vss_obs     | 19.0228851 | 19.0228851 | 0          |
| 3       | VSSO                       | Vss_obs     | 12.4353504 | 12.4353504 | 0          |
| 4       | VSSO                       | Vss_obs     | 17.2181012 | 17.2181012 | 0          |
| 5       | VSSO                       | Vss_obs     | 22.5106044 | 22.5106044 | 0          |
| 6       | VSSO                       | Vss_obs     | 16.0767951 | 16.0767951 | 0          |
| 1       | VSSP                       | Vss_pred    | 35.1433309 | 35.1433309 | 0          |
| 2       | VSSP                       | Vss_pred    | 18.8108371 | 18.8108371 | 0          |
| 3       | VSSP                       | Vss_pred    | 11.2432438 | 11.2432438 | 0          |
| 4       | VSSP                       | Vss_pred    | 15.6290886 | 15.6290886 | 0          |
| 5       | VSSP                       | Vss_pred    | 21.4660427 | 21.4660427 | 0          |
| 6       | VSSP                       | Vss_pred    | 14.8507925 | 14.8507925 | 0          |

#### A.4 Test 4: Indometh (n=6), Log, IV Bolus

```
table_wres_rres(Wres4, Rres4,
  Caption = 'Indometh (n=6), Log, IV Bolus')
```

Table 5: Indometh (n=6), Log, IV Bolus

| Subject | Pharmacokinetic Parameters |              | Values     |            | Difference |
|---------|----------------------------|--------------|------------|------------|------------|
|         | PPTESTCD                   | WNL          | NonCompart | WinNonlin  |            |
| 1       | R2                         | Rsq          | 0.9970667  | 0.9970667  | 0          |
| 2       | R2                         | Rsq          | 0.9476691  | 0.9476691  | 0          |
| 3       | R2                         | Rsq          | 0.8758261  | 0.8758261  | 0          |
| 4       | R2                         | Rsq          | 0.8728249  | 0.8728249  | 0          |
| 5       | R2                         | Rsq          | 0.8752442  | 0.8752442  | 0          |
| 6       | R2                         | Rsq          | 0.9039538  | 0.9039538  | 0          |
| 1       | R2ADJ                      | Rsq_adjusted | 0.9941335  | 0.9941335  | 0          |
| 2       | R2ADJ                      | Rsq_adjusted | 0.9401933  | 0.9401933  | 0          |
| 3       | R2ADJ                      | Rsq_adjusted | 0.8603043  | 0.8603043  | 0          |
| 4       | R2ADJ                      | Rsq_adjusted | 0.8586943  | 0.8586943  | 0          |
| 5       | R2ADJ                      | Rsq_adjusted | 0.8544516  | 0.8544516  | 0          |
| 6       | R2ADJ                      | Rsq_adjusted | 0.8902329  | 0.8902329  | 0          |
| 1       | CORRXY                     | Corr_XY      | -0.9985323 | -0.9985323 | 0          |
| 2       | CORRXY                     | Corr_XY      | -0.9734830 | -0.9734830 | 0          |
| 3       | CORRXY                     | Corr_XY      | -0.9358558 | -0.9358558 | 0          |
| 4       | CORRXY                     | Corr_XY      | -0.9342510 | -0.9342510 | 0          |
| 5       | CORRXY                     | Corr_XY      | -0.9355449 | -0.9355449 | 0          |

Table 5: Indometh (n=6), Log, IV Bolus (*continued*)

| Subject | Pharmacokinetic Parameters |                    | Values     |            | Difference |
|---------|----------------------------|--------------------|------------|------------|------------|
|         | PPTESTCD                   | WNL                | NonCompart | WinNonlin  |            |
| 6       | CORRXY                     | Corr_XY            | -0.9507649 | -0.9507649 | 0          |
| 1       | LAMZNPT                    | No_points_lambda_z | 3.0000000  | 3.0000000  | 0          |
| 2       | LAMZNPT                    | No_points_lambda_z | 9.0000000  | 9.0000000  | 0          |
| 3       | LAMZNPT                    | No_points_lambda_z | 10.0000000 | 10.0000000 | 0          |
| 4       | LAMZNPT                    | No_points_lambda_z | 11.0000000 | 11.0000000 | 0          |
| 5       | LAMZNPT                    | No_points_lambda_z | 8.0000000  | 8.0000000  | 0          |
| 6       | LAMZNPT                    | No_points_lambda_z | 9.0000000  | 9.0000000  | 0          |
| 1       | LAMZ                       | Lambda_z           | 0.1583205  | 0.1583205  | 0          |
| 2       | LAMZ                       | Lambda_z           | 0.3022800  | 0.3022800  | 0          |
| 3       | LAMZ                       | Lambda_z           | 0.4218926  | 0.4218926  | 0          |
| 4       | LAMZ                       | Lambda_z           | 0.4554455  | 0.4554455  | 0          |
| 5       | LAMZ                       | Lambda_z           | 0.2527478  | 0.2527478  | 0          |
| 6       | LAMZ                       | Lambda_z           | 0.3535205  | 0.3535205  | 0          |
| 1       | LAMZLL                     | Lambda_z_lower     | 5.0000000  | 5.0000000  | 0          |
| 2       | LAMZLL                     | Lambda_z_lower     | 0.7500000  | 0.7500000  | 0          |
| 3       | LAMZLL                     | Lambda_z_lower     | 0.5000000  | 0.5000000  | 0          |
| 4       | LAMZLL                     | Lambda_z_lower     | 0.2500000  | 0.2500000  | 0          |
| 5       | LAMZLL                     | Lambda_z_lower     | 1.0000000  | 1.0000000  | 0          |
| 6       | LAMZLL                     | Lambda_z_lower     | 0.7500000  | 0.7500000  | 0          |
| 1       | LAMZUL                     | Lambda_z_upper     | 8.0000000  | 8.0000000  | 0          |
| 2       | LAMZUL                     | Lambda_z_upper     | 8.0000000  | 8.0000000  | 0          |
| 3       | LAMZUL                     | Lambda_z_upper     | 8.0000000  | 8.0000000  | 0          |
| 4       | LAMZUL                     | Lambda_z_upper     | 8.0000000  | 8.0000000  | 0          |
| 5       | LAMZUL                     | Lambda_z_upper     | 8.0000000  | 8.0000000  | 0          |
| 6       | LAMZUL                     | Lambda_z_upper     | 8.0000000  | 8.0000000  | 0          |
| 1       | LAMZHL                     | HL_Lambda_z        | 4.3781270  | 4.3781270  | 0          |
| 2       | LAMZHL                     | HL_Lambda_z        | 2.2930632  | 2.2930632  | 0          |
| 3       | LAMZHL                     | HL_Lambda_z        | 1.6429468  | 1.6429468  | 0          |
| 4       | LAMZHL                     | HL_Lambda_z        | 1.5219104  | 1.5219104  | 0          |
| 5       | LAMZHL                     | HL_Lambda_z        | 2.7424461  | 2.7424461  | 0          |
| 6       | LAMZHL                     | HL_Lambda_z        | 1.9606986  | 1.9606986  | 0          |
| 1       | TMAX                       | Tmax               | 0.2500000  | 0.2500000  | 0          |
| 2       | TMAX                       | Tmax               | 0.2500000  | 0.2500000  | 0          |
| 3       | TMAX                       | Tmax               | 0.2500000  | 0.2500000  | 0          |
| 4       | TMAX                       | Tmax               | 0.2500000  | 0.2500000  | 0          |
| 5       | TMAX                       | Tmax               | 0.2500000  | 0.2500000  | 0          |
| 6       | TMAX                       | Tmax               | 0.2500000  | 0.2500000  | 0          |
| 1       | CMAX                       | Cmax               | 1.5000000  | 1.5000000  | 0          |
| 2       | CMAX                       | Cmax               | 2.0300000  | 2.0300000  | 0          |
| 3       | CMAX                       | Cmax               | 2.7200000  | 2.7200000  | 0          |
| 4       | CMAX                       | Cmax               | 1.8500000  | 1.8500000  | 0          |
| 5       | CMAX                       | Cmax               | 2.0500000  | 2.0500000  | 0          |
| 6       | CMAX                       | Cmax               | 2.3100000  | 2.3100000  | 0          |
| 1       | CMAXD                      | Cmax_D             | 0.0600000  | 0.0600000  | 0          |
| 2       | CMAXD                      | Cmax_D             | 0.0812000  | 0.0812000  | 0          |

Table 5: Indometh (n=6), Log, IV Bolus (*continued*)

| Subject | Pharmacokinetic Parameters |              | Values     |           | Difference |
|---------|----------------------------|--------------|------------|-----------|------------|
|         | PPTESTCD                   | WNL          | NonCompart | WinNonlin |            |
| 3       | CMAXD                      | Cmax_D       | 0.1088000  | 0.1088000 | 0          |
| 4       | CMAXD                      | Cmax_D       | 0.0740000  | 0.0740000 | 0          |
| 5       | CMAXD                      | Cmax_D       | 0.0820000  | 0.0820000 | 0          |
| 6       | CMAXD                      | Cmax_D       | 0.0924000  | 0.0924000 | 0          |
| 1       | C0                         | C0           | 2.3936170  | 2.3936170 | 0          |
| 2       | C0                         | C0           | 2.5281595  | 2.5281595 | 0          |
| 3       | C0                         | C0           | 4.9653691  | 4.9653691 | 0          |
| 4       | C0                         | C0           | 2.4622302  | 2.4622302 | 0          |
| 5       | C0                         | C0           | 4.0408654  | 4.0408654 | 0          |
| 6       | C0                         | C0           | 3.7056250  | 3.7056250 | 0          |
| 1       | TLST                       | Tlast        | 8.0000000  | 8.0000000 | 0          |
| 2       | TLST                       | Tlast        | 8.0000000  | 8.0000000 | 0          |
| 3       | TLST                       | Tlast        | 8.0000000  | 8.0000000 | 0          |
| 4       | TLST                       | Tlast        | 8.0000000  | 8.0000000 | 0          |
| 5       | TLST                       | Tlast        | 8.0000000  | 8.0000000 | 0          |
| 6       | TLST                       | Tlast        | 8.0000000  | 8.0000000 | 0          |
| 1       | CLST                       | Clast        | 0.0500000  | 0.0500000 | 0          |
| 2       | CLST                       | Clast        | 0.0800000  | 0.0800000 | 0          |
| 3       | CLST                       | Clast        | 0.0800000  | 0.0800000 | 0          |
| 4       | CLST                       | Clast        | 0.0700000  | 0.0700000 | 0          |
| 5       | CLST                       | Clast        | 0.0600000  | 0.0600000 | 0          |
| 6       | CLST                       | Clast        | 0.0900000  | 0.0900000 | 0          |
| 1       | AUCLST                     | AUClast      | 2.0098984  | 2.0098984 | 0          |
| 2       | AUCLST                     | AUClast      | 3.2028878  | 3.2028878 | 0          |
| 3       | AUCLST                     | AUClast      | 3.4743971  | 3.4743971 | 0          |
| 4       | AUCLST                     | AUClast      | 2.7483832  | 2.7483832 | 0          |
| 5       | AUCLST                     | AUClast      | 2.3983736  | 2.3983736 | 0          |
| 6       | AUCLST                     | AUClast      | 3.2908266  | 3.2908266 | 0          |
| 1       | AUCALL                     | AUCall       | 2.0098984  | 2.0098984 | 0          |
| 2       | AUCALL                     | AUCall       | 3.2028878  | 3.2028878 | 0          |
| 3       | AUCALL                     | AUCall       | 3.4743971  | 3.4743971 | 0          |
| 4       | AUCALL                     | AUCall       | 2.7483832  | 2.7483832 | 0          |
| 5       | AUCALL                     | AUCall       | 2.3983736  | 2.3983736 | 0          |
| 6       | AUCALL                     | AUCall       | 3.2908266  | 3.2908266 | 0          |
| 1       | AUCIFO                     | AUCINF_obs   | 2.3257135  | 2.3257135 | 0          |
| 2       | AUCIFO                     | AUCINF_obs   | 3.4675431  | 3.4675431 | 0          |
| 3       | AUCIFO                     | AUCINF_obs   | 3.6640188  | 3.6640188 | 0          |
| 4       | AUCIFO                     | AUCINF_obs   | 2.9020789  | 2.9020789 | 0          |
| 5       | AUCIFO                     | AUCINF_obs   | 2.6357645  | 2.6357645 | 0          |
| 6       | AUCIFO                     | AUCINF_obs   | 3.5454087  | 3.5454087 | 0          |
| 1       | AUCIFOD                    | AUCINF_D_obs | 0.0930285  | 0.0930285 | 0          |
| 2       | AUCIFOD                    | AUCINF_D_obs | 0.1387017  | 0.1387017 | 0          |
| 3       | AUCIFOD                    | AUCINF_D_obs | 0.1465608  | 0.1465608 | 0          |
| 4       | AUCIFOD                    | AUCINF_D_obs | 0.1160832  | 0.1160832 | 0          |
| 5       | AUCIFOD                    | AUCINF_D_obs | 0.1054306  | 0.1054306 | 0          |

Table 5: Indometh (n=6), Log, IV Bolus (*continued*)

| Subject | Pharmacokinetic Parameters |                    | Values     |            | Difference |
|---------|----------------------------|--------------------|------------|------------|------------|
|         | PPTESTCD                   | WNL                | NonCompart | WinNonlin  |            |
| 6       | AUCIFOD                    | AUCINF_D_obs       | 0.1418163  | 0.1418163  | 0          |
| 1       | AUCPEO                     | AUC_.Extrap_obs    | 13.5792780 | 13.5792780 | 0          |
| 2       | AUCPEO                     | AUC_.Extrap_obs    | 7.6323571  | 7.6323571  | 0          |
| 3       | AUCPEO                     | AUC_.Extrap_obs    | 5.1752381  | 5.1752381  | 0          |
| 4       | AUCPEO                     | AUC_.Extrap_obs    | 5.2960545  | 5.2960545  | 0          |
| 5       | AUCPEO                     | AUC_.Extrap_obs    | 9.0065258  | 9.0065258  | 0          |
| 6       | AUCPEO                     | AUC_.Extrap_obs    | 7.1806138  | 7.1806138  | 0          |
| 1       | AUCPBEO                    | AUC_.Back_Ext_obs  | 20.5542573 | 20.5542573 | 0          |
| 2       | AUCPBEO                    | AUC_.Back_Ext_obs  | 16.3658871 | 16.3658871 | 0          |
| 3       | AUCPBEO                    | AUC_.Back_Ext_obs  | 25.4552663 | 25.4552663 | 0          |
| 4       | AUCPBEO                    | AUC_.Back_Ext_obs  | 18.4484084 | 18.4484084 | 0          |
| 5       | AUCPBEO                    | AUC_.Back_Ext_obs  | 27.8259014 | 27.8259014 | 0          |
| 6       | AUCPBEO                    | AUC_.Back_Ext_obs  | 20.8230657 | 20.8230657 | 0          |
| 1       | VZO                        | Vz_obs             | 67.8963898 | 67.8963898 | 0          |
| 2       | VZO                        | Vz_obs             | 23.8511160 | 23.8511160 | 0          |
| 3       | VZO                        | Vz_obs             | 16.1726192 | 16.1726192 | 0          |
| 4       | VZO                        | Vz_obs             | 18.9144805 | 18.9144805 | 0          |
| 5       | VZO                        | Vz_obs             | 37.5271908 | 37.5271908 | 0          |
| 6       | VZO                        | Vz_obs             | 19.9461495 | 19.9461495 | 0          |
| 1       | CLO                        | Cl_obs             | 10.7493892 | 10.7493892 | 0          |
| 2       | CLO                        | Cl_obs             | 7.2097158  | 7.2097158  | 0          |
| 3       | CLO                        | Cl_obs             | 6.8231092  | 6.8231092  | 0          |
| 4       | CLO                        | Cl_obs             | 8.6145142  | 8.6145142  | 0          |
| 5       | CLO                        | Cl_obs             | 9.4849143  | 9.4849143  | 0          |
| 6       | CLO                        | Cl_obs             | 7.0513732  | 7.0513732  | 0          |
| 1       | AUCIFP                     | AUCINF_pred        | 2.3272832  | 2.3272832  | 0          |
| 2       | AUCIFP                     | AUCINF_pred        | 3.4501946  | 3.4501946  | 0          |
| 3       | AUCIFP                     | AUCINF_pred        | 3.5691429  | 3.5691429  | 0          |
| 4       | AUCIFP                     | AUCINF_pred        | 2.8185565  | 2.8185565  | 0          |
| 5       | AUCIFP                     | AUCINF_pred        | 2.5945039  | 2.5945039  | 0          |
| 6       | AUCIFP                     | AUCINF_pred        | 3.4499191  | 3.4499191  | 0          |
| 1       | AUCIFPD                    | AUCINF_D_pred      | 0.0930913  | 0.0930913  | 0          |
| 2       | AUCIFPD                    | AUCINF_D_pred      | 0.1380078  | 0.1380078  | 0          |
| 3       | AUCIFPD                    | AUCINF_D_pred      | 0.1427657  | 0.1427657  | 0          |
| 4       | AUCIFPD                    | AUCINF_D_pred      | 0.1127423  | 0.1127423  | 0          |
| 5       | AUCIFPD                    | AUCINF_D_pred      | 0.1037802  | 0.1037802  | 0          |
| 6       | AUCIFPD                    | AUCINF_D_pred      | 0.1379968  | 0.1379968  | 0          |
| 1       | AUCPEP                     | AUC_.Extrap_pred   | 13.6375646 | 13.6375646 | 0          |
| 2       | AUCPEP                     | AUC_.Extrap_pred   | 7.1679092  | 7.1679092  | 0          |
| 3       | AUCPEP                     | AUC_.Extrap_pred   | 2.6545826  | 2.6545826  | 0          |
| 4       | AUCPEP                     | AUC_.Extrap_pred   | 2.4896893  | 2.4896893  | 0          |
| 5       | AUCPEP                     | AUC_.Extrap_pred   | 7.5594516  | 7.5594516  | 0          |
| 6       | AUCPEP                     | AUC_.Extrap_pred   | 4.6114853  | 4.6114853  | 0          |
| 1       | AUCPBEP                    | AUC_.Back_Ext_pred | 20.5403945 | 20.5403945 | 0          |
| 2       | AUCPBEP                    | AUC_.Back_Ext_pred | 16.4481790 | 16.4481790 | 0          |



Table 5: Indometh (n=6), Log, IV Bolus (*continued*)

| Subject | Pharmacokinetic Parameters |                    | Values     |            | Difference |
|---------|----------------------------|--------------------|------------|------------|------------|
|         | PPTESTCD                   | WNL                | NonCompart | WinNonlin  |            |
| 3       | AUCPBEP                    | AUC_.Back_Ext_pred | 26.1319245 | 26.1319245 | 0          |
| 4       | AUCPBEP                    | AUC_.Back_Ext_pred | 18.9950907 | 18.9950907 | 0          |
| 5       | AUCPBEP                    | AUC_.Back_Ext_pred | 28.2684182 | 28.2684182 | 0          |
| 6       | AUCPBEP                    | AUC_.Back_Ext_pred | 21.3994230 | 21.3994230 | 0          |
| 1       | VZP                        | Vz_pred            | 67.8505969 | 67.8505969 | 0          |
| 2       | VZP                        | Vz_pred            | 23.9710455 | 23.9710455 | 0          |
| 3       | VZP                        | Vz_pred            | 16.6025238 | 16.6025238 | 0          |
| 4       | VZP                        | Vz_pred            | 19.4749739 | 19.4749739 | 0          |
| 5       | VZP                        | Vz_pred            | 38.1239878 | 38.1239878 | 0          |
| 6       | VZP                        | Vz_pred            | 20.4982349 | 20.4982349 | 0          |
| 1       | CLP                        | Cl_pred            | 10.7421392 | 10.7421392 | 0          |
| 2       | CLP                        | Cl_pred            | 7.2459681  | 7.2459681  | 0          |
| 3       | CLP                        | Cl_pred            | 7.0044827  | 7.0044827  | 0          |
| 4       | CLP                        | Cl_pred            | 8.8697884  | 8.8697884  | 0          |
| 5       | CLP                        | Cl_pred            | 9.6357534  | 9.6357534  | 0          |
| 6       | CLP                        | Cl_pred            | 7.2465467  | 7.2465467  | 0          |
| 1       | AUMCLST                    | AUMClast           | 3.3047961  | 3.3047961  | 0          |
| 2       | AUMCLST                    | AUMClast           | 6.4131687  | 6.4131687  | 0          |
| 3       | AUMCLST                    | AUMClast           | 5.0552993  | 5.0552993  | 0          |
| 4       | AUMCLST                    | AUMClast           | 4.4049718  | 4.4049718  | 0          |
| 5       | AUMCLST                    | AUMClast           | 3.7472994  | 3.7472994  | 0          |
| 6       | AUMCLST                    | AUMClast           | 5.5904206  | 5.5904206  | 0          |
| 1       | AUMCIFO                    | AUMCINF_obs        | 7.8261005  | 7.8261005  | 0          |
| 2       | AUMCIFO                    | AUMCINF_obs        | 9.4059410  | 9.4059410  | 0          |
| 3       | AUMCIFO                    | AUMCINF_obs        | 7.0217278  | 7.0217278  | 0          |
| 4       | AUMCIFO                    | AUMCINF_obs        | 5.9719996  | 5.9719996  | 0          |
| 5       | AUMCIFO                    | AUMCINF_obs        | 6.5856658  | 6.5856658  | 0          |
| 6       | AUMCIFO                    | AUMCINF_obs        | 8.3472113  | 8.3472113  | 0          |
| 1       | AUMCPEO                    | AUMC_.Extrap_obs   | 57.7721236 | 57.7721236 | 0          |
| 2       | AUMCPEO                    | AUMC_.Extrap_obs   | 31.8178935 | 31.8178935 | 0          |
| 3       | AUMCPEO                    | AUMC_.Extrap_obs   | 28.0049084 | 28.0049084 | 0          |
| 4       | AUMCPEO                    | AUMC_.Extrap_obs   | 26.2395827 | 26.2395827 | 0          |
| 5       | AUMCPEO                    | AUMC_.Extrap_obs   | 43.0991557 | 43.0991557 | 0          |
| 6       | AUMCPEO                    | AUMC_.Extrap_obs   | 33.0264883 | 33.0264883 | 0          |
| 1       | AUMCIFP                    | AUMCINF_pred       | 7.8485720  | 7.8485720  | 0          |
| 2       | AUMCIFP                    | AUMCINF_pred       | 9.2097614  | 9.2097614  | 0          |
| 3       | AUMCIFP                    | AUMCINF_pred       | 6.0378395  | 6.0378395  | 0          |
| 4       | AUMCIFP                    | AUMCINF_pred       | 5.1204344  | 5.1204344  | 0          |
| 5       | AUMCIFP                    | AUMCINF_pred       | 6.0923336  | 6.0923336  | 0          |
| 6       | AUMCIFP                    | AUMCINF_pred       | 7.3131841  | 7.3131841  | 0          |
| 1       | AUMCPEP                    | AUMC_.Extrap_pred  | 57.8930274 | 57.8930274 | 0          |
| 2       | AUMCPEP                    | AUMC_.Extrap_pred  | 30.3655279 | 30.3655279 | 0          |
| 3       | AUMCPEP                    | AUMC_.Extrap_pred  | 16.2730417 | 16.2730417 | 0          |
| 4       | AUMCPEP                    | AUMC_.Extrap_pred  | 13.9726930 | 13.9726930 | 0          |
| 5       | AUMCPEP                    | AUMC_.Extrap_pred  | 38.4915588 | 38.4915588 | 0          |

Table 5: Indometh (n=6), Log, IV Bolus (*continued*)

| Subject | Pharmacokinetic Parameters |                  | Values     |            | Difference |
|---------|----------------------------|------------------|------------|------------|------------|
|         | PPTESTCD                   | WNL              | NonCompart | WinNonlin  |            |
| 6       | AUMCPEP                    | AUMC_Extrap_pred | 23.5569554 | 23.5569554 | 0          |
| 1       | MRTIVLST                   | MRTlast          | 1.6442602  | 1.6442602  | 0          |
| 2       | MRTIVLST                   | MRTlast          | 2.0023083  | 2.0023083  | 0          |
| 3       | MRTIVLST                   | MRTlast          | 1.4550148  | 1.4550148  | 0          |
| 4       | MRTIVLST                   | MRTlast          | 1.6027502  | 1.6027502  | 0          |
| 5       | MRTIVLST                   | MRTlast          | 1.5624335  | 1.5624335  | 0          |
| 6       | MRTIVLST                   | MRTlast          | 1.6987892  | 1.6987892  | 0          |
| 1       | MRTIVIFO                   | MRTINF_obs       | 3.3650320  | 3.3650320  | 0          |
| 2       | MRTIVIFO                   | MRTINF_obs       | 2.7125665  | 2.7125665  | 0          |
| 3       | MRTIVIFO                   | MRTINF_obs       | 1.9164006  | 1.9164006  | 0          |
| 4       | MRTIVIFO                   | MRTINF_obs       | 2.0578350  | 2.0578350  | 0          |
| 5       | MRTIVIFO                   | MRTINF_obs       | 2.4985790  | 2.4985790  | 0          |
| 6       | MRTIVIFO                   | MRTINF_obs       | 2.3543721  | 2.3543721  | 0          |
| 1       | MRTIVIFP                   | MRTINF_pred      | 3.3724181  | 3.3724181  | 0          |
| 2       | MRTIVIFP                   | MRTINF_pred      | 2.6693455  | 2.6693455  | 0          |
| 3       | MRTIVIFP                   | MRTINF_pred      | 1.6916777  | 1.6916777  | 0          |
| 4       | MRTIVIFP                   | MRTINF_pred      | 1.8166868  | 1.8166868  | 0          |
| 5       | MRTIVIFP                   | MRTINF_pred      | 2.3481690  | 2.3481690  | 0          |
| 6       | MRTIVIFP                   | MRTINF_pred      | 2.1198132  | 2.1198132  | 0          |
| 1       | VSSO                       | Vss_obs          | 36.1720388 | 36.1720388 | 0          |
| 2       | VSSO                       | Vss_obs          | 19.5568334 | 19.5568334 | 0          |
| 3       | VSSO                       | Vss_obs          | 13.0758105 | 13.0758105 | 0          |
| 4       | VSSO                       | Vss_obs          | 17.7272490 | 17.7272490 | 0          |
| 5       | VSSO                       | Vss_obs          | 23.6988080 | 23.6988080 | 0          |
| 6       | VSSO                       | Vss_obs          | 16.6015562 | 16.6015562 | 0          |
| 1       | VSSP                       | Vss_pred         | 36.2269851 | 36.2269851 | 0          |
| 2       | VSSP                       | Vss_pred         | 19.3419923 | 19.3419923 | 0          |
| 3       | VSSP                       | Vss_pred         | 11.8493272 | 11.8493272 | 0          |
| 4       | VSSP                       | Vss_pred         | 16.1136274 | 16.1136274 | 0          |
| 5       | VSSP                       | Vss_pred         | 22.6263772 | 22.6263772 | 0          |
| 6       | VSSP                       | Vss_pred         | 15.3613252 | 15.3613252 | 0          |

## A.5 Test 5: Indometh (n=6), Linear, IV Infusion (0.25hr)

```
table_wres_rres(Wres5, Rres5,
  Caption = 'Indometh (n=6), Linear, IV Infusion (0.25hr)')
```

Table 6: Indometh (n=6), Linear, IV Infusion (0.25hr)

| Subject | Pharmacokinetic Parameters |     | Values     |           | Difference |
|---------|----------------------------|-----|------------|-----------|------------|
|         | PPTESTCD                   | WNL | NonCompart | WinNonlin |            |
| 1       | R2                         | Rsq | 0.9970667  | 0.9970667 | 0          |
| 2       | R2                         | Rsq | 0.9476691  | 0.9476691 | 0          |

Table 6: Indometh (n=6), Linear, IV Infusion (0.25hr) (*continued*)

| Subject | Pharmacokinetic Parameters |                    | Values     |            | Difference |
|---------|----------------------------|--------------------|------------|------------|------------|
|         | PPTTESTCD                  | WNL                | NonCompart | WinNonlin  |            |
| 3       | R2                         | Rsqr               | 0.8758261  | 0.8758261  | 0          |
| 4       | R2                         | Rsqr               | 0.8671179  | 0.8671179  | 0          |
| 5       | R2                         | Rsqr               | 0.8752442  | 0.8752442  | 0          |
| 6       | R2                         | Rsqr               | 0.9039538  | 0.9039538  | 0          |
| 1       | R2ADJ                      | Rsqr_adjusted      | 0.9941335  | 0.9941335  | 0          |
| 2       | R2ADJ                      | Rsqr_adjusted      | 0.9401933  | 0.9401933  | 0          |
| 3       | R2ADJ                      | Rsqr_adjusted      | 0.8603043  | 0.8603043  | 0          |
| 4       | R2ADJ                      | Rsqr_adjusted      | 0.8505077  | 0.8505077  | 0          |
| 5       | R2ADJ                      | Rsqr_adjusted      | 0.8544516  | 0.8544516  | 0          |
| 6       | R2ADJ                      | Rsqr_adjusted      | 0.8902329  | 0.8902329  | 0          |
| 1       | CORRXY                     | Corr_XY            | -0.9985323 | -0.9985323 | 0          |
| 2       | CORRXY                     | Corr_XY            | -0.9734830 | -0.9734830 | 0          |
| 3       | CORRXY                     | Corr_XY            | -0.9358558 | -0.9358558 | 0          |
| 4       | CORRXY                     | Corr_XY            | -0.9311917 | -0.9311917 | 0          |
| 5       | CORRXY                     | Corr_XY            | -0.9355449 | -0.9355449 | 0          |
| 6       | CORRXY                     | Corr_XY            | -0.9507649 | -0.9507649 | 0          |
| 1       | LAMZNPT                    | No_points_lambda_z | 3.0000000  | 3.0000000  | 0          |
| 2       | LAMZNPT                    | No_points_lambda_z | 9.0000000  | 9.0000000  | 0          |
| 3       | LAMZNPT                    | No_points_lambda_z | 10.0000000 | 10.0000000 | 0          |
| 4       | LAMZNPT                    | No_points_lambda_z | 10.0000000 | 10.0000000 | 0          |
| 5       | LAMZNPT                    | No_points_lambda_z | 8.0000000  | 8.0000000  | 0          |
| 6       | LAMZNPT                    | No_points_lambda_z | 9.0000000  | 9.0000000  | 0          |
| 1       | LAMZ                       | Lambda_z           | 0.1583205  | 0.1583205  | 0          |
| 2       | LAMZ                       | Lambda_z           | 0.3022800  | 0.3022800  | 0          |
| 3       | LAMZ                       | Lambda_z           | 0.4218926  | 0.4218926  | 0          |
| 4       | LAMZ                       | Lambda_z           | 0.4290762  | 0.4290762  | 0          |
| 5       | LAMZ                       | Lambda_z           | 0.2527478  | 0.2527478  | 0          |
| 6       | LAMZ                       | Lambda_z           | 0.3535205  | 0.3535205  | 0          |
| 1       | LAMZLL                     | Lambda_z_lower     | 5.0000000  | 5.0000000  | 0          |
| 2       | LAMZLL                     | Lambda_z_lower     | 0.7500000  | 0.7500000  | 0          |
| 3       | LAMZLL                     | Lambda_z_lower     | 0.5000000  | 0.5000000  | 0          |
| 4       | LAMZLL                     | Lambda_z_lower     | 0.5000000  | 0.5000000  | 0          |
| 5       | LAMZLL                     | Lambda_z_lower     | 1.0000000  | 1.0000000  | 0          |
| 6       | LAMZLL                     | Lambda_z_lower     | 0.7500000  | 0.7500000  | 0          |
| 1       | LAMZUL                     | Lambda_z_upper     | 8.0000000  | 8.0000000  | 0          |
| 2       | LAMZUL                     | Lambda_z_upper     | 8.0000000  | 8.0000000  | 0          |
| 3       | LAMZUL                     | Lambda_z_upper     | 8.0000000  | 8.0000000  | 0          |
| 4       | LAMZUL                     | Lambda_z_upper     | 8.0000000  | 8.0000000  | 0          |
| 5       | LAMZUL                     | Lambda_z_upper     | 8.0000000  | 8.0000000  | 0          |
| 6       | LAMZUL                     | Lambda_z_upper     | 8.0000000  | 8.0000000  | 0          |
| 1       | LAMZHL                     | HL_Lambda_z        | 4.3781270  | 4.3781270  | 0          |
| 2       | LAMZHL                     | HL_Lambda_z        | 2.2930632  | 2.2930632  | 0          |
| 3       | LAMZHL                     | HL_Lambda_z        | 1.6429468  | 1.6429468  | 0          |
| 4       | LAMZHL                     | HL_Lambda_z        | 1.6154409  | 1.6154409  | 0          |
| 5       | LAMZHL                     | HL_Lambda_z        | 2.7424461  | 2.7424461  | 0          |

Table 6: Indometh (n=6), Linear, IV Infusion (0.25hr) (*continued*)

| Subject | Pharmacokinetic Parameters |             | Values     |           | Difference |
|---------|----------------------------|-------------|------------|-----------|------------|
|         | PPTTESTCD                  | WNL         | NonCompart | WinNonlin |            |
| 6       | LAMZHL                     | HL_Lambda_z | 1.9606986  | 1.9606986 | 0          |
| 1       | TMAX                       | Tmax        | 0.2500000  | 0.2500000 | 0          |
| 2       | TMAX                       | Tmax        | 0.2500000  | 0.2500000 | 0          |
| 3       | TMAX                       | Tmax        | 0.2500000  | 0.2500000 | 0          |
| 4       | TMAX                       | Tmax        | 0.2500000  | 0.2500000 | 0          |
| 5       | TMAX                       | Tmax        | 0.2500000  | 0.2500000 | 0          |
| 6       | TMAX                       | Tmax        | 0.2500000  | 0.2500000 | 0          |
| 1       | CMAX                       | Cmax        | 1.5000000  | 1.5000000 | 0          |
| 2       | CMAX                       | Cmax        | 2.0300000  | 2.0300000 | 0          |
| 3       | CMAX                       | Cmax        | 2.7200000  | 2.7200000 | 0          |
| 4       | CMAX                       | Cmax        | 1.8500000  | 1.8500000 | 0          |
| 5       | CMAX                       | Cmax        | 2.0500000  | 2.0500000 | 0          |
| 6       | CMAX                       | Cmax        | 2.3100000  | 2.3100000 | 0          |
| 1       | CMAXD                      | Cmax_D      | 0.0600000  | 0.0600000 | 0          |
| 2       | CMAXD                      | Cmax_D      | 0.0812000  | 0.0812000 | 0          |
| 3       | CMAXD                      | Cmax_D      | 0.1088000  | 0.1088000 | 0          |
| 4       | CMAXD                      | Cmax_D      | 0.0740000  | 0.0740000 | 0          |
| 5       | CMAXD                      | Cmax_D      | 0.0820000  | 0.0820000 | 0          |
| 6       | CMAXD                      | Cmax_D      | 0.0924000  | 0.0924000 | 0          |
| 1       | TLST                       | Tlast       | 8.0000000  | 8.0000000 | 0          |
| 2       | TLST                       | Tlast       | 8.0000000  | 8.0000000 | 0          |
| 3       | TLST                       | Tlast       | 8.0000000  | 8.0000000 | 0          |
| 4       | TLST                       | Tlast       | 8.0000000  | 8.0000000 | 0          |
| 5       | TLST                       | Tlast       | 8.0000000  | 8.0000000 | 0          |
| 6       | TLST                       | Tlast       | 8.0000000  | 8.0000000 | 0          |
| 1       | CLST                       | Clast       | 0.0500000  | 0.0500000 | 0          |
| 2       | CLST                       | Clast       | 0.0800000  | 0.0800000 | 0          |
| 3       | CLST                       | Clast       | 0.0800000  | 0.0800000 | 0          |
| 4       | CLST                       | Clast       | 0.0700000  | 0.0700000 | 0          |
| 5       | CLST                       | Clast       | 0.0600000  | 0.0600000 | 0          |
| 6       | CLST                       | Clast       | 0.0900000  | 0.0900000 | 0          |
| 1       | AUCLST                     | AUClast     | 1.7412500  | 1.7412500 | 0          |
| 2       | AUCLST                     | AUClast     | 2.9325000  | 2.9325000 | 0          |
| 3       | AUCLST                     | AUClast     | 2.9337500  | 2.9337500 | 0          |
| 4       | AUCLST                     | AUClast     | 2.4775000  | 2.4775000 | 0          |
| 5       | AUCLST                     | AUClast     | 1.9537500  | 1.9537500 | 0          |
| 6       | AUCLST                     | AUClast     | 2.8725000  | 2.8725000 | 0          |
| 1       | AUCALL                     | AUCall      | 1.7412500  | 1.7412500 | 0          |
| 2       | AUCALL                     | AUCall      | 2.9325000  | 2.9325000 | 0          |
| 3       | AUCALL                     | AUCall      | 2.9337500  | 2.9337500 | 0          |
| 4       | AUCALL                     | AUCall      | 2.4775000  | 2.4775000 | 0          |
| 5       | AUCALL                     | AUCall      | 1.9537500  | 1.9537500 | 0          |
| 6       | AUCALL                     | AUCall      | 2.8725000  | 2.8725000 | 0          |
| 1       | AUCIFO                     | AUCINF_obs  | 2.0570651  | 2.0570651 | 0          |
| 2       | AUCIFO                     | AUCINF_obs  | 3.1971553  | 3.1971553 | 0          |

Table 6: Indometh (n=6), Linear, IV Infusion (0.25hr) (*continued*)

| Subject | Pharmacokinetic Parameters |                  | Values     |            | Difference |
|---------|----------------------------|------------------|------------|------------|------------|
|         | PPTTESTCD                  | WNL              | NonCompart | WinNonlin  |            |
| 3       | AUCIFO                     | AUCINF_obs       | 3.1233717  | 3.1233717  | 0          |
| 4       | AUCIFO                     | AUCINF_obs       | 2.6406412  | 2.6406412  | 0          |
| 5       | AUCIFO                     | AUCINF_obs       | 2.1911408  | 2.1911408  | 0          |
| 6       | AUCIFO                     | AUCINF_obs       | 3.1270821  | 3.1270821  | 0          |
| 1       | AUCIFOD                    | AUCINF_D_obs     | 0.0822826  | 0.0822826  | 0          |
| 2       | AUCIFOD                    | AUCINF_D_obs     | 0.1278862  | 0.1278862  | 0          |
| 3       | AUCIFOD                    | AUCINF_D_obs     | 0.1249349  | 0.1249349  | 0          |
| 4       | AUCIFOD                    | AUCINF_D_obs     | 0.1056256  | 0.1056256  | 0          |
| 5       | AUCIFOD                    | AUCINF_D_obs     | 0.0876456  | 0.0876456  | 0          |
| 6       | AUCIFOD                    | AUCINF_D_obs     | 0.1250833  | 0.1250833  | 0          |
| 1       | AUCPEO                     | AUC_.Extrap_obs  | 15.3527035 | 15.3527035 | 0          |
| 2       | AUCPEO                     | AUC_.Extrap_obs  | 8.2778360  | 8.2778360  | 0          |
| 3       | AUCPEO                     | AUC_.Extrap_obs  | 6.0710577  | 6.0710577  | 0          |
| 4       | AUCPEO                     | AUC_.Extrap_obs  | 6.1780905  | 6.1780905  | 0          |
| 5       | AUCPEO                     | AUC_.Extrap_obs  | 10.8341191 | 10.8341191 | 0          |
| 6       | AUCPEO                     | AUC_.Extrap_obs  | 8.1412032  | 8.1412032  | 0          |
| 1       | VZO                        | Vz_obs           | 76.7635175 | 76.7635175 | 0          |
| 2       | VZO                        | Vz_obs           | 25.8682374 | 25.8682374 | 0          |
| 3       | VZO                        | Vz_obs           | 18.9720552 | 18.9720552 | 0          |
| 4       | VZO                        | Vz_obs           | 22.0646091 | 22.0646091 | 0          |
| 5       | VZO                        | Vz_obs           | 45.1421631 | 45.1421631 | 0          |
| 6       | VZO                        | Vz_obs           | 22.6144534 | 22.6144534 | 0          |
| 1       | CLO                        | Cl_obs           | 12.1532371 | 12.1532371 | 0          |
| 2       | CLO                        | Cl_obs           | 7.8194513  | 7.8194513  | 0          |
| 3       | CLO                        | Cl_obs           | 8.0041706  | 8.0041706  | 0          |
| 4       | CLO                        | Cl_obs           | 9.4673975  | 9.4673975  | 0          |
| 5       | CLO                        | Cl_obs           | 11.4095817 | 11.4095817 | 0          |
| 6       | CLO                        | Cl_obs           | 7.9946733  | 7.9946733  | 0          |
| 1       | AUCIFP                     | AUCINF_pred      | 2.0586347  | 2.0586347  | 0          |
| 2       | AUCIFP                     | AUCINF_pred      | 3.1798068  | 3.1798068  | 0          |
| 3       | AUCIFP                     | AUCINF_pred      | 3.0284958  | 3.0284958  | 0          |
| 4       | AUCIFP                     | AUCINF_pred      | 2.5577884  | 2.5577884  | 0          |
| 5       | AUCIFP                     | AUCINF_pred      | 2.1498803  | 2.1498803  | 0          |
| 6       | AUCIFP                     | AUCINF_pred      | 3.0315925  | 3.0315925  | 0          |
| 1       | AUCIFPD                    | AUCINF_D_pred    | 0.0823454  | 0.0823454  | 0          |
| 2       | AUCIFPD                    | AUCINF_D_pred    | 0.1271923  | 0.1271923  | 0          |
| 3       | AUCIFPD                    | AUCINF_D_pred    | 0.1211398  | 0.1211398  | 0          |
| 4       | AUCIFPD                    | AUCINF_D_pred    | 0.1023115  | 0.1023115  | 0          |
| 5       | AUCIFPD                    | AUCINF_D_pred    | 0.0859952  | 0.0859952  | 0          |
| 6       | AUCIFPD                    | AUCINF_D_pred    | 0.1212637  | 0.1212637  | 0          |
| 1       | AUCPEP                     | AUC_.Extrap_pred | 15.4172443 | 15.4172443 | 0          |
| 2       | AUCPEP                     | AUC_.Extrap_pred | 7.7774164  | 7.7774164  | 0          |
| 3       | AUCPEP                     | AUC_.Extrap_pred | 3.1284787  | 3.1284787  | 0          |
| 4       | AUCPEP                     | AUC_.Extrap_pred | 3.1389787  | 3.1389787  | 0          |
| 5       | AUCPEP                     | AUC_.Extrap_pred | 9.1228460  | 9.1228460  | 0          |

Table 6: Indometh (n=6), Linear, IV Infusion (0.25hr) (*continued*)

| Subject | Pharmacokinetic Parameters |                   | Values     |            | Difference |
|---------|----------------------------|-------------------|------------|------------|------------|
|         | PPTTESTCD                  | WNL               | NonCompart | WinNonlin  |            |
| 6       | AUCPEP                     | AUC_.Extrap_pred  | 5.2478198  | 5.2478198  | 0          |
| 1       | VZP                        | Vz_pred           | 76.7049878 | 76.7049878 | 0          |
| 2       | VZP                        | Vz_pred           | 26.0093699 | 26.0093699 | 0          |
| 3       | VZP                        | Vz_pred           | 19.5664063 | 19.5664063 | 0          |
| 4       | VZP                        | Vz_pred           | 22.7793336 | 22.7793336 | 0          |
| 5       | VZP                        | Vz_pred           | 46.0085322 | 46.0085322 | 0          |
| 6       | VZP                        | Vz_pred           | 23.3267671 | 23.3267671 | 0          |
| 1       | CLP                        | Cl_pred           | 12.1439707 | 12.1439707 | 0          |
| 2       | CLP                        | Cl_pred           | 7.8621128  | 7.8621128  | 0          |
| 3       | CLP                        | Cl_pred           | 8.2549230  | 8.2549230  | 0          |
| 4       | CLP                        | Cl_pred           | 9.7740688  | 9.7740688  | 0          |
| 5       | CLP                        | Cl_pred           | 11.6285546 | 11.6285546 | 0          |
| 6       | CLP                        | Cl_pred           | 8.2464909  | 8.2464909  | 0          |
| 1       | AUMCLST                    | AUMClast          | 3.2712500  | 3.2712500  | 0          |
| 2       | AUMCLST                    | AUMClast          | 6.3987500  | 6.3987500  | 0          |
| 3       | AUMCLST                    | AUMClast          | 5.0062500  | 5.0062500  | 0          |
| 4       | AUMCLST                    | AUMClast          | 4.3818750  | 4.3818750  | 0          |
| 5       | AUMCLST                    | AUMClast          | 3.7075000  | 3.7075000  | 0          |
| 6       | AUMCLST                    | AUMClast          | 5.5325000  | 5.5325000  | 0          |
| 1       | AUMCIFO                    | AUMCINF_obs       | 7.7925545  | 7.7925545  | 0          |
| 2       | AUMCIFO                    | AUMCINF_obs       | 9.3915223  | 9.3915223  | 0          |
| 3       | AUMCIFO                    | AUMCINF_obs       | 6.9726784  | 6.9726784  | 0          |
| 4       | AUMCIFO                    | AUMCINF_obs       | 6.0672197  | 6.0672197  | 0          |
| 5       | AUMCIFO                    | AUMCINF_obs       | 6.5458663  | 6.5458663  | 0          |
| 6       | AUMCIFO                    | AUMCINF_obs       | 8.2892908  | 8.2892908  | 0          |
| 1       | AUMCPEO                    | AUMC_.Extrap_obs  | 58.0208261 | 58.0208261 | 0          |
| 2       | AUMCPEO                    | AUMC_.Extrap_obs  | 31.8667432 | 31.8667432 | 0          |
| 3       | AUMCPEO                    | AUMC_.Extrap_obs  | 28.2019090 | 28.2019090 | 0          |
| 4       | AUMCPEO                    | AUMC_.Extrap_obs  | 27.7778746 | 27.7778746 | 0          |
| 5       | AUMCPEO                    | AUMC_.Extrap_obs  | 43.3612023 | 43.3612023 | 0          |
| 6       | AUMCPEO                    | AUMC_.Extrap_obs  | 33.2572574 | 33.2572574 | 0          |
| 1       | AUMCIFP                    | AUMCINF_pred      | 7.8150259  | 7.8150259  | 0          |
| 2       | AUMCIFP                    | AUMCINF_pred      | 9.1953427  | 9.1953427  | 0          |
| 3       | AUMCIFP                    | AUMCINF_pred      | 5.9887901  | 5.9887901  | 0          |
| 4       | AUMCIFP                    | AUMCINF_pred      | 5.2113018  | 5.2113018  | 0          |
| 5       | AUMCIFP                    | AUMCINF_pred      | 6.0525342  | 6.0525342  | 0          |
| 6       | AUMCIFP                    | AUMCINF_pred      | 7.2552635  | 7.2552635  | 0          |
| 1       | AUMCPEP                    | AUMC_.Extrap_pred | 58.1415337 | 58.1415337 | 0          |
| 2       | AUMCPEP                    | AUMC_.Extrap_pred | 30.4131425 | 30.4131425 | 0          |
| 3       | AUMCPEP                    | AUMC_.Extrap_pred | 16.4063210 | 16.4063210 | 0          |
| 4       | AUMCPEP                    | AUMC_.Extrap_pred | 15.9159231 | 15.9159231 | 0          |
| 5       | AUMCPEP                    | AUMC_.Extrap_pred | 38.7446663 | 38.7446663 | 0          |
| 6       | AUMCPEP                    | AUMC_.Extrap_pred | 23.7450164 | 23.7450164 | 0          |
| 1       | MRTIVLST                   | MRTlast           | 1.7536791  | 1.7536791  | 0          |
| 2       | MRTIVLST                   | MRTlast           | 2.0570119  | 2.0570119  | 0          |

Table 6: Indometh (n=6), Linear, IV Infusion (0.25hr) (*continued*)

| Subject | Pharmacokinetic Parameters |             | Values     |            | Difference |
|---------|----------------------------|-------------|------------|------------|------------|
|         | PPTTESTCD                  | WNL         | NonCompart | WinNonlin  |            |
| 3       | MRTIVLST                   | MRTlast     | 1.5814337  | 1.5814337  | 0          |
| 4       | MRTIVLST                   | MRTlast     | 1.6436680  | 1.6436680  | 0          |
| 5       | MRTIVLST                   | MRTlast     | 1.7726328  | 1.7726328  | 0          |
| 6       | MRTIVLST                   | MRTlast     | 1.8010226  | 1.8010226  | 0          |
| 1       | MRTIVIFO                   | MRTINF_obs  | 3.6631905  | 3.6631905  | 0          |
| 2       | MRTIVIFO                   | MRTINF_obs  | 2.8124621  | 2.8124621  | 0          |
| 3       | MRTIVIFO                   | MRTINF_obs  | 2.1074203  | 2.1074203  | 0          |
| 4       | MRTIVIFO                   | MRTINF_obs  | 2.1726312  | 2.1726312  | 0          |
| 5       | MRTIVIFO                   | MRTINF_obs  | 2.8624239  | 2.8624239  | 0          |
| 6       | MRTIVIFO                   | MRTINF_obs  | 2.5258069  | 2.5258069  | 0          |
| 1       | MRTIVIFP                   | MRTINF_pred | 3.6712178  | 3.6712178  | 0          |
| 2       | MRTIVIFP                   | MRTINF_pred | 2.7667929  | 2.7667929  | 0          |
| 3       | MRTIVIFP                   | MRTINF_pred | 1.8524801  | 1.8524801  | 0          |
| 4       | MRTIVIFP                   | MRTINF_pred | 1.9124249  | 1.9124249  | 0          |
| 5       | MRTIVIFP                   | MRTINF_pred | 2.6902890  | 2.6902890  | 0          |
| 6       | MRTIVIFP                   | MRTINF_pred | 2.2682186  | 2.2682186  | 0          |
| 1       | VSSO                       | Vss_obs     | 44.5196227 | 44.5196227 | 0          |
| 2       | VSSO                       | Vss_obs     | 21.9919102 | 21.9919102 | 0          |
| 3       | VSSO                       | Vss_obs     | 16.8681518 | 16.8681518 | 0          |
| 4       | VSSO                       | Vss_obs     | 20.5691634 | 20.5691634 | 0          |
| 5       | VSSO                       | Vss_obs     | 32.6590590 | 32.6590590 | 0          |
| 6       | VSSO                       | Vss_obs     | 20.1930009 | 20.1930009 | 0          |
| 1       | VSSP                       | Vss_pred    | 44.5831617 | 44.5831617 | 0          |
| 2       | VSSP                       | Vss_pred    | 21.7528377 | 21.7528377 | 0          |
| 3       | VSSP                       | Vss_pred    | 15.2920802 | 15.2920802 | 0          |
| 4       | VSSP                       | Vss_pred    | 18.6921722 | 18.6921722 | 0          |
| 5       | VSSP                       | Vss_pred    | 31.2841719 | 31.2841719 | 0          |
| 6       | VSSP                       | Vss_pred    | 18.7048438 | 18.7048438 | 0          |

## A.6 Test 6: Indometh (n=6), Log, IV Infusion (0.25hr)

```
table_wres_rres(Wres6, Rres6,
  Caption = 'Indometh (n=6), Log, IV Infusion (0.25hr)')
```

Table 7: Indometh (n=6), Log, IV Infusion (0.25hr)

| Subject | Pharmacokinetic Parameters |      | Values     |           | Difference |
|---------|----------------------------|------|------------|-----------|------------|
|         | PPTTESTCD                  | WNL  | NonCompart | WinNonlin |            |
| 1       | R2                         | Rsqr | 0.9970667  | 0.9970667 | 0          |
| 2       | R2                         | Rsqr | 0.9476691  | 0.9476691 | 0          |
| 3       | R2                         | Rsqr | 0.8758261  | 0.8758261 | 0          |
| 4       | R2                         | Rsqr | 0.8671179  | 0.8671179 | 0          |
| 5       | R2                         | Rsqr | 0.8752442  | 0.8752442 | 0          |

Table 7: Indometh (n=6), Log, IV Infusion (0.25hr) (*continued*)

| Subject | Pharmacokinetic Parameters |                    | Values     |            | Difference |
|---------|----------------------------|--------------------|------------|------------|------------|
|         | PPTTESTCD                  | WNL                | NonCompart | WinNonlin  |            |
| 6       | R2                         | Rsqr               | 0.9039538  | 0.9039538  | 0          |
| 1       | R2ADJ                      | Rsqr_adjusted      | 0.9941335  | 0.9941335  | 0          |
| 2       | R2ADJ                      | Rsqr_adjusted      | 0.9401933  | 0.9401933  | 0          |
| 3       | R2ADJ                      | Rsqr_adjusted      | 0.8603043  | 0.8603043  | 0          |
| 4       | R2ADJ                      | Rsqr_adjusted      | 0.8505077  | 0.8505077  | 0          |
| 5       | R2ADJ                      | Rsqr_adjusted      | 0.8544516  | 0.8544516  | 0          |
| 6       | R2ADJ                      | Rsqr_adjusted      | 0.8902329  | 0.8902329  | 0          |
| 1       | CORRXY                     | Corr_XY            | -0.9985323 | -0.9985323 | 0          |
| 2       | CORRXY                     | Corr_XY            | -0.9734830 | -0.9734830 | 0          |
| 3       | CORRXY                     | Corr_XY            | -0.9358558 | -0.9358558 | 0          |
| 4       | CORRXY                     | Corr_XY            | -0.9311917 | -0.9311917 | 0          |
| 5       | CORRXY                     | Corr_XY            | -0.9355449 | -0.9355449 | 0          |
| 6       | CORRXY                     | Corr_XY            | -0.9507649 | -0.9507649 | 0          |
| 1       | LAMZNPT                    | No_points_lambda_z | 3.0000000  | 3.0000000  | 0          |
| 2       | LAMZNPT                    | No_points_lambda_z | 9.0000000  | 9.0000000  | 0          |
| 3       | LAMZNPT                    | No_points_lambda_z | 10.0000000 | 10.0000000 | 0          |
| 4       | LAMZNPT                    | No_points_lambda_z | 10.0000000 | 10.0000000 | 0          |
| 5       | LAMZNPT                    | No_points_lambda_z | 8.0000000  | 8.0000000  | 0          |
| 6       | LAMZNPT                    | No_points_lambda_z | 9.0000000  | 9.0000000  | 0          |
| 1       | LAMZ                       | Lambda_z           | 0.1583205  | 0.1583205  | 0          |
| 2       | LAMZ                       | Lambda_z           | 0.3022800  | 0.3022800  | 0          |
| 3       | LAMZ                       | Lambda_z           | 0.4218926  | 0.4218926  | 0          |
| 4       | LAMZ                       | Lambda_z           | 0.4290762  | 0.4290762  | 0          |
| 5       | LAMZ                       | Lambda_z           | 0.2527478  | 0.2527478  | 0          |
| 6       | LAMZ                       | Lambda_z           | 0.3535205  | 0.3535205  | 0          |
| 1       | LAMZLL                     | Lambda_z_lower     | 5.0000000  | 5.0000000  | 0          |
| 2       | LAMZLL                     | Lambda_z_lower     | 0.7500000  | 0.7500000  | 0          |
| 3       | LAMZLL                     | Lambda_z_lower     | 0.5000000  | 0.5000000  | 0          |
| 4       | LAMZLL                     | Lambda_z_lower     | 0.5000000  | 0.5000000  | 0          |
| 5       | LAMZLL                     | Lambda_z_lower     | 1.0000000  | 1.0000000  | 0          |
| 6       | LAMZLL                     | Lambda_z_lower     | 0.7500000  | 0.7500000  | 0          |
| 1       | LAMZUL                     | Lambda_z_upper     | 8.0000000  | 8.0000000  | 0          |
| 2       | LAMZUL                     | Lambda_z_upper     | 8.0000000  | 8.0000000  | 0          |
| 3       | LAMZUL                     | Lambda_z_upper     | 8.0000000  | 8.0000000  | 0          |
| 4       | LAMZUL                     | Lambda_z_upper     | 8.0000000  | 8.0000000  | 0          |
| 5       | LAMZUL                     | Lambda_z_upper     | 8.0000000  | 8.0000000  | 0          |
| 6       | LAMZUL                     | Lambda_z_upper     | 8.0000000  | 8.0000000  | 0          |
| 1       | LAMZHL                     | HL_Lambda_z        | 4.3781270  | 4.3781270  | 0          |
| 2       | LAMZHL                     | HL_Lambda_z        | 2.2930632  | 2.2930632  | 0          |
| 3       | LAMZHL                     | HL_Lambda_z        | 1.6429468  | 1.6429468  | 0          |
| 4       | LAMZHL                     | HL_Lambda_z        | 1.6154409  | 1.6154409  | 0          |
| 5       | LAMZHL                     | HL_Lambda_z        | 2.7424461  | 2.7424461  | 0          |
| 6       | LAMZHL                     | HL_Lambda_z        | 1.9606986  | 1.9606986  | 0          |
| 1       | TMAX                       | Tmax               | 0.2500000  | 0.2500000  | 0          |
| 2       | TMAX                       | Tmax               | 0.2500000  | 0.2500000  | 0          |



Table 7: Indometh (n=6), Log, IV Infusion (0.25hr) (*continued*)

| Subject | Pharmacokinetic Parameters |            | Values     |           | Difference |
|---------|----------------------------|------------|------------|-----------|------------|
|         | PPTSTCD                    | WNL        | NonCompart | WinNonlin |            |
| 3       | TMAX                       | Tmax       | 0.2500000  | 0.2500000 | 0          |
| 4       | TMAX                       | Tmax       | 0.2500000  | 0.2500000 | 0          |
| 5       | TMAX                       | Tmax       | 0.2500000  | 0.2500000 | 0          |
| 6       | TMAX                       | Tmax       | 0.2500000  | 0.2500000 | 0          |
| 1       | CMAX                       | Cmax       | 1.5000000  | 1.5000000 | 0          |
| 2       | CMAX                       | Cmax       | 2.0300000  | 2.0300000 | 0          |
| 3       | CMAX                       | Cmax       | 2.7200000  | 2.7200000 | 0          |
| 4       | CMAX                       | Cmax       | 1.8500000  | 1.8500000 | 0          |
| 5       | CMAX                       | Cmax       | 2.0500000  | 2.0500000 | 0          |
| 6       | CMAX                       | Cmax       | 2.3100000  | 2.3100000 | 0          |
| 1       | CMAXD                      | Cmax_D     | 0.0600000  | 0.0600000 | 0          |
| 2       | CMAXD                      | Cmax_D     | 0.0812000  | 0.0812000 | 0          |
| 3       | CMAXD                      | Cmax_D     | 0.1088000  | 0.1088000 | 0          |
| 4       | CMAXD                      | Cmax_D     | 0.0740000  | 0.0740000 | 0          |
| 5       | CMAXD                      | Cmax_D     | 0.0820000  | 0.0820000 | 0          |
| 6       | CMAXD                      | Cmax_D     | 0.0924000  | 0.0924000 | 0          |
| 1       | TLST                       | Tlast      | 8.0000000  | 8.0000000 | 0          |
| 2       | TLST                       | Tlast      | 8.0000000  | 8.0000000 | 0          |
| 3       | TLST                       | Tlast      | 8.0000000  | 8.0000000 | 0          |
| 4       | TLST                       | Tlast      | 8.0000000  | 8.0000000 | 0          |
| 5       | TLST                       | Tlast      | 8.0000000  | 8.0000000 | 0          |
| 6       | TLST                       | Tlast      | 8.0000000  | 8.0000000 | 0          |
| 1       | CLST                       | Clast      | 0.0500000  | 0.0500000 | 0          |
| 2       | CLST                       | Clast      | 0.0800000  | 0.0800000 | 0          |
| 3       | CLST                       | Clast      | 0.0800000  | 0.0800000 | 0          |
| 4       | CLST                       | Clast      | 0.0700000  | 0.0700000 | 0          |
| 5       | CLST                       | Clast      | 0.0600000  | 0.0600000 | 0          |
| 6       | CLST                       | Clast      | 0.0900000  | 0.0900000 | 0          |
| 1       | AUCLST                     | AUClast    | 1.7193653  | 1.7193653 | 0          |
| 2       | AUCLST                     | AUClast    | 2.8891436  | 2.8891436 | 0          |
| 3       | AUCLST                     | AUClast    | 2.8817113  | 2.8817113 | 0          |
| 4       | AUCLST                     | AUClast    | 2.4442459  | 2.4442459 | 0          |
| 5       | AUCLST                     | AUClast    | 1.9211984  | 1.9211984 | 0          |
| 6       | AUCLST                     | AUClast    | 2.8413138  | 2.8413138 | 0          |
| 1       | AUCALL                     | AUCall     | 1.7193653  | 1.7193653 | 0          |
| 2       | AUCALL                     | AUCall     | 2.8891436  | 2.8891436 | 0          |
| 3       | AUCALL                     | AUCall     | 2.8817113  | 2.8817113 | 0          |
| 4       | AUCALL                     | AUCall     | 2.4442459  | 2.4442459 | 0          |
| 5       | AUCALL                     | AUCall     | 1.9211984  | 1.9211984 | 0          |
| 6       | AUCALL                     | AUCall     | 2.8413138  | 2.8413138 | 0          |
| 1       | AUCIFO                     | AUCINF_obs | 2.0351804  | 2.0351804 | 0          |
| 2       | AUCIFO                     | AUCINF_obs | 3.1537989  | 3.1537989 | 0          |
| 3       | AUCIFO                     | AUCINF_obs | 3.0713330  | 3.0713330 | 0          |
| 4       | AUCIFO                     | AUCINF_obs | 2.6073871  | 2.6073871 | 0          |
| 5       | AUCIFO                     | AUCINF_obs | 2.1585892  | 2.1585892 | 0          |

Table 7: Indometh (n=6), Log, IV Infusion (0.25hr) (*continued*)

| Subject | Pharmacokinetic Parameters |                  | Values     |            | Difference |
|---------|----------------------------|------------------|------------|------------|------------|
|         | Pptestcd                   | WNL              | NonCompart | WinNonlin  |            |
| 6       | AUCIFO                     | AUCINF_obs       | 3.0958959  | 3.0958959  | 0          |
| 1       | AUCIFOD                    | AUCINF_D_obs     | 0.0814072  | 0.0814072  | 0          |
| 2       | AUCIFOD                    | AUCINF_D_obs     | 0.1261520  | 0.1261520  | 0          |
| 3       | AUCIFOD                    | AUCINF_D_obs     | 0.1228533  | 0.1228533  | 0          |
| 4       | AUCIFOD                    | AUCINF_D_obs     | 0.1042955  | 0.1042955  | 0          |
| 5       | AUCIFOD                    | AUCINF_D_obs     | 0.0863436  | 0.0863436  | 0          |
| 6       | AUCIFOD                    | AUCINF_D_obs     | 0.1238358  | 0.1238358  | 0          |
| 1       | AUCPEO                     | AUC_.Extrap_obs  | 15.5177942 | 15.5177942 | 0          |
| 2       | AUCPEO                     | AUC_.Extrap_obs  | 8.3916343  | 8.3916343  | 0          |
| 3       | AUCPEO                     | AUC_.Extrap_obs  | 6.1739217  | 6.1739217  | 0          |
| 4       | AUCPEO                     | AUC_.Extrap_obs  | 6.2568848  | 6.2568848  | 0          |
| 5       | AUCPEO                     | AUC_.Extrap_obs  | 10.9974979 | 10.9974979 | 0          |
| 6       | AUCPEO                     | AUC_.Extrap_obs  | 8.2232127  | 8.2232127  | 0          |
| 1       | VZO                        | Vz_obs           | 77.5889712 | 77.5889712 | 0          |
| 2       | VZO                        | Vz_obs           | 26.2238573 | 26.2238573 | 0          |
| 3       | VZO                        | Vz_obs           | 19.2935053 | 19.2935053 | 0          |
| 4       | VZO                        | Vz_obs           | 22.3460171 | 22.3460171 | 0          |
| 5       | VZO                        | Vz_obs           | 45.8229078 | 45.8229078 | 0          |
| 6       | VZO                        | Vz_obs           | 22.8422576 | 22.8422576 | 0          |
| 1       | CLO                        | Cl_obs           | 12.2839234 | 12.2839234 | 0          |
| 2       | CLO                        | Cl_obs           | 7.9269481  | 7.9269481  | 0          |
| 3       | CLO                        | Cl_obs           | 8.1397881  | 8.1397881  | 0          |
| 4       | CLO                        | Cl_obs           | 9.5881430  | 9.5881430  | 0          |
| 5       | CLO                        | Cl_obs           | 11.5816384 | 11.5816384 | 0          |
| 6       | CLO                        | Cl_obs           | 8.0752068  | 8.0752068  | 0          |
| 1       | AUCIFP                     | AUCINF_pred      | 2.0367500  | 2.0367500  | 0          |
| 2       | AUCIFP                     | AUCINF_pred      | 3.1364504  | 3.1364504  | 0          |
| 3       | AUCIFP                     | AUCINF_pred      | 2.9764572  | 2.9764572  | 0          |
| 4       | AUCIFP                     | AUCINF_pred      | 2.5245343  | 2.5245343  | 0          |
| 5       | AUCIFP                     | AUCINF_pred      | 2.1173287  | 2.1173287  | 0          |
| 6       | AUCIFP                     | AUCINF_pred      | 3.0004063  | 3.0004063  | 0          |
| 1       | AUCIFPD                    | AUCINF_D_pred    | 0.0814700  | 0.0814700  | 0          |
| 2       | AUCIFPD                    | AUCINF_D_pred    | 0.1254580  | 0.1254580  | 0          |
| 3       | AUCIFPD                    | AUCINF_D_pred    | 0.1190583  | 0.1190583  | 0          |
| 4       | AUCIFPD                    | AUCINF_D_pred    | 0.1009814  | 0.1009814  | 0          |
| 5       | AUCIFPD                    | AUCINF_D_pred    | 0.0846931  | 0.0846931  | 0          |
| 6       | AUCIFPD                    | AUCINF_D_pred    | 0.1200163  | 0.1200163  | 0          |
| 1       | AUCPEP                     | AUC_.Extrap_pred | 15.5829013 | 15.5829013 | 0          |
| 2       | AUCPEP                     | AUC_.Extrap_pred | 7.8849267  | 7.8849267  | 0          |
| 3       | AUCPEP                     | AUC_.Extrap_pred | 3.1831752  | 3.1831752  | 0          |
| 4       | AUCPEP                     | AUC_.Extrap_pred | 3.1803265  | 3.1803265  | 0          |
| 5       | AUCPEP                     | AUC_.Extrap_pred | 9.2630996  | 9.2630996  | 0          |
| 6       | AUCPEP                     | AUC_.Extrap_pred | 5.3023656  | 5.3023656  | 0          |
| 1       | VZP                        | Vz_pred          | 77.5291765 | 77.5291765 | 0          |
| 2       | VZP                        | Vz_pred          | 26.3689077 | 26.3689077 | 0          |

Table 7: Indometh (n=6), Log, IV Infusion (0.25hr) (*continued*)

| Subject | Pharmacokinetic Parameters |                   | Values     |            | Difference |
|---------|----------------------------|-------------------|------------|------------|------------|
|         | PPTTESTCD                  | WNL               | NonCompart | WinNonlin  |            |
| 3       | VZP                        | Vz_pred           | 19.9084941 | 19.9084941 | 0          |
| 4       | VZP                        | Vz_pred           | 23.0793917 | 23.0793917 | 0          |
| 5       | VZP                        | Vz_pred           | 46.7158621 | 46.7158621 | 0          |
| 6       | VZP                        | Vz_pred           | 23.5692251 | 23.5692251 | 0          |
| 1       | CLP                        | Cl_pred           | 12.2744566 | 12.2744566 | 0          |
| 2       | CLP                        | Cl_pred           | 7.9707940  | 7.9707940  | 0          |
| 3       | CLP                        | Cl_pred           | 8.3992473  | 8.3992473  | 0          |
| 4       | CLP                        | Cl_pred           | 9.9028165  | 9.9028165  | 0          |
| 5       | CLP                        | Cl_pred           | 11.8073306 | 11.8073306 | 0          |
| 6       | CLP                        | Cl_pred           | 8.3322048  | 8.3322048  | 0          |
| 1       | AUMCLST                    | AUMClast          | 3.2965543  | 3.2965543  | 0          |
| 2       | AUMCLST                    | AUMClast          | 6.4082620  | 6.4082620  | 0          |
| 3       | AUMCLST                    | AUMClast          | 5.0353383  | 5.0353383  | 0          |
| 4       | AUMCLST                    | AUMClast          | 4.3990453  | 4.3990453  | 0          |
| 5       | AUMCLST                    | AUMClast          | 3.7299741  | 3.7299741  | 0          |
| 6       | AUMCLST                    | AUMClast          | 5.5775672  | 5.5775672  | 0          |
| 1       | AUMCIFO                    | AUMCINF_obs       | 7.8178588  | 7.8178588  | 0          |
| 2       | AUMCIFO                    | AUMCINF_obs       | 9.4010343  | 9.4010343  | 0          |
| 3       | AUMCIFO                    | AUMCINF_obs       | 7.0017667  | 7.0017667  | 0          |
| 4       | AUMCIFO                    | AUMCINF_obs       | 6.0843899  | 6.0843899  | 0          |
| 5       | AUMCIFO                    | AUMCINF_obs       | 6.5683405  | 6.5683405  | 0          |
| 6       | AUMCIFO                    | AUMCINF_obs       | 8.3343579  | 8.3343579  | 0          |
| 1       | AUMCPEO                    | AUMC_.Extrap_obs  | 57.8330281 | 57.8330281 | 0          |
| 2       | AUMCPEO                    | AUMC_.Extrap_obs  | 31.8345005 | 31.8345005 | 0          |
| 3       | AUMCPEO                    | AUMC_.Extrap_obs  | 28.0847466 | 28.0847466 | 0          |
| 4       | AUMCPEO                    | AUMC_.Extrap_obs  | 27.6994849 | 27.6994849 | 0          |
| 5       | AUMCPEO                    | AUMC_.Extrap_obs  | 43.2128382 | 43.2128382 | 0          |
| 6       | AUMCPEO                    | AUMC_.Extrap_obs  | 33.0774222 | 33.0774222 | 0          |
| 1       | AUMCIFP                    | AUMCINF_pred      | 7.8403303  | 7.8403303  | 0          |
| 2       | AUMCIFP                    | AUMCINF_pred      | 9.2048546  | 9.2048546  | 0          |
| 3       | AUMCIFP                    | AUMCINF_pred      | 6.0178784  | 6.0178784  | 0          |
| 4       | AUMCIFP                    | AUMCINF_pred      | 5.2284721  | 5.2284721  | 0          |
| 5       | AUMCIFP                    | AUMCINF_pred      | 6.0750083  | 6.0750083  | 0          |
| 6       | AUMCIFP                    | AUMCINF_pred      | 7.3003307  | 7.3003307  | 0          |
| 1       | AUMCPEP                    | AUMC_.Extrap_pred | 57.9538845 | 57.9538845 | 0          |
| 2       | AUMCPEP                    | AUMC_.Extrap_pred | 30.3817147 | 30.3817147 | 0          |
| 3       | AUMCPEP                    | AUMC_.Extrap_pred | 16.3270188 | 16.3270188 | 0          |
| 4       | AUMCPEP                    | AUMC_.Extrap_pred | 15.8636553 | 15.8636553 | 0          |
| 5       | AUMCPEP                    | AUMC_.Extrap_pred | 38.6013327 | 38.6013327 | 0          |
| 6       | AUMCPEP                    | AUMC_.Extrap_pred | 23.5984312 | 23.5984312 | 0          |
| 1       | MRTIVLST                   | MRTlast           | 1.7923089  | 1.7923089  | 0          |
| 2       | MRTIVLST                   | MRTlast           | 2.0930490  | 2.0930490  | 0          |
| 3       | MRTIVLST                   | MRTlast           | 1.6223430  | 1.6223430  | 0          |
| 4       | MRTIVLST                   | MRTlast           | 1.6747556  | 1.6747556  | 0          |
| 5       | MRTIVLST                   | MRTlast           | 1.8164830  | 1.8164830  | 0          |

Table 7: Indometh (n=6), Log, IV Infusion (0.25hr) (*continued*)

| Subject | Pharmacokinetic Parameters |             | Values     |            | Difference |
|---------|----------------------------|-------------|------------|------------|------------|
|         | Pptestcd                   | WNL         | NonCompart | WinNonlin  |            |
| 6       | MRTIVLST                   | MRTlast     | 1.8380240  | 1.8380240  | 0          |
| 1       | MRTIVIFO                   | MRTINF_obs  | 3.7163591  | 3.7163591  | 0          |
| 2       | MRTIVIFO                   | MRTINF_obs  | 2.8558604  | 2.8558604  | 0          |
| 3       | MRTIVIFO                   | MRTINF_obs  | 2.1547159  | 2.1547159  | 0          |
| 4       | MRTIVIFO                   | MRTINF_obs  | 2.2085200  | 2.2085200  | 0          |
| 5       | MRTIVIFO                   | MRTINF_obs  | 2.9178858  | 2.9178858  | 0          |
| 6       | MRTIVIFO                   | MRTINF_obs  | 2.5670666  | 2.5670666  | 0          |
| 1       | MRTIVIFP                   | MRTINF_pred | 3.7244318  | 3.7244318  | 0          |
| 2       | MRTIVIFP                   | MRTINF_pred | 2.8098000  | 2.8098000  | 0          |
| 3       | MRTIVIFP                   | MRTINF_pred | 1.8968260  | 1.8968260  | 0          |
| 4       | MRTIVIFP                   | MRTINF_pred | 1.9460640  | 1.9460640  | 0          |
| 5       | MRTIVIFP                   | MRTINF_pred | 2.7441853  | 2.7441853  | 0          |
| 6       | MRTIVIFP                   | MRTINF_pred | 2.3081140  | 2.3081140  | 0          |
| 1       | VSSO                       | Vss_obs     | 45.6514707 | 45.6514707 | 0          |
| 2       | VSSO                       | Vss_obs     | 22.6382575 | 22.6382575 | 0          |
| 3       | VSSO                       | Vss_obs     | 17.5389306 | 17.5389306 | 0          |
| 4       | VSSO                       | Vss_obs     | 21.1756058 | 21.1756058 | 0          |
| 5       | VSSO                       | Vss_obs     | 33.7938980 | 33.7938980 | 0          |
| 6       | VSSO                       | Vss_obs     | 20.7295934 | 20.7295934 | 0          |
| 1       | VSSP                       | Vss_pred    | 45.7153760 | 45.7153760 | 0          |
| 2       | VSSP                       | Vss_pred    | 22.3963368 | 22.3963368 | 0          |
| 3       | VSSP                       | Vss_pred    | 15.9319103 | 15.9319103 | 0          |
| 4       | VSSP                       | Vss_pred    | 19.2715146 | 19.2715146 | 0          |
| 5       | VSSP                       | Vss_pred    | 32.4015028 | 32.4015028 | 0          |
| 6       | VSSP                       | Vss_pred    | 19.2316785 | 19.2316785 | 0          |

### A.7 Test 7: Indometh (n=6), Linear, Extravascular

```
table_wres_rres(Wres7, Rres7,
  Caption = 'Indometh (n=6), Linear, Extravascular')
```

Table 8: Indometh (n=6), Linear, Extravascular

| Subject | Pharmacokinetic Parameters |               | Values     |           | Difference |
|---------|----------------------------|---------------|------------|-----------|------------|
|         | Pptestcd                   | WNL           | NonCompart | WinNonlin |            |
| 1       | R2                         | Rsqr          | 0.9970667  | 0.9970667 | 0          |
| 2       | R2                         | Rsqr          | 0.9476691  | 0.9476691 | 0          |
| 3       | R2                         | Rsqr          | 0.8758261  | 0.8758261 | 0          |
| 4       | R2                         | Rsqr          | 0.8671179  | 0.8671179 | 0          |
| 5       | R2                         | Rsqr          | 0.8752442  | 0.8752442 | 0          |
| 6       | R2                         | Rsqr          | 0.9039538  | 0.9039538 | 0          |
| 1       | R2ADJ                      | Rsqr_adjusted | 0.9941335  | 0.9941335 | 0          |
| 2       | R2ADJ                      | Rsqr_adjusted | 0.9401933  | 0.9401933 | 0          |

Table 8: Indometh (n=6), Linear, Extravascular (*continued*)

| Subject | Pharmacokinetic Parameters |                    | Values     |            | Difference |
|---------|----------------------------|--------------------|------------|------------|------------|
|         | PPTTESTCD                  | WNL                | NonCompart | WinNonlin  |            |
| 3       | R2ADJ                      | Rsqr_adjusted      | 0.8603043  | 0.8603043  | 0          |
| 4       | R2ADJ                      | Rsqr_adjusted      | 0.8505077  | 0.8505077  | 0          |
| 5       | R2ADJ                      | Rsqr_adjusted      | 0.8544516  | 0.8544516  | 0          |
| 6       | R2ADJ                      | Rsqr_adjusted      | 0.8902329  | 0.8902329  | 0          |
| 1       | CORRXY                     | Corr_XY            | -0.9985323 | -0.9985323 | 0          |
| 2       | CORRXY                     | Corr_XY            | -0.9734830 | -0.9734830 | 0          |
| 3       | CORRXY                     | Corr_XY            | -0.9358558 | -0.9358558 | 0          |
| 4       | CORRXY                     | Corr_XY            | -0.9311917 | -0.9311917 | 0          |
| 5       | CORRXY                     | Corr_XY            | -0.9355449 | -0.9355449 | 0          |
| 6       | CORRXY                     | Corr_XY            | -0.9507649 | -0.9507649 | 0          |
| 1       | LAMZNPT                    | No_points_lambda_z | 3.0000000  | 3.0000000  | 0          |
| 2       | LAMZNPT                    | No_points_lambda_z | 9.0000000  | 9.0000000  | 0          |
| 3       | LAMZNPT                    | No_points_lambda_z | 10.0000000 | 10.0000000 | 0          |
| 4       | LAMZNPT                    | No_points_lambda_z | 10.0000000 | 10.0000000 | 0          |
| 5       | LAMZNPT                    | No_points_lambda_z | 8.0000000  | 8.0000000  | 0          |
| 6       | LAMZNPT                    | No_points_lambda_z | 9.0000000  | 9.0000000  | 0          |
| 1       | LAMZ                       | Lambda_z           | 0.1583205  | 0.1583205  | 0          |
| 2       | LAMZ                       | Lambda_z           | 0.3022800  | 0.3022800  | 0          |
| 3       | LAMZ                       | Lambda_z           | 0.4218926  | 0.4218926  | 0          |
| 4       | LAMZ                       | Lambda_z           | 0.4290762  | 0.4290762  | 0          |
| 5       | LAMZ                       | Lambda_z           | 0.2527478  | 0.2527478  | 0          |
| 6       | LAMZ                       | Lambda_z           | 0.3535205  | 0.3535205  | 0          |
| 1       | LAMZLL                     | Lambda_z_lower     | 5.0000000  | 5.0000000  | 0          |
| 2       | LAMZLL                     | Lambda_z_lower     | 0.7500000  | 0.7500000  | 0          |
| 3       | LAMZLL                     | Lambda_z_lower     | 0.5000000  | 0.5000000  | 0          |
| 4       | LAMZLL                     | Lambda_z_lower     | 0.5000000  | 0.5000000  | 0          |
| 5       | LAMZLL                     | Lambda_z_lower     | 1.0000000  | 1.0000000  | 0          |
| 6       | LAMZLL                     | Lambda_z_lower     | 0.7500000  | 0.7500000  | 0          |
| 1       | LAMZUL                     | Lambda_z_upper     | 8.0000000  | 8.0000000  | 0          |
| 2       | LAMZUL                     | Lambda_z_upper     | 8.0000000  | 8.0000000  | 0          |
| 3       | LAMZUL                     | Lambda_z_upper     | 8.0000000  | 8.0000000  | 0          |
| 4       | LAMZUL                     | Lambda_z_upper     | 8.0000000  | 8.0000000  | 0          |
| 5       | LAMZUL                     | Lambda_z_upper     | 8.0000000  | 8.0000000  | 0          |
| 6       | LAMZUL                     | Lambda_z_upper     | 8.0000000  | 8.0000000  | 0          |
| 1       | LAMZHL                     | HL_Lambda_z        | 4.3781270  | 4.3781270  | 0          |
| 2       | LAMZHL                     | HL_Lambda_z        | 2.2930632  | 2.2930632  | 0          |
| 3       | LAMZHL                     | HL_Lambda_z        | 1.6429468  | 1.6429468  | 0          |
| 4       | LAMZHL                     | HL_Lambda_z        | 1.6154409  | 1.6154409  | 0          |
| 5       | LAMZHL                     | HL_Lambda_z        | 2.7424461  | 2.7424461  | 0          |
| 6       | LAMZHL                     | HL_Lambda_z        | 1.9606986  | 1.9606986  | 0          |
| 1       | TLAG                       | Tlag               | 0.0000000  | 0.0000000  | 0          |
| 2       | TLAG                       | Tlag               | 0.0000000  | 0.0000000  | 0          |
| 3       | TLAG                       | Tlag               | 0.0000000  | 0.0000000  | 0          |
| 4       | TLAG                       | Tlag               | 0.0000000  | 0.0000000  | 0          |
| 5       | TLAG                       | Tlag               | 0.0000000  | 0.0000000  | 0          |

Table 8: Indometh (n=6), Linear, Extravascular (*continued*)

| Subject | Pharmacokinetic Parameters |            | Values     |           | Difference |
|---------|----------------------------|------------|------------|-----------|------------|
|         | PPTSTCD                    | WNL        | NonCompart | WinNonlin |            |
| 6       | TLAG                       | Tlag       | 0.000000   | 0.000000  | 0          |
| 1       | TMAX                       | Tmax       | 0.250000   | 0.250000  | 0          |
| 2       | TMAX                       | Tmax       | 0.250000   | 0.250000  | 0          |
| 3       | TMAX                       | Tmax       | 0.250000   | 0.250000  | 0          |
| 4       | TMAX                       | Tmax       | 0.250000   | 0.250000  | 0          |
| 5       | TMAX                       | Tmax       | 0.250000   | 0.250000  | 0          |
| 6       | TMAX                       | Tmax       | 0.250000   | 0.250000  | 0          |
| 1       | CMAX                       | Cmax       | 1.500000   | 1.500000  | 0          |
| 2       | CMAX                       | Cmax       | 2.030000   | 2.030000  | 0          |
| 3       | CMAX                       | Cmax       | 2.720000   | 2.720000  | 0          |
| 4       | CMAX                       | Cmax       | 1.850000   | 1.850000  | 0          |
| 5       | CMAX                       | Cmax       | 2.050000   | 2.050000  | 0          |
| 6       | CMAX                       | Cmax       | 2.310000   | 2.310000  | 0          |
| 1       | CMAXD                      | Cmax_D     | 0.060000   | 0.060000  | 0          |
| 2       | CMAXD                      | Cmax_D     | 0.081200   | 0.081200  | 0          |
| 3       | CMAXD                      | Cmax_D     | 0.108800   | 0.108800  | 0          |
| 4       | CMAXD                      | Cmax_D     | 0.074000   | 0.074000  | 0          |
| 5       | CMAXD                      | Cmax_D     | 0.082000   | 0.082000  | 0          |
| 6       | CMAXD                      | Cmax_D     | 0.092400   | 0.092400  | 0          |
| 1       | TLST                       | Tlast      | 8.000000   | 8.000000  | 0          |
| 2       | TLST                       | Tlast      | 8.000000   | 8.000000  | 0          |
| 3       | TLST                       | Tlast      | 8.000000   | 8.000000  | 0          |
| 4       | TLST                       | Tlast      | 8.000000   | 8.000000  | 0          |
| 5       | TLST                       | Tlast      | 8.000000   | 8.000000  | 0          |
| 6       | TLST                       | Tlast      | 8.000000   | 8.000000  | 0          |
| 1       | CLST                       | Clast      | 0.050000   | 0.050000  | 0          |
| 2       | CLST                       | Clast      | 0.080000   | 0.080000  | 0          |
| 3       | CLST                       | Clast      | 0.080000   | 0.080000  | 0          |
| 4       | CLST                       | Clast      | 0.070000   | 0.070000  | 0          |
| 5       | CLST                       | Clast      | 0.060000   | 0.060000  | 0          |
| 6       | CLST                       | Clast      | 0.090000   | 0.090000  | 0          |
| 1       | AUCLST                     | AUClast    | 1.741250   | 1.741250  | 0          |
| 2       | AUCLST                     | AUClast    | 2.932500   | 2.932500  | 0          |
| 3       | AUCLST                     | AUClast    | 2.933750   | 2.933750  | 0          |
| 4       | AUCLST                     | AUClast    | 2.477500   | 2.477500  | 0          |
| 5       | AUCLST                     | AUClast    | 1.953750   | 1.953750  | 0          |
| 6       | AUCLST                     | AUClast    | 2.872500   | 2.872500  | 0          |
| 1       | AUCALL                     | AUCall     | 1.741250   | 1.741250  | 0          |
| 2       | AUCALL                     | AUCall     | 2.932500   | 2.932500  | 0          |
| 3       | AUCALL                     | AUCall     | 2.933750   | 2.933750  | 0          |
| 4       | AUCALL                     | AUCall     | 2.477500   | 2.477500  | 0          |
| 5       | AUCALL                     | AUCall     | 1.953750   | 1.953750  | 0          |
| 6       | AUCALL                     | AUCall     | 2.872500   | 2.872500  | 0          |
| 1       | AUCIFO                     | AUCINF_obs | 2.0570651  | 2.0570651 | 0          |
| 2       | AUCIFO                     | AUCINF_obs | 3.1971553  | 3.1971553 | 0          |

Table 8: Indometh (n=6), Linear, Extravascular (*continued*)

| Subject | Pharmacokinetic Parameters |                  | Values     |            | Difference |
|---------|----------------------------|------------------|------------|------------|------------|
|         | PPTTESTCD                  | WNL              | NonCompart | WinNonlin  |            |
| 3       | AUCIFO                     | AUCINF_obs       | 3.1233717  | 3.1233717  | 0          |
| 4       | AUCIFO                     | AUCINF_obs       | 2.6406412  | 2.6406412  | 0          |
| 5       | AUCIFO                     | AUCINF_obs       | 2.1911408  | 2.1911408  | 0          |
| 6       | AUCIFO                     | AUCINF_obs       | 3.1270821  | 3.1270821  | 0          |
| 1       | AUCIFOD                    | AUCINF_D_obs     | 0.0822826  | 0.0822826  | 0          |
| 2       | AUCIFOD                    | AUCINF_D_obs     | 0.1278862  | 0.1278862  | 0          |
| 3       | AUCIFOD                    | AUCINF_D_obs     | 0.1249349  | 0.1249349  | 0          |
| 4       | AUCIFOD                    | AUCINF_D_obs     | 0.1056256  | 0.1056256  | 0          |
| 5       | AUCIFOD                    | AUCINF_D_obs     | 0.0876456  | 0.0876456  | 0          |
| 6       | AUCIFOD                    | AUCINF_D_obs     | 0.1250833  | 0.1250833  | 0          |
| 1       | AUCPEO                     | AUC_.Extrap_obs  | 15.3527035 | 15.3527035 | 0          |
| 2       | AUCPEO                     | AUC_.Extrap_obs  | 8.2778360  | 8.2778360  | 0          |
| 3       | AUCPEO                     | AUC_.Extrap_obs  | 6.0710577  | 6.0710577  | 0          |
| 4       | AUCPEO                     | AUC_.Extrap_obs  | 6.1780905  | 6.1780905  | 0          |
| 5       | AUCPEO                     | AUC_.Extrap_obs  | 10.8341191 | 10.8341191 | 0          |
| 6       | AUCPEO                     | AUC_.Extrap_obs  | 8.1412032  | 8.1412032  | 0          |
| 1       | VZFO                       | Vz_F_obs         | 76.7635175 | 76.7635175 | 0          |
| 2       | VZFO                       | Vz_F_obs         | 25.8682374 | 25.8682374 | 0          |
| 3       | VZFO                       | Vz_F_obs         | 18.9720552 | 18.9720552 | 0          |
| 4       | VZFO                       | Vz_F_obs         | 22.0646091 | 22.0646091 | 0          |
| 5       | VZFO                       | Vz_F_obs         | 45.1421631 | 45.1421631 | 0          |
| 6       | VZFO                       | Vz_F_obs         | 22.6144534 | 22.6144534 | 0          |
| 1       | CLFO                       | Cl_F_obs         | 12.1532371 | 12.1532371 | 0          |
| 2       | CLFO                       | Cl_F_obs         | 7.8194513  | 7.8194513  | 0          |
| 3       | CLFO                       | Cl_F_obs         | 8.0041706  | 8.0041706  | 0          |
| 4       | CLFO                       | Cl_F_obs         | 9.4673975  | 9.4673975  | 0          |
| 5       | CLFO                       | Cl_F_obs         | 11.4095817 | 11.4095817 | 0          |
| 6       | CLFO                       | Cl_F_obs         | 7.9946733  | 7.9946733  | 0          |
| 1       | AUCIFP                     | AUCINF_pred      | 2.0586347  | 2.0586347  | 0          |
| 2       | AUCIFP                     | AUCINF_pred      | 3.1798068  | 3.1798068  | 0          |
| 3       | AUCIFP                     | AUCINF_pred      | 3.0284958  | 3.0284958  | 0          |
| 4       | AUCIFP                     | AUCINF_pred      | 2.5577884  | 2.5577884  | 0          |
| 5       | AUCIFP                     | AUCINF_pred      | 2.1498803  | 2.1498803  | 0          |
| 6       | AUCIFP                     | AUCINF_pred      | 3.0315925  | 3.0315925  | 0          |
| 1       | AUCIFPD                    | AUCINF_D_pred    | 0.0823454  | 0.0823454  | 0          |
| 2       | AUCIFPD                    | AUCINF_D_pred    | 0.1271923  | 0.1271923  | 0          |
| 3       | AUCIFPD                    | AUCINF_D_pred    | 0.1211398  | 0.1211398  | 0          |
| 4       | AUCIFPD                    | AUCINF_D_pred    | 0.1023115  | 0.1023115  | 0          |
| 5       | AUCIFPD                    | AUCINF_D_pred    | 0.0859952  | 0.0859952  | 0          |
| 6       | AUCIFPD                    | AUCINF_D_pred    | 0.1212637  | 0.1212637  | 0          |
| 1       | AUCPEP                     | AUC_.Extrap_pred | 15.4172443 | 15.4172443 | 0          |
| 2       | AUCPEP                     | AUC_.Extrap_pred | 7.7774164  | 7.7774164  | 0          |
| 3       | AUCPEP                     | AUC_.Extrap_pred | 3.1284787  | 3.1284787  | 0          |
| 4       | AUCPEP                     | AUC_.Extrap_pred | 3.1389787  | 3.1389787  | 0          |
| 5       | AUCPEP                     | AUC_.Extrap_pred | 9.1228460  | 9.1228460  | 0          |

Table 8: Indometh (n=6), Linear, Extravascular (*continued*)

| Subject | Pharmacokinetic Parameters |                   | Values     |            | Difference |
|---------|----------------------------|-------------------|------------|------------|------------|
|         | PPTTESTCD                  | WNL               | NonCompart | WinNonlin  |            |
| 6       | AUCPEP                     | AUC_.Extrap_pred  | 5.2478198  | 5.2478198  | 0          |
| 1       | VZFP                       | Vz_F_pred         | 76.7049878 | 76.7049878 | 0          |
| 2       | VZFP                       | Vz_F_pred         | 26.0093699 | 26.0093699 | 0          |
| 3       | VZFP                       | Vz_F_pred         | 19.5664063 | 19.5664063 | 0          |
| 4       | VZFP                       | Vz_F_pred         | 22.7793336 | 22.7793336 | 0          |
| 5       | VZFP                       | Vz_F_pred         | 46.0085322 | 46.0085322 | 0          |
| 6       | VZFP                       | Vz_F_pred         | 23.3267671 | 23.3267671 | 0          |
| 1       | CLFP                       | Cl_F_pred         | 12.1439707 | 12.1439707 | 0          |
| 2       | CLFP                       | Cl_F_pred         | 7.8621128  | 7.8621128  | 0          |
| 3       | CLFP                       | Cl_F_pred         | 8.2549230  | 8.2549230  | 0          |
| 4       | CLFP                       | Cl_F_pred         | 9.7740688  | 9.7740687  | 0          |
| 5       | CLFP                       | Cl_F_pred         | 11.6285546 | 11.6285546 | 0          |
| 6       | CLFP                       | Cl_F_pred         | 8.2464909  | 8.2464909  | 0          |
| 1       | AUMCLST                    | AUMClast          | 3.2712500  | 3.2712500  | 0          |
| 2       | AUMCLST                    | AUMClast          | 6.3987500  | 6.3987500  | 0          |
| 3       | AUMCLST                    | AUMClast          | 5.0062500  | 5.0062500  | 0          |
| 4       | AUMCLST                    | AUMClast          | 4.3818750  | 4.3818750  | 0          |
| 5       | AUMCLST                    | AUMClast          | 3.7075000  | 3.7075000  | 0          |
| 6       | AUMCLST                    | AUMClast          | 5.5325000  | 5.5325000  | 0          |
| 1       | AUMCIFO                    | AUMCINF_obs       | 7.7925545  | 7.7925545  | 0          |
| 2       | AUMCIFO                    | AUMCINF_obs       | 9.3915223  | 9.3915223  | 0          |
| 3       | AUMCIFO                    | AUMCINF_obs       | 6.9726784  | 6.9726784  | 0          |
| 4       | AUMCIFO                    | AUMCINF_obs       | 6.0672197  | 6.0672197  | 0          |
| 5       | AUMCIFO                    | AUMCINF_obs       | 6.5458663  | 6.5458663  | 0          |
| 6       | AUMCIFO                    | AUMCINF_obs       | 8.2892908  | 8.2892908  | 0          |
| 1       | AUMCPEO                    | AUMC_.Extrap_obs  | 58.0208261 | 58.0208261 | 0          |
| 2       | AUMCPEO                    | AUMC_.Extrap_obs  | 31.8667432 | 31.8667432 | 0          |
| 3       | AUMCPEO                    | AUMC_.Extrap_obs  | 28.2019090 | 28.2019090 | 0          |
| 4       | AUMCPEO                    | AUMC_.Extrap_obs  | 27.7778746 | 27.7778746 | 0          |
| 5       | AUMCPEO                    | AUMC_.Extrap_obs  | 43.3612023 | 43.3612023 | 0          |
| 6       | AUMCPEO                    | AUMC_.Extrap_obs  | 33.2572574 | 33.2572574 | 0          |
| 1       | AUMCIFP                    | AUMCINF_pred      | 7.8150259  | 7.8150259  | 0          |
| 2       | AUMCIFP                    | AUMCINF_pred      | 9.1953427  | 9.1953427  | 0          |
| 3       | AUMCIFP                    | AUMCINF_pred      | 5.9887901  | 5.9887901  | 0          |
| 4       | AUMCIFP                    | AUMCINF_pred      | 5.2113018  | 5.2113018  | 0          |
| 5       | AUMCIFP                    | AUMCINF_pred      | 6.0525342  | 6.0525342  | 0          |
| 6       | AUMCIFP                    | AUMCINF_pred      | 7.2552635  | 7.2552635  | 0          |
| 1       | AUMCPEP                    | AUMC_.Extrap_pred | 58.1415337 | 58.1415337 | 0          |
| 2       | AUMCPEP                    | AUMC_.Extrap_pred | 30.4131425 | 30.4131425 | 0          |
| 3       | AUMCPEP                    | AUMC_.Extrap_pred | 16.4063210 | 16.4063210 | 0          |
| 4       | AUMCPEP                    | AUMC_.Extrap_pred | 15.9159231 | 15.9159230 | 0          |
| 5       | AUMCPEP                    | AUMC_.Extrap_pred | 38.7446663 | 38.7446663 | 0          |
| 6       | AUMCPEP                    | AUMC_.Extrap_pred | 23.7450164 | 23.7450164 | 0          |
| 1       | MRTEVLST                   | MRTlast           | 1.8786791  | 1.8786791  | 0          |
| 2       | MRTEVLST                   | MRTlast           | 2.1820119  | 2.1820119  | 0          |



Table 8: Indometh (n=6), Linear, Extravascular (*continued*)

| Subject | Pharmacokinetic Parameters |             | Values     |           | Difference |
|---------|----------------------------|-------------|------------|-----------|------------|
|         | PPTSTCD                    | WNL         | NonCompart | WinNonlin |            |
| 3       | MRTEVLST                   | MRTlast     | 1.7064337  | 1.7064337 | 0          |
| 4       | MRTEVLST                   | MRTlast     | 1.7686680  | 1.7686680 | 0          |
| 5       | MRTEVLST                   | MRTlast     | 1.8976328  | 1.8976328 | 0          |
| 6       | MRTEVLST                   | MRTlast     | 1.9260226  | 1.9260226 | 0          |
| 1       | MRTEVIFO                   | MRTINF_obs  | 3.7881905  | 3.7881905 | 0          |
| 2       | MRTEVIFO                   | MRTINF_obs  | 2.9374621  | 2.9374621 | 0          |
| 3       | MRTEVIFO                   | MRTINF_obs  | 2.2324203  | 2.2324203 | 0          |
| 4       | MRTEVIFO                   | MRTINF_obs  | 2.2976312  | 2.2976312 | 0          |
| 5       | MRTEVIFO                   | MRTINF_obs  | 2.9874239  | 2.9874239 | 0          |
| 6       | MRTEVIFO                   | MRTINF_obs  | 2.6508069  | 2.6508069 | 0          |
| 1       | MRTEVIFP                   | MRTINF_pred | 3.7962178  | 3.7962178 | 0          |
| 2       | MRTEVIFP                   | MRTINF_pred | 2.8917929  | 2.8917929 | 0          |
| 3       | MRTEVIFP                   | MRTINF_pred | 1.9774801  | 1.9774801 | 0          |
| 4       | MRTEVIFP                   | MRTINF_pred | 2.0374249  | 2.0374249 | 0          |
| 5       | MRTEVIFP                   | MRTINF_pred | 2.8152890  | 2.8152890 | 0          |
| 6       | MRTEVIFP                   | MRTINF_pred | 2.3932186  | 2.3932186 | 0          |

## A.8 Test 8: Indometh (n=6), Log, Extravascular

```
table_wres_rres(Wres8, Rres8,
  Caption = 'Indometh (n=6), Log, Extravascular')
```

Table 9: Indometh (n=6), Log, Extravascular

| Subject | Pharmacokinetic Parameters |               | Values     |            | Difference |
|---------|----------------------------|---------------|------------|------------|------------|
|         | PPTSTCD                    | WNL           | NonCompart | WinNonlin  |            |
| 1       | R2                         | Rsqr          | 0.9970667  | 0.9970667  | 0          |
| 2       | R2                         | Rsqr          | 0.9476691  | 0.9476691  | 0          |
| 3       | R2                         | Rsqr          | 0.8758261  | 0.8758261  | 0          |
| 4       | R2                         | Rsqr          | 0.8671179  | 0.8671179  | 0          |
| 5       | R2                         | Rsqr          | 0.8752442  | 0.8752442  | 0          |
| 6       | R2                         | Rsqr          | 0.9039538  | 0.9039538  | 0          |
| 1       | R2ADJ                      | Rsqr_adjusted | 0.9941335  | 0.9941335  | 0          |
| 2       | R2ADJ                      | Rsqr_adjusted | 0.9401933  | 0.9401933  | 0          |
| 3       | R2ADJ                      | Rsqr_adjusted | 0.8603043  | 0.8603043  | 0          |
| 4       | R2ADJ                      | Rsqr_adjusted | 0.8505077  | 0.8505077  | 0          |
| 5       | R2ADJ                      | Rsqr_adjusted | 0.8544516  | 0.8544516  | 0          |
| 6       | R2ADJ                      | Rsqr_adjusted | 0.8902329  | 0.8902329  | 0          |
| 1       | CORRXY                     | Corr_XY       | -0.9985323 | -0.9985323 | 0          |
| 2       | CORRXY                     | Corr_XY       | -0.9734830 | -0.9734830 | 0          |
| 3       | CORRXY                     | Corr_XY       | -0.9358558 | -0.9358558 | 0          |
| 4       | CORRXY                     | Corr_XY       | -0.9311917 | -0.9311917 | 0          |
| 5       | CORRXY                     | Corr_XY       | -0.9355449 | -0.9355449 | 0          |

Table 9: Indometh (n=6), Log, Extravascular (*continued*)

| Subject | Pharmacokinetic Parameters |                    | Values     |            | Difference |
|---------|----------------------------|--------------------|------------|------------|------------|
|         | PPTTESTCD                  | WNL                | NonCompart | WinNonlin  |            |
| 6       | CORRXY                     | Corr_XY            | -0.9507649 | -0.9507649 | 0          |
| 1       | LAMZNPT                    | No_points_lambda_z | 3.0000000  | 3.0000000  | 0          |
| 2       | LAMZNPT                    | No_points_lambda_z | 9.0000000  | 9.0000000  | 0          |
| 3       | LAMZNPT                    | No_points_lambda_z | 10.0000000 | 10.0000000 | 0          |
| 4       | LAMZNPT                    | No_points_lambda_z | 10.0000000 | 10.0000000 | 0          |
| 5       | LAMZNPT                    | No_points_lambda_z | 8.0000000  | 8.0000000  | 0          |
| 6       | LAMZNPT                    | No_points_lambda_z | 9.0000000  | 9.0000000  | 0          |
| 1       | LAMZ                       | Lambda_z           | 0.1583205  | 0.1583205  | 0          |
| 2       | LAMZ                       | Lambda_z           | 0.3022800  | 0.3022800  | 0          |
| 3       | LAMZ                       | Lambda_z           | 0.4218926  | 0.4218926  | 0          |
| 4       | LAMZ                       | Lambda_z           | 0.4290762  | 0.4290762  | 0          |
| 5       | LAMZ                       | Lambda_z           | 0.2527478  | 0.2527478  | 0          |
| 6       | LAMZ                       | Lambda_z           | 0.3535205  | 0.3535205  | 0          |
| 1       | LAMZLL                     | Lambda_z_lower     | 5.0000000  | 5.0000000  | 0          |
| 2       | LAMZLL                     | Lambda_z_lower     | 0.7500000  | 0.7500000  | 0          |
| 3       | LAMZLL                     | Lambda_z_lower     | 0.5000000  | 0.5000000  | 0          |
| 4       | LAMZLL                     | Lambda_z_lower     | 0.5000000  | 0.5000000  | 0          |
| 5       | LAMZLL                     | Lambda_z_lower     | 1.0000000  | 1.0000000  | 0          |
| 6       | LAMZLL                     | Lambda_z_lower     | 0.7500000  | 0.7500000  | 0          |
| 1       | LAMZUL                     | Lambda_z_upper     | 8.0000000  | 8.0000000  | 0          |
| 2       | LAMZUL                     | Lambda_z_upper     | 8.0000000  | 8.0000000  | 0          |
| 3       | LAMZUL                     | Lambda_z_upper     | 8.0000000  | 8.0000000  | 0          |
| 4       | LAMZUL                     | Lambda_z_upper     | 8.0000000  | 8.0000000  | 0          |
| 5       | LAMZUL                     | Lambda_z_upper     | 8.0000000  | 8.0000000  | 0          |
| 6       | LAMZUL                     | Lambda_z_upper     | 8.0000000  | 8.0000000  | 0          |
| 1       | LAMZHL                     | HL_Lambda_z        | 4.3781270  | 4.3781270  | 0          |
| 2       | LAMZHL                     | HL_Lambda_z        | 2.2930632  | 2.2930632  | 0          |
| 3       | LAMZHL                     | HL_Lambda_z        | 1.6429468  | 1.6429468  | 0          |
| 4       | LAMZHL                     | HL_Lambda_z        | 1.6154409  | 1.6154409  | 0          |
| 5       | LAMZHL                     | HL_Lambda_z        | 2.7424461  | 2.7424461  | 0          |
| 6       | LAMZHL                     | HL_Lambda_z        | 1.9606986  | 1.9606986  | 0          |
| 1       | TLAG                       | Tlag               | 0.0000000  | 0.0000000  | 0          |
| 2       | TLAG                       | Tlag               | 0.0000000  | 0.0000000  | 0          |
| 3       | TLAG                       | Tlag               | 0.0000000  | 0.0000000  | 0          |
| 4       | TLAG                       | Tlag               | 0.0000000  | 0.0000000  | 0          |
| 5       | TLAG                       | Tlag               | 0.0000000  | 0.0000000  | 0          |
| 6       | TLAG                       | Tlag               | 0.0000000  | 0.0000000  | 0          |
| 1       | TMAX                       | Tmax               | 0.2500000  | 0.2500000  | 0          |
| 2       | TMAX                       | Tmax               | 0.2500000  | 0.2500000  | 0          |
| 3       | TMAX                       | Tmax               | 0.2500000  | 0.2500000  | 0          |
| 4       | TMAX                       | Tmax               | 0.2500000  | 0.2500000  | 0          |
| 5       | TMAX                       | Tmax               | 0.2500000  | 0.2500000  | 0          |
| 6       | TMAX                       | Tmax               | 0.2500000  | 0.2500000  | 0          |
| 1       | CMAX                       | Cmax               | 1.5000000  | 1.5000000  | 0          |
| 2       | CMAX                       | Cmax               | 2.0300000  | 2.0300000  | 0          |

Table 9: Indometh (n=6), Log, Extravascular (*continued*)

| Subject | Pharmacokinetic Parameters |              | Values     |           | Difference |
|---------|----------------------------|--------------|------------|-----------|------------|
|         | PPTSTCD                    | WNL          | NonCompart | WinNonlin |            |
| 3       | CMAx                       | Cmax         | 2.7200000  | 2.7200000 | 0          |
| 4       | CMAx                       | Cmax         | 1.8500000  | 1.8500000 | 0          |
| 5       | CMAx                       | Cmax         | 2.0500000  | 2.0500000 | 0          |
| 6       | CMAx                       | Cmax         | 2.3100000  | 2.3100000 | 0          |
| 1       | CMAxD                      | Cmax_D       | 0.0600000  | 0.0600000 | 0          |
| 2       | CMAxD                      | Cmax_D       | 0.0812000  | 0.0812000 | 0          |
| 3       | CMAxD                      | Cmax_D       | 0.1088000  | 0.1088000 | 0          |
| 4       | CMAxD                      | Cmax_D       | 0.0740000  | 0.0740000 | 0          |
| 5       | CMAxD                      | Cmax_D       | 0.0820000  | 0.0820000 | 0          |
| 6       | CMAxD                      | Cmax_D       | 0.0924000  | 0.0924000 | 0          |
| 1       | TLST                       | Tlast        | 8.0000000  | 8.0000000 | 0          |
| 2       | TLST                       | Tlast        | 8.0000000  | 8.0000000 | 0          |
| 3       | TLST                       | Tlast        | 8.0000000  | 8.0000000 | 0          |
| 4       | TLST                       | Tlast        | 8.0000000  | 8.0000000 | 0          |
| 5       | TLST                       | Tlast        | 8.0000000  | 8.0000000 | 0          |
| 6       | TLST                       | Tlast        | 8.0000000  | 8.0000000 | 0          |
| 1       | CLST                       | Clast        | 0.0500000  | 0.0500000 | 0          |
| 2       | CLST                       | Clast        | 0.0800000  | 0.0800000 | 0          |
| 3       | CLST                       | Clast        | 0.0800000  | 0.0800000 | 0          |
| 4       | CLST                       | Clast        | 0.0700000  | 0.0700000 | 0          |
| 5       | CLST                       | Clast        | 0.0600000  | 0.0600000 | 0          |
| 6       | CLST                       | Clast        | 0.0900000  | 0.0900000 | 0          |
| 1       | AUCLST                     | AUClast      | 1.7193653  | 1.7193653 | 0          |
| 2       | AUCLST                     | AUClast      | 2.8891436  | 2.8891436 | 0          |
| 3       | AUCLST                     | AUClast      | 2.8817113  | 2.8817113 | 0          |
| 4       | AUCLST                     | AUClast      | 2.4442459  | 2.4442459 | 0          |
| 5       | AUCLST                     | AUClast      | 1.9211984  | 1.9211984 | 0          |
| 6       | AUCLST                     | AUClast      | 2.8413138  | 2.8413138 | 0          |
| 1       | AUCALL                     | AUCall       | 1.7193653  | 1.7193653 | 0          |
| 2       | AUCALL                     | AUCall       | 2.8891436  | 2.8891436 | 0          |
| 3       | AUCALL                     | AUCall       | 2.8817113  | 2.8817113 | 0          |
| 4       | AUCALL                     | AUCall       | 2.4442459  | 2.4442459 | 0          |
| 5       | AUCALL                     | AUCall       | 1.9211984  | 1.9211984 | 0          |
| 6       | AUCALL                     | AUCall       | 2.8413138  | 2.8413138 | 0          |
| 1       | AUCIFO                     | AUCINF_obs   | 2.0351804  | 2.0351804 | 0          |
| 2       | AUCIFO                     | AUCINF_obs   | 3.1537989  | 3.1537989 | 0          |
| 3       | AUCIFO                     | AUCINF_obs   | 3.0713330  | 3.0713330 | 0          |
| 4       | AUCIFO                     | AUCINF_obs   | 2.6073871  | 2.6073871 | 0          |
| 5       | AUCIFO                     | AUCINF_obs   | 2.1585892  | 2.1585892 | 0          |
| 6       | AUCIFO                     | AUCINF_obs   | 3.0958959  | 3.0958959 | 0          |
| 1       | AUCIFOD                    | AUCINF_D_obs | 0.0814072  | 0.0814072 | 0          |
| 2       | AUCIFOD                    | AUCINF_D_obs | 0.1261520  | 0.1261520 | 0          |
| 3       | AUCIFOD                    | AUCINF_D_obs | 0.1228533  | 0.1228533 | 0          |
| 4       | AUCIFOD                    | AUCINF_D_obs | 0.1042955  | 0.1042955 | 0          |
| 5       | AUCIFOD                    | AUCINF_D_obs | 0.0863436  | 0.0863436 | 0          |

Table 9: Indometh (n=6), Log, Extravascular (*continued*)

| Subject | Pharmacokinetic Parameters |                  | Values     |            | Difference |
|---------|----------------------------|------------------|------------|------------|------------|
|         | PPTTESTCD                  | WNL              | NonCompart | WinNonlin  |            |
| 6       | AUCIFOD                    | AUCINF_D_obs     | 0.1238358  | 0.1238358  | 0          |
| 1       | AUCPEO                     | AUC_.Extrap_obs  | 15.5177942 | 15.5177942 | 0          |
| 2       | AUCPEO                     | AUC_.Extrap_obs  | 8.3916343  | 8.3916343  | 0          |
| 3       | AUCPEO                     | AUC_.Extrap_obs  | 6.1739217  | 6.1739217  | 0          |
| 4       | AUCPEO                     | AUC_.Extrap_obs  | 6.2568848  | 6.2568848  | 0          |
| 5       | AUCPEO                     | AUC_.Extrap_obs  | 10.9974979 | 10.9974979 | 0          |
| 6       | AUCPEO                     | AUC_.Extrap_obs  | 8.2232127  | 8.2232127  | 0          |
| 1       | VZFO                       | Vz_F_obs         | 77.5889712 | 77.5889712 | 0          |
| 2       | VZFO                       | Vz_F_obs         | 26.2238573 | 26.2238573 | 0          |
| 3       | VZFO                       | Vz_F_obs         | 19.2935053 | 19.2935053 | 0          |
| 4       | VZFO                       | Vz_F_obs         | 22.3460171 | 22.3460171 | 0          |
| 5       | VZFO                       | Vz_F_obs         | 45.8229078 | 45.8229078 | 0          |
| 6       | VZFO                       | Vz_F_obs         | 22.8422576 | 22.8422576 | 0          |
| 1       | CLFO                       | Cl_F_obs         | 12.2839234 | 12.2839234 | 0          |
| 2       | CLFO                       | Cl_F_obs         | 7.9269481  | 7.9269481  | 0          |
| 3       | CLFO                       | Cl_F_obs         | 8.1397881  | 8.1397881  | 0          |
| 4       | CLFO                       | Cl_F_obs         | 9.5881430  | 9.5881430  | 0          |
| 5       | CLFO                       | Cl_F_obs         | 11.5816384 | 11.5816384 | 0          |
| 6       | CLFO                       | Cl_F_obs         | 8.0752068  | 8.0752068  | 0          |
| 1       | AUCIFP                     | AUCINF_pred      | 2.0367500  | 2.0367500  | 0          |
| 2       | AUCIFP                     | AUCINF_pred      | 3.1364504  | 3.1364504  | 0          |
| 3       | AUCIFP                     | AUCINF_pred      | 2.9764572  | 2.9764572  | 0          |
| 4       | AUCIFP                     | AUCINF_pred      | 2.5245343  | 2.5245343  | 0          |
| 5       | AUCIFP                     | AUCINF_pred      | 2.1173287  | 2.1173287  | 0          |
| 6       | AUCIFP                     | AUCINF_pred      | 3.0004063  | 3.0004063  | 0          |
| 1       | AUCIFPD                    | AUCINF_D_pred    | 0.0814700  | 0.0814700  | 0          |
| 2       | AUCIFPD                    | AUCINF_D_pred    | 0.1254580  | 0.1254580  | 0          |
| 3       | AUCIFPD                    | AUCINF_D_pred    | 0.1190583  | 0.1190583  | 0          |
| 4       | AUCIFPD                    | AUCINF_D_pred    | 0.1009814  | 0.1009814  | 0          |
| 5       | AUCIFPD                    | AUCINF_D_pred    | 0.0846931  | 0.0846931  | 0          |
| 6       | AUCIFPD                    | AUCINF_D_pred    | 0.1200163  | 0.1200163  | 0          |
| 1       | AUCPEP                     | AUC_.Extrap_pred | 15.5829013 | 15.5829013 | 0          |
| 2       | AUCPEP                     | AUC_.Extrap_pred | 7.8849267  | 7.8849267  | 0          |
| 3       | AUCPEP                     | AUC_.Extrap_pred | 3.1831752  | 3.1831752  | 0          |
| 4       | AUCPEP                     | AUC_.Extrap_pred | 3.1803265  | 3.1803265  | 0          |
| 5       | AUCPEP                     | AUC_.Extrap_pred | 9.2630996  | 9.2630996  | 0          |
| 6       | AUCPEP                     | AUC_.Extrap_pred | 5.3023656  | 5.3023656  | 0          |
| 1       | VZFP                       | Vz_F_pred        | 77.5291765 | 77.5291765 | 0          |
| 2       | VZFP                       | Vz_F_pred        | 26.3689077 | 26.3689077 | 0          |
| 3       | VZFP                       | Vz_F_pred        | 19.9084941 | 19.9084941 | 0          |
| 4       | VZFP                       | Vz_F_pred        | 23.0793917 | 23.0793917 | 0          |
| 5       | VZFP                       | Vz_F_pred        | 46.7158621 | 46.7158621 | 0          |
| 6       | VZFP                       | Vz_F_pred        | 23.5692251 | 23.5692252 | 0          |
| 1       | CLFP                       | Cl_F_pred        | 12.2744566 | 12.2744566 | 0          |
| 2       | CLFP                       | Cl_F_pred        | 7.9707940  | 7.9707940  | 0          |

Table 9: Indometh (n=6), Log, Extravascular (*continued*)

| Subject | Pharmacokinetic Parameters |                   | Values     |            | Difference |
|---------|----------------------------|-------------------|------------|------------|------------|
|         | PPTTESTCD                  | WNL               | NonCompart | WinNonlin  |            |
| 3       | CLFP                       | Cl_F_pred         | 8.3992473  | 8.3992473  | 0          |
| 4       | CLFP                       | Cl_F_pred         | 9.9028165  | 9.9028165  | 0          |
| 5       | CLFP                       | Cl_F_pred         | 11.8073306 | 11.8073306 | 0          |
| 6       | CLFP                       | Cl_F_pred         | 8.3322048  | 8.3322048  | 0          |
| 1       | AUMCLST                    | AUMClast          | 3.2965543  | 3.2965543  | 0          |
| 2       | AUMCLST                    | AUMClast          | 6.4082620  | 6.4082620  | 0          |
| 3       | AUMCLST                    | AUMClast          | 5.0353383  | 5.0353382  | 0          |
| 4       | AUMCLST                    | AUMClast          | 4.3990453  | 4.3990453  | 0          |
| 5       | AUMCLST                    | AUMClast          | 3.7299741  | 3.7299741  | 0          |
| 6       | AUMCLST                    | AUMClast          | 5.5775672  | 5.5775672  | 0          |
| 1       | AUMCIFO                    | AUMCINF_obs       | 7.8178588  | 7.8178588  | 0          |
| 2       | AUMCIFO                    | AUMCINF_obs       | 9.4010343  | 9.4010343  | 0          |
| 3       | AUMCIFO                    | AUMCINF_obs       | 7.0017667  | 7.0017667  | 0          |
| 4       | AUMCIFO                    | AUMCINF_obs       | 6.0843899  | 6.0843899  | 0          |
| 5       | AUMCIFO                    | AUMCINF_obs       | 6.5683405  | 6.5683405  | 0          |
| 6       | AUMCIFO                    | AUMCINF_obs       | 8.3343579  | 8.3343579  | 0          |
| 1       | AUMCPEO                    | AUMC_.Extrap_obs  | 57.8330281 | 57.8330281 | 0          |
| 2       | AUMCPEO                    | AUMC_.Extrap_obs  | 31.8345005 | 31.8345005 | 0          |
| 3       | AUMCPEO                    | AUMC_.Extrap_obs  | 28.0847466 | 28.0847466 | 0          |
| 4       | AUMCPEO                    | AUMC_.Extrap_obs  | 27.6994849 | 27.6994849 | 0          |
| 5       | AUMCPEO                    | AUMC_.Extrap_obs  | 43.2128382 | 43.2128382 | 0          |
| 6       | AUMCPEO                    | AUMC_.Extrap_obs  | 33.0774222 | 33.0774222 | 0          |
| 1       | AUMCIFP                    | AUMCINF_pred      | 7.8403303  | 7.8403303  | 0          |
| 2       | AUMCIFP                    | AUMCINF_pred      | 9.2048546  | 9.2048546  | 0          |
| 3       | AUMCIFP                    | AUMCINF_pred      | 6.0178784  | 6.0178784  | 0          |
| 4       | AUMCIFP                    | AUMCINF_pred      | 5.2284721  | 5.2284721  | 0          |
| 5       | AUMCIFP                    | AUMCINF_pred      | 6.0750083  | 6.0750083  | 0          |
| 6       | AUMCIFP                    | AUMCINF_pred      | 7.3003307  | 7.3003307  | 0          |
| 1       | AUMCPEP                    | AUMC_.Extrap_pred | 57.9538845 | 57.9538845 | 0          |
| 2       | AUMCPEP                    | AUMC_.Extrap_pred | 30.3817147 | 30.3817147 | 0          |
| 3       | AUMCPEP                    | AUMC_.Extrap_pred | 16.3270188 | 16.3270188 | 0          |
| 4       | AUMCPEP                    | AUMC_.Extrap_pred | 15.8636553 | 15.8636553 | 0          |
| 5       | AUMCPEP                    | AUMC_.Extrap_pred | 38.6013327 | 38.6013327 | 0          |
| 6       | AUMCPEP                    | AUMC_.Extrap_pred | 23.5984312 | 23.5984312 | 0          |
| 1       | MRTEVLST                   | MRTlast           | 1.9173089  | 1.9173089  | 0          |
| 2       | MRTEVLST                   | MRTlast           | 2.2180490  | 2.2180490  | 0          |
| 3       | MRTEVLST                   | MRTlast           | 1.7473430  | 1.7473430  | 0          |
| 4       | MRTEVLST                   | MRTlast           | 1.7997556  | 1.7997556  | 0          |
| 5       | MRTEVLST                   | MRTlast           | 1.9414830  | 1.9414830  | 0          |
| 6       | MRTEVLST                   | MRTlast           | 1.9630240  | 1.9630240  | 0          |
| 1       | MRTEVIFO                   | MRTINF_obs        | 3.8413591  | 3.8413591  | 0          |
| 2       | MRTEVIFO                   | MRTINF_obs        | 2.9808604  | 2.9808604  | 0          |
| 3       | MRTEVIFO                   | MRTINF_obs        | 2.2797159  | 2.2797159  | 0          |
| 4       | MRTEVIFO                   | MRTINF_obs        | 2.3335200  | 2.3335200  | 0          |
| 5       | MRTEVIFO                   | MRTINF_obs        | 3.0428858  | 3.0428858  | 0          |

Table 9: Indometh (n=6), Log, Extravascular (*continued*)

| Subject | Pharmacokinetic Parameters |             | Values     |           | Difference |
|---------|----------------------------|-------------|------------|-----------|------------|
|         | PPTESTCD                   | WNL         | NonCompart | WinNonlin |            |
| 6       | MRTEVIFO                   | MRTINF_obs  | 2.6920666  | 2.6920666 | 0          |
| 1       | MRTEVIFP                   | MRTINF_pred | 3.8494318  | 3.8494318 | 0          |
| 2       | MRTEVIFP                   | MRTINF_pred | 2.9348000  | 2.9348000 | 0          |
| 3       | MRTEVIFP                   | MRTINF_pred | 2.0218260  | 2.0218260 | 0          |
| 4       | MRTEVIFP                   | MRTINF_pred | 2.0710640  | 2.0710640 | 0          |
| 5       | MRTEVIFP                   | MRTINF_pred | 2.8691853  | 2.8691853 | 0          |
| 6       | MRTEVIFP                   | MRTINF_pred | 2.4331140  | 2.4331140 | 0          |

## B Session Information

```
devtools::session_info()
```

```
## setting value
## version R version 3.5.0 (2018-04-23)
## system x86_64, mingw32
## ui RTerm
## language (EN)
## collate Korean_Korea.949
## tz Asia/Seoul
## date 2018-05-11
##
## package * version date source
## assertthat 0.2.0 2017-04-11 CRAN (R 3.4.0)
## backports 1.1.2 2017-12-13 CRAN (R 3.5.0)
## base * 3.5.0 2018-04-23 local
## bindr 0.1.1 2018-03-13 CRAN (R 3.4.3)
## bindrcpp * 0.2.2 2018-03-29 CRAN (R 3.5.0)
## bookdown 0.7 2018-02-18 CRAN (R 3.4.3)
## colorspace 1.3-2 2016-12-14 CRAN (R 3.5.0)
## compiler 3.5.0 2018-04-23 local
## datasets * 3.5.0 2018-04-23 local
## devtools 1.13.5 2018-02-18 CRAN (R 3.5.0)
## digest 0.6.15 2018-01-28 CRAN (R 3.5.0)
## dplyr * 0.7.4 2017-09-28 CRAN (R 3.5.0)
## evaluate 0.10.1 2017-06-24 CRAN (R 3.4.1)
## glue 1.2.0 2017-10-29 CRAN (R 3.5.0)
## graphics * 3.5.0 2018-04-23 local
## grDevices * 3.5.0 2018-04-23 local
## highr 0.6 2016-05-09 CRAN (R 3.4.0)
## hms 0.4.2 2018-03-10 CRAN (R 3.4.3)
## htmltools 0.3.6 2017-04-28 CRAN (R 3.5.0)
## httr 1.3.1 2017-08-20 CRAN (R 3.4.1)
## kableExtra * 0.8.0 2018-04-05 CRAN (R 3.4.4)
## knitr * 1.20 2018-02-20 CRAN (R 3.4.3)
## magrittr 1.5 2014-11-22 CRAN (R 3.4.0)
## memoise 1.1.0 2017-04-21 CRAN (R 3.4.0)
```

```
## methods      * 3.5.0    2018-04-23 local
## munsell       0.4.3    2016-02-13 CRAN (R 3.4.0)
## NonCompart   * 0.4.2    2018-05-11 CRAN (R 3.4.4)
## pillar       1.2.2    2018-04-26 CRAN (R 3.5.0)
## pkgconfig    2.0.1    2017-03-21 CRAN (R 3.4.0)
## plyr         1.8.4    2016-06-08 CRAN (R 3.5.0)
## purrr        0.2.4    2017-10-18 CRAN (R 3.5.0)
## R6           2.2.2    2017-06-17 CRAN (R 3.4.1)
## Rcpp         0.12.16  2018-03-13 CRAN (R 3.5.0)
## readr        1.1.1    2017-05-16 CRAN (R 3.5.0)
## rlang        0.2.0    2018-02-20 CRAN (R 3.5.0)
## rmarkdown    1.9      2018-03-01 CRAN (R 3.4.3)
## rprojroot    1.3-2    2018-01-03 CRAN (R 3.4.3)
## rstudioapi   0.7      2017-09-07 CRAN (R 3.4.1)
## rvest        0.3.2    2016-06-17 CRAN (R 3.4.0)
## scales       0.5.0    2017-08-24 CRAN (R 3.5.0)
## stats        * 3.5.0    2018-04-23 local
## stringi      1.2.2    2018-05-02 CRAN (R 3.5.0)
## stringr      1.3.1    2018-05-10 CRAN (R 3.5.0)
## tibble       1.4.2    2018-01-22 CRAN (R 3.5.0)
## tidyr        * 0.8.0    2018-01-29 CRAN (R 3.5.0)
## tidyselect   0.2.4    2018-02-26 CRAN (R 3.5.0)
## tools        3.5.0    2018-04-23 local
## utils        * 3.5.0    2018-04-23 local
## viridisLite  0.3.0    2018-02-01 CRAN (R 3.4.3)
## withr        2.1.2    2018-03-15 CRAN (R 3.4.4)
## xfun         0.1      2018-01-22 CRAN (R 3.4.3)
## xml2         1.2.0    2018-01-24 CRAN (R 3.5.0)
## yaml         2.1.19   2018-05-01 CRAN (R 3.5.0)
```

## References

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- Kim, Hyungsub, Sungpil Han, Yong-Soon Cho, Seok-Kyu Yoon, and Kyun-Seop Bae. 2018. “Development of R Packages: ‘NonCompart’ and ‘Ncar’ for Noncompartmental Analysis (Nca).” *Translational and Clinical Pharmacology* 26 (1). Korean Society for Clinical Pharmacology; Therapeutics (KAMJE):10–15. <http://www.tcpharm.org/Data/Journal/2/358.pdf>.