MetidaNCA validation report

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2024-07-17

Contents

1 Introduction and package description

This is Non-compartment anlysis software. The package is designed for batch processing of pharmacokinetic data.

See documentation:

- Dev: https://pharmcat.github.io/MetidaNCA.jl/dev/
- Stable: https://pharmcat.github.io/MetidaNCA.jl/stable/

1.1 Validation purpose

The main validation purpose is confirmation by examination and provision of objective evidence that software specifications conform to user needs and intended uses, and that the particular requirements implemented through software can be consistently fulfilled.

1.2 Requirements

- Julia 1.6 (or higher) installed for Operating System/OS Version/Architecture in Tier 1 list

Tier 1: Julia is guaranteed to build from source and pass all tests on these platforms when built with the default options. Official binaries are always available and CI is run on every commit to ensure support is actively maintained.

1.3 Developer software life cycle

- Development stage
- Testing procedures development
- Performing testing procedures on local machine
- Push to development branch
- Make pull request to main branch
- Performing testing procedures with GitHub Actions
- Make pull request to the official registry of general Julia packages (if nessesary)
- Make release (if previous completed)

1.3.1 Versions

- X.Y.Z - patch release (no breaking changes)
- X.Y.0 - minor release (may include breaking changes if X = 0)
- X.0.0 - major release (breaking changes, changes in public API)
- 0.#.# - no stable public API
- 1.#.# or higher - stable public API

1.4 Build support

1.4.1 Tier 1

- julia-version: 1.6, 1.7, 1.8
- julia-arch: x64
- os: ubuntu-latest, macOS-latest, windows-latest

2 Installation

2.1 System information

- Julia version: v“1.8.5”
- Current machine: “x86_64-linux-gnu”

2.2 Installation method

MetidaNCA.jl can be installed by executing the following command in REPL:

```
import Pkg; Pkg.add("MetidaNCA")
```

2.3 Version check

The installation process is checking within each testing job via GitHub Actions. Also GitHub Action chek performed before merging into JuliaRegistries/General repository (see Automatic merging of pull requests).

Current package version: “0.5.11”

3 Operation qualification

This part of validation based on testing procedures entails running software products under known conditions with defined inputs and documented outcomes that can be compared to their predefined expectations. All documented public API included in testing procedures and part of critical internal methods. Testing procedures can be found in `test` directory.

3.1 Coverage

Code coverage report available on Codecov.io. Test procedures include all public API methods check.

- Coverage goal: >= 90.0%

3.2 Data

Validation data available in the repository and included in the package. See Appendix 1.

3.3 Testing results

```
Pkg.test("MetidaNCA")
```

4 Performance qualification

Purpose of this testing procedures to demonstrate performance for some critical tasks. Results from MetidaNCA compared with Phoenix WinNonlin 8.0 results, see Appendix 2.

4.1 Parameter's names description

Table 1: Parameter description

Name	Description
Cmax	Maximum concentration
Tmax	Time at Cmax
Cdose	Concentration at dose time
Clast	Last non-zero concentration
AUClast	AUC to Clast
AUMClast	AUMC to Clast
AUCall	AUC with all values
Rsq	r square
ARsq	Adjusted r square
Kel	Terminal elimination constant
HL	Half live or T1/2
LZint	Intercept
Clast_pred	Predicted Clast
AUCinf	AUC extrapolated to infinity
AUCpct	Percentage AUClast from AUCinf
MRTlast	Mean Residence Time (last)
MRTinf	Mean Residence Time (inf)
Clinf	Clearence
Vzinf	Volume of distribution
AUCtau	AUC in Tau range
AUMCtau	AUMC in Tau range
MRTtauinf	MRT based on Tau
Cltau	Clearence in Tau range
Vztau	Volume of distribution in Tau range

4.2 Output example

Import data:

```
pkdata2  = CSV.File(
joinpath(dirname(pathof(MetidaNCA)), "..", "test", "csv", "pkdata2.csv")
) |> DataFrame
ds = pkimport(pkdata2, :Time, :Concentration, [:Subject, :Formulation];
dosetime = DoseTime(dose = 100, time = 0))
sort!(ds, :Subject)
```

Execute NCA:

```
MetidaNCA.nca!(ds[1], adm = :ev, calcm = :lint, verbose = 1)
```

```
 Non-compartmental Pharmacokinetic Analysis
   Subject: Subject => 1; Formulation => T;
   Settings:
   Method: lint; Dose: 100; Dose time: 0
------ ------- ------- -------- ---------- ---------- ------
 Time   Conc.     AUC      AUC        AUMC        AUMC   Info
                         (cum.)                 (cum.)
------ ------- ------- -------- ---------- ---------- ------
    0       0       0        0          0          0      D
  0.5   178.9   44.74    44.74      22.37      22.37
    1   190.9   92.45    137.2      70.09      92.45
  1.5   164.9   88.95    226.1      109.6        202
    2     140   76.22    302.4      131.8      333.8
  2.5   129.6   67.39    369.8        151      484.8
    3   131.4   65.24      435      179.5      664.3
    4   150.9   141.1    576.1      498.8       1163
    5   121.2     136    712.1      604.8       1768
    6   139.2   130.2    842.4      720.8       2489
    8   128.5   267.7     1110       1864       4352
   10   143.2   271.8     1382       2461       6813      E
   12     145   288.2     1670       3172       9985      E
   24   133.2    1669     3339   2.961e+04   3.96e+04      E
   48   137.3    3245     6584   1.174e+05   1.57e+05      E
   72   112.8    3001     9585   1.766e+05   3.336e+05     E
------ ------- ------- -------- ---------- ---------- ------

   Cdose: 0.0, Dose time: 0
   Kel start: 10.0; end: 72.0

 PK/PD subject NCA result
------------ -------------
   Parameter         Value
------------ -------------
        Rsqn           3.0
      Vzlast       3.08222
        Tmax           1.0
```

ARsq	0.714769
AUClast	9585.42
MRTinf	293.162
AUCinf_pred	44242.6
LZ	-0.00338474
LZint	5.00849
Obsnum	16.0
Clast	112.846
Dose	100.0
Tlag	0.0
Cdose	0.0
Vssinf	0.682964
AUCall	9585.42

---------- ----------

15 rows omitted

4.3 Results

4.3.1 Linear-trapezoidal rule; Extravascular; Dosetime 0.0; No Tau; Dose 100

Code:

```
nca!(ds, adm = :ev, calcm = :lint)
```

Table 2: Plasma data results, Linear-trapezoidal rule, Extravascular

Parameter	Subject	Value	Reference	Difference
$Cmax$	1	190.869	190.869	0.0
$Cmax$	2	261.177	261.177	0.0
$Cmax$	3	105.345	105.345	0.0
$Cmax$	4	208.542	208.542	0.0
$Cmax$	5	169.334	169.334	0.0
$Cmax$	6	154.648	154.648	0.0
$Cmax$	7	153.254	153.254	0.0
$Cmax$	8	138.327	138.327	0.0
$Cmax$	9	167.347	167.347	0.0
$Cmax$	10	125.482	125.482	0.0
$Tmax$	1	1.0	1.0	0.0
$Tmax$	2	1.0	1.0	0.0
$Tmax$	3	1.5	1.5	0.0
$Tmax$	4	1.0	1.0	0.0
$Tmax$	5	4.0	4.0	0.0
$Tmax$	6	2.5	2.5	0.0
$Tmax$	7	2.5	2.5	0.0
$Tmax$	8	4.0	4.0	0.0
$Tmax$	9	3.0	3.0	0.0
$Tmax$	10	2.0	2.0	0.0
$Cdose$	1	0.0	0.0	0.0
$Cdose$	2	0.0	0.0	0.0
$Cdose$	3	0.0	0.0	0.0
$Cdose$	4	0.0	0.0	0.0
$Cdose$	5	0.0	0.0	0.0
$Cdose$	6	0.0	0.0	0.0
$Cdose$	7	0.0	0.0	0.0
$Cdose$	8	0.0	0.0	0.0
$Cdose$	9	0.0	0.0	0.0
$Cdose$	10	0.0	0.0	0.0
$Clast$	1	112.846	112.846	0.0
$Clast$	2	85.241	85.241	0.0
$Clast$	3	67.901	67.901	0.0
$Clast$	4	97.625	97.625	0.0
$Clast$	5	110.778	110.778	0.0
$Clast$	6	69.501	69.501	0.0
$Clast$	7	58.051	58.051	0.0
$Clast$	8	74.437	74.437	0.0

Parameter	Subject	Value	Reference	Difference
$Clast$	9	93.44	93.44	0.0
$Clast$	10	42.191	42.191	0.0
$AUClast$	1	9585.42	9585.42	0.0
$AUClast$	2	10112.2	10112.2	0.0
$AUClast$	3	5396.55	5396.55	0.0
$AUClast$	4	9317.84	9317.84	0.0
$AUClast$	5	9561.26	9561.26	0.0
$AUClast$	6	6966.6	6966.6	0.0
$AUClast$	7	7029.57	7029.57	0.0
$AUClast$	8	7110.67	7110.67	0.0
$AUClast$	9	8315.08	8315.08	0.0
$AUClast$	10	5620.89	5620.89	0.0
$AUMClast$	1	333582.0	333582.0	0.0
$AUMClast$	2	298701.0	298701.0	0.0
$AUMClast$	3	186032.0	186032.0	0.0
$AUMClast$	4	313956.0	313956.0	0.0
$AUMClast$	5	315182.0	315182.0	0.0
$AUMClast$	6	226977.0	226977.0	0.0
$AUMClast$	7	219798.0	219798.0	0.0
$AUMClast$	8	240526.0	240526.0	0.0
$AUMClast$	9	277614.0	277614.0	0.0
$AUMClast$	10	154893.0	154893.0	0.0
$AUCall$	1	9585.42	9585.42	0.0
$AUCall$	2	10112.2	10112.2	0.0
$AUCall$	3	5396.55	5396.55	0.0
$AUCall$	4	9317.84	9317.84	0.0
$AUCall$	5	9561.26	9561.26	0.0
$AUCall$	6	6966.6	6966.6	0.0
$AUCall$	7	7029.57	7029.57	0.0
$AUCall$	8	7110.67	7110.67	0.0
$AUCall$	9	8315.08	8315.08	0.0
$AUCall$	10	5620.89	5620.89	0.0
Rsq	1	0.786077	0.786077	0.0
Rsq	2	0.992764	0.992764	0.0
Rsq	3	0.813589	0.813589	0.0
Rsq	4	0.918859	0.918859	0.0
Rsq	5	0.85336	0.85336	0.0
Rsq	6	0.950119	0.950119	0.0
Rsq	7	0.970312	0.970312	0.0
Rsq	8	0.947969	0.947969	0.0
Rsq	9	0.947538	0.947538	0.0
Rsq	10	0.880923	0.880923	0.0
$ARsq$	1	0.714769	0.714769	0.0
$ARsq$	2	0.990351	0.990351	0.0
$ARsq$	3	0.776307	0.776307	0.0
$ARsq$	4	0.837717	0.837717	0.0
$ARsq$	5	0.82892	0.82892	0.0
$ARsq$	6	0.925179	0.925179	0.0

Parameter	Subject	Value	Reference	Difference
$ARsq$	7	0.960416	0.960416	0.0
$ARsq$	8	0.921954	0.921954	0.0
$ARsq$	9	0.921307	0.921307	0.0
$ARsq$	10	0.863912	0.863912	0.0
Kel	1	0.00338474	0.00338474	0.0
Kel	2	0.0141063	0.0141063	0.0
Kel	3	0.00329143	0.00329143	0.0
Kel	4	0.00769534	0.00769534	0.0
Kel	5	0.00681333	0.00681333	0.0
Kel	6	0.00769228	0.00769228	0.0
Kel	7	0.012459	0.012459	0.0
Kel	8	0.00893008	0.00893008	0.0
Kel	9	0.00564586	0.00564586	0.0
Kel	10	0.0171897	0.0171897	0.0
HL	1	204.786	204.786	0.0
HL	2	49.1374	49.1374	0.0
HL	3	210.591	210.591	0.0
HL	4	90.0736	90.0736	0.0
HL	5	101.734	101.734	0.0
HL	6	90.1095	90.1095	0.0
HL	7	55.6345	55.6345	0.0
HL	8	77.6194	77.6194	0.0
HL	9	122.771	122.771	0.0
HL	10	40.3233	40.3233	0.0
$Clast_{pred}$	1	117.306	117.306	0.0
$Clast_{pred}$	2	82.5367	82.5367	0.0
$Clast_{pred}$	3	66.9311	66.9311	0.0
$Clast_{pred}$	4	100.768	100.768	0.0
$Clast_{pred}$	5	105.298	105.298	0.0
$Clast_{pred}$	6	71.9399	71.9399	0.0
$Clast_{pred}$	7	61.1727	61.1727	0.0
$Clast_{pred}$	8	75.6043	75.6043	0.0
$Clast_{pred}$	9	93.7618	93.7618	0.0
$Clast_{pred}$	10	38.8109	38.8109	0.0
$AUCinf$	1	42925.0	42925.0	0.0
$AUCinf$	2	16154.9	16154.9	0.0
$AUCinf$	3	26026.2	26026.2	0.0
$AUCinf$	4	22004.1	22004.1	0.0
$AUCinf$	5	25820.3	25820.3	0.0
$AUCinf$	6	16001.8	16001.8	0.0
$AUCinf$	7	11689.0	11689.0	0.0
$AUCinf$	8	15446.2	15446.2	0.0
$AUCinf$	9	24865.2	24865.2	0.0
$AUCinf$	10	8075.32	8075.32	0.0
$AUCpct$	1	77.6694	77.6694	0.0
$AUCpct$	2	37.405	37.405	0.0
$AUCpct$	3	79.2649	79.2649	0.0

Parameter	Subject	Value	Reference	Difference
$AUCpct$	4	57.6541	57.6541	0.0
$AUCpct$	5	62.97	62.97	0.0
$AUCpct$	6	56.4636	56.4636	0.0
$AUCpct$	7	39.8614	39.8614	0.0
$AUCpct$	8	53.9649	53.9649	0.0
$AUCpct$	9	66.5594	66.5594	0.0
$AUCpct$	10	30.3942	30.3942	0.0
$MRTlast$	1	34.801	34.801	0.0
$MRTlast$	2	29.5388	29.5388	0.0
$MRTlast$	3	34.4724	34.4724	0.0
$MRTlast$	4	33.6941	33.6941	0.0
$MRTlast$	5	32.9644	32.9644	0.0
$MRTlast$	6	32.5808	32.5808	0.0
$MRTlast$	7	31.2676	31.2676	0.0
$MRTlast$	8	33.8261	33.8261	0.0
$MRTlast$	9	33.3868	33.3868	0.0
$MRTlast$	10	27.5567	27.5567	0.0
$MRTinf$	1	293.162	293.162	0.0
$MRTinf$	2	71.9379	71.9379	0.0
$MRTinf$	3	305.041	305.041	0.0
$MRTinf$	4	130.7	130.7	0.0
$MRTinf$	5	149.967	149.967	0.0
$MRTinf$	6	128.241	128.241	0.0
$MRTinf$	7	79.4983	79.4983	0.0
$MRTinf$	8	114.857	114.857	0.0
$MRTinf$	9	176.978	176.978	0.0
$MRTinf$	10	58.7464	58.7464	0.0
$Clinf$	1	0.00232964	0.00232964	0.0
$Clinf$	2	0.00619006	0.00619006	0.0
$Clinf$	3	0.00384228	0.00384228	0.0
$Clinf$	4	0.00454461	0.00454461	0.0
$Clinf$	5	0.00387293	0.00387293	0.0
$Clinf$	6	0.00624931	0.00624931	0.0
$Clinf$	7	0.00855509	0.00855509	0.0
$Clinf$	8	0.00647408	0.00647408	0.0
$Clinf$	9	0.00402168	0.00402168	0.0
$Clinf$	10	0.0123834	0.0123834	0.0
$Vzinf$	1	0.688278	0.688278	0.0
$Vzinf$	2	0.438815	0.438815	0.0
$Vzinf$	3	1.16736	1.16736	0.0
$Vzinf$	4	0.590566	0.590566	0.0
$Vzinf$	5	0.568434	0.568434	0.0
$Vzinf$	6	0.812414	0.812414	0.0
$Vzinf$	7	0.686662	0.686662	0.0
$Vzinf$	8	0.724974	0.724974	0.0
$Vzinf$	9	0.712323	0.712323	0.0
$Vzinf$	10	0.720395	0.720395	0.0

4.3.2 Linear-Up Log-Down; Extravascular; Dosetime 0.25; Tau 9; Dose 100

Code:

```
setdosetime!(ds, DoseTime(dose = 100, time = 0.25, tau = 9))
nca!(ds, adm = :ev, calcm = :luld)
```

Table 3: Plasma data results, Linear-Up Log-Down, Extravascular

Parameter	Subject	Value	Reference	Difference
$Cmax$	1	190.869	190.869	0.0
$Cmax$	2	261.177	261.177	0.0
$Cmax$	3	105.345	105.345	0.0
$Cmax$	4	208.542	208.542	0.0
$Cmax$	5	169.334	169.334	0.0
$Cmax$	6	154.648	154.648	0.0
$Cmax$	7	153.254	153.254	0.0
$Cmax$	8	138.327	138.327	0.0
$Cmax$	9	167.347	167.347	0.0
$Cmax$	10	125.482	125.482	0.0
$Tmax$	1	1.0	1.0	0.0
$Tmax$	2	1.0	1.0	0.0
$Tmax$	3	1.5	1.5	0.0
$Tmax$	4	1.0	1.0	0.0
$Tmax$	5	4.0	4.0	0.0
$Tmax$	6	2.5	2.5	0.0
$Tmax$	7	2.5	2.5	0.0
$Tmax$	8	4.0	4.0	0.0
$Tmax$	9	3.0	3.0	0.0
$Tmax$	10	2.0	2.0	0.0
$Cdose$	1	121.239	121.239	0.0
$Cdose$	2	62.222	62.222	0.0
$Cdose$	3	49.849	49.849	0.0
$Cdose$	4	52.421	52.421	0.0
$Cdose$	5	0.0	0.0	0.0
$Cdose$	6	57.882	57.882	0.0
$Cdose$	7	19.95	19.95	0.0
$Cdose$	8	22.724	22.724	0.0
$Cdose$	9	105.438	105.438	0.0
$Cdose$	10	13.634	13.634	0.0
$Clast$	1	112.846	112.846	0.0
$Clast$	2	85.241	85.241	0.0
$Clast$	3	67.901	67.901	0.0
$Clast$	4	97.625	97.625	0.0
$Clast$	5	110.778	110.778	0.0
$Clast$	6	69.501	69.501	0.0
$Clast$	7	58.051	58.051	0.0
$Clast$	8	74.437	74.437	0.0
$Clast$	9	93.44	93.44	0.0

Parameter	Subject	Value	Reference	Difference
$Clast$	10	42.191	42.191	0.0
$AUClast$	1	9566.6	9566.6	0.0
$AUClast$	2	10054.3	10054.3	0.0
$AUClast$	3	5392.46	5392.46	0.0
$AUClast$	4	9297.1	9297.1	0.0
$AUClast$	5	9519.18	9519.18	0.0
$AUClast$	6	6948.99	6948.99	0.0
$AUClast$	7	6988.77	6988.77	0.0
$AUClast$	8	7058.82	7058.82	0.0
$AUClast$	9	8302.37	8302.37	0.0
$AUClast$	10	5486.84	5486.84	0.0
$AUCtau$	1	1268.28	1268.28	0.0
$AUCtau$	2	1831.82	1831.82	0.0
$AUCtau$	3	754.649	754.649	0.0
$AUCtau$	4	1336.48	1336.48	0.0
$AUCtau$	5	1310.9	1310.9	0.0
$AUCtau$	6	1114.24	1114.24	0.0
$AUCtau$	7	1079.37	1079.37	0.0
$AUCtau$	8	766.62	766.62	0.0
$AUCtau$	9	1219.63	1219.63	0.0
$AUCtau$	10	970.306	970.306	0.0
$AUMCtau$	1	5477.2	5477.2	0.0
$AUMCtau$	2	8367.57	8367.57	0.0
$AUMCtau$	3	3455.35	3455.35	0.0
$AUMCtau$	4	6014.65	6014.65	0.0
$AUMCtau$	5	6609.79	6609.79	0.0
$AUMCtau$	6	5064.72	5064.72	0.0
$AUMCtau$	7	4976.96	4976.96	0.0
$AUMCtau$	8	2863.01	2863.01	0.0
$AUMCtau$	9	5386.88	5386.88	0.0
$AUMCtau$	10	4713.48	4713.48	0.0
$AUCall$	1	9566.6	9566.6	0.0
$AUCall$	2	10054.3	10054.3	0.0
$AUCall$	3	5392.46	5392.46	0.0
$AUCall$	4	9297.1	9297.1	0.0
$AUCall$	5	9519.18	9519.18	0.0
$AUCall$	6	6948.99	6948.99	0.0
$AUCall$	7	6988.77	6988.77	0.0
$AUCall$	8	7058.82	7058.82	0.0
$AUCall$	9	8302.37	8302.37	0.0
$AUCall$	10	5486.84	5486.84	0.0
Rsq	1	0.786077	0.786077	0.0
Rsq	2	0.992764	0.992764	0.0
Rsq	3	0.813589	0.813589	0.0
Rsq	4	0.918859	0.918859	0.0
Rsq	5	0.85336	0.85336	0.0
Rsq	6	0.950119	0.950119	0.0
Rsq	7	0.970312	0.970312	0.0

Parameter	Subject	Value	Reference	Difference
Rsq	8	0.947969	0.947969	0.0
Rsq	9	0.947538	0.947538	0.0
Rsq	10	0.880923	0.880923	0.0
$ARsq$	1	0.714769	0.714769	0.0
$ARsq$	2	0.990351	0.990351	0.0
$ARsq$	3	0.776307	0.776307	0.0
$ARsq$	4	0.837717	0.837717	0.0
$ARsq$	5	0.82892	0.82892	0.0
$ARsq$	6	0.925179	0.925179	0.0
$ARsq$	7	0.960416	0.960416	0.0
$ARsq$	8	0.921954	0.921954	0.0
$ARsq$	9	0.921307	0.921307	0.0
$ARsq$	10	0.863912	0.863912	0.0
Kel	1	0.00338474	0.00338474	0.0
Kel	2	0.0141063	0.0141063	0.0
Kel	3	0.00329143	0.00329143	0.0
Kel	4	0.00769534	0.00769534	0.0
Kel	5	0.00681333	0.00681333	0.0
Kel	6	0.00769228	0.00769228	0.0
Kel	7	0.012459	0.012459	0.0
Kel	8	0.00893008	0.00893008	0.0
Kel	9	0.00564586	0.00564586	0.0
Kel	10	0.0171897	0.0171897	0.0
HL	1	204.786	204.786	0.0
HL	2	49.1374	49.1374	0.0
HL	3	210.591	210.591	0.0
HL	4	90.0736	90.0736	0.0
HL	5	101.734	101.734	0.0
HL	6	90.1095	90.1095	0.0
HL	7	55.6345	55.6345	0.0
HL	8	77.6194	77.6194	0.0
HL	9	122.771	122.771	0.0
HL	10	40.3233	40.3233	0.0
$Clast_{pred}$	1	117.306	117.306	0.0
$Clast_{pred}$	2	82.5367	82.5367	0.0
$Clast_{pred}$	3	66.9311	66.9311	0.0
$Clast_{pred}$	4	100.768	100.768	0.0
$Clast_{pred}$	5	105.298	105.298	0.0
$Clast_{pred}$	6	71.9399	71.9399	0.0
$Clast_{pred}$	7	61.1727	61.1727	0.0
$Clast_{pred}$	8	75.6043	75.6043	0.0
$Clast_{pred}$	9	93.7618	93.7618	0.0
$Clast_{pred}$	10	38.8109	38.8109	0.0
$AUCinf$	1	42906.2	42906.2	0.0
$AUCinf$	2	16097.0	16097.0	0.0
$AUCinf$	3	26022.1	26022.1	0.0
$AUCinf$	4	21983.3	21983.3	0.0

Parameter	Subject	Value	Reference	Difference
$AUCinf$	5	25778.2	25778.2	0.0
$AUCinf$	6	15984.1	15984.1	0.0
$AUCinf$	7	11648.2	11648.2	0.0
$AUCinf$	8	15394.4	15394.4	0.0
$AUCinf$	9	24852.5	24852.5	0.0
$AUCinf$	10	7941.27	7941.27	0.0
$AUCpct$	1	77.7035	77.7035	0.0
$AUCpct$	2	37.5395	37.5395	0.0
$AUCpct$	3	79.2774	79.2774	0.0
$AUCpct$	4	57.7084	57.7084	0.0
$AUCpct$	5	63.0727	63.0727	0.0
$AUCpct$	6	56.5258	56.5258	0.0
$AUCpct$	7	40.001	40.001	0.0
$AUCpct$	8	54.1467	54.1467	0.0
$AUCpct$	9	66.5935	66.5935	0.0
$AUCpct$	10	30.9073	30.9073	0.0
$MRTtauinf$	1	299.792	299.792	0.0
$MRTtauinf$	2	74.655	74.655	0.0
$MRTtauinf$	3	305.92	305.92	0.0
$MRTtauinf$	4	143.538	143.538	0.0
$MRTtauinf$	5	173.022	173.022	0.0
$MRTtauinf$	6	124.653	124.653	0.0
$MRTtauinf$	7	92.7359	92.7359	0.0
$MRTtauinf$	8	175.462	175.462	0.0
$MRTtauinf$	9	178.811	178.811	0.0
$MRTtauinf$	10	69.5163	69.5163	0.0
$Cltau$	1	0.0788472	0.0788472	0.0
$Cltau$	2	0.0545905	0.0545905	0.0
$Cltau$	3	0.132512	0.132512	0.0
$Cltau$	4	0.0748234	0.0748234	0.0
$Cltau$	5	0.0762832	0.0762832	0.0
$Cltau$	6	0.0897472	0.0897472	0.0
$Cltau$	7	0.0926469	0.0926469	0.0
$Cltau$	8	0.130443	0.130443	0.0
$Cltau$	9	0.081992	0.081992	0.0
$Cltau$	10	0.10306	0.10306	0.0
$Vztau$	1	23.2949	23.2949	0.0
$Vztau$	2	3.86993	3.86993	0.0
$Vztau$	3	40.2597	40.2597	0.0
$Vztau$	4	9.7232	9.7232	0.0
$Vztau$	5	11.1962	11.1962	0.0
$Vztau$	6	11.6672	11.6672	0.0
$Vztau$	7	7.43617	7.43617	0.0
$Vztau$	8	14.6071	14.6071	0.0
$Vztau$	9	14.5225	14.5225	0.0
$Vztau$	10	5.99545	5.99545	0.0

4.3.3 Linear-trapezoidal rule; Intravascular; Dosetime 0.0; Tau 12; Dose 120

Code:

```
setdosetime!(ds, DoseTime(dose = 120, time = 0.0, tau = 12))
nca!(ds, adm = :iv, calcm = :lint)
```

Table 4: Plasma data results, Linear-trapezoidal rule, Intravascular

Parameter	Subject	Value	Reference	Difference
$Cmax$	1	190.869	190.869	0.0
$Cmax$	2	261.177	261.177	0.0
$Cmax$	3	105.345	105.345	0.0
$Cmax$	4	208.542	208.542	0.0
$Cmax$	5	169.334	169.334	0.0
$Cmax$	6	154.648	154.648	0.0
$Cmax$	7	153.254	153.254	0.0
$Cmax$	8	138.327	138.327	0.0
$Cmax$	9	167.347	167.347	0.0
$Cmax$	10	125.482	125.482	0.0
$Tmax$	1	1.0	1.0	0.0
$Tmax$	2	1.0	1.0	0.0
$Tmax$	3	1.5	1.5	0.0
$Tmax$	4	1.0	1.0	0.0
$Tmax$	5	4.0	4.0	0.0
$Tmax$	6	2.5	2.5	0.0
$Tmax$	7	2.5	2.5	0.0
$Tmax$	8	4.0	4.0	0.0
$Tmax$	9	3.0	3.0	0.0
$Tmax$	10	2.0	2.0	0.0
$Cdose$	1	0.0	0.0	0.0
$Cdose$	2	0.0	0.0	0.0
$Cdose$	3	0.0	0.0	0.0
$Cdose$	4	0.0	0.0	0.0
$Cdose$	5	0.0	0.0	0.0
$Cdose$	6	0.0	0.0	0.0
$Cdose$	7	0.0	0.0	0.0
$Cdose$	8	0.0	0.0	0.0
$Cdose$	9	0.0	0.0	0.0
$Cdose$	10	0.0	0.0	0.0
$Clast$	1	112.846	112.846	0.0
$Clast$	2	85.241	85.241	0.0
$Clast$	3	67.901	67.901	0.0
$Clast$	4	97.625	97.625	0.0
$Clast$	5	110.778	110.778	0.0
$Clast$	6	69.501	69.501	0.0
$Clast$	7	58.051	58.051	0.0
$Clast$	8	74.437	74.437	0.0
$Clast$	9	93.44	93.44	0.0

Parameter	Subject	Value	Reference	Difference
$Clast$	10	42.191	42.191	0.0
$AUClast$	1	9585.42	9585.42	0.0
$AUClast$	2	10112.2	10112.2	0.0
$AUClast$	3	5396.55	5396.55	0.0
$AUClast$	4	9317.84	9317.84	0.0
$AUClast$	5	9561.26	9561.26	0.0
$AUClast$	6	6966.6	6966.6	0.0
$AUClast$	7	7029.57	7029.57	0.0
$AUClast$	8	7110.67	7110.67	0.0
$AUClast$	9	8315.08	8315.08	0.0
$AUClast$	10	5620.89	5620.89	0.0
$AUCtau$	1	1670.1	1670.1	0.0
$AUCtau$	2	2380.27	2380.27	0.0
$AUCtau$	3	980.346	980.346	0.0
$AUCtau$	4	1711.04	1711.04	0.0
$AUCtau$	5	1738.46	1738.46	0.0
$AUCtau$	6	1410.0	1410.0	0.0
$AUCtau$	7	1436.56	1436.56	0.0
$AUCtau$	8	1105.07	1105.07	0.0
$AUCtau$	9	1638.19	1638.19	0.0
$AUCtau$	10	1293.71	1293.71	0.0
$AUMCtau$	1	9984.82	9984.82	0.0
$AUMCtau$	2	14630.1	14630.1	0.0
$AUMCtau$	3	6024.5	6024.5	0.0
$AUMCtau$	4	10299.7	10299.7	0.0
$AUMCtau$	5	11466.1	11466.1	0.0
$AUMCtau$	6	8467.36	8467.36	0.0
$AUMCtau$	7	9003.02	9003.02	0.0
$AUMCtau$	8	6457.01	6457.01	0.0
$AUMCtau$	9	10095.8	10095.8	0.0
$AUMCtau$	10	8367.3	8367.3	0.0
$AUCall$	1	9585.42	9585.42	0.0
$AUCall$	2	10112.2	10112.2	0.0
$AUCall$	3	5396.55	5396.55	0.0
$AUCall$	4	9317.84	9317.84	0.0
$AUCall$	5	9561.26	9561.26	0.0
$AUCall$	6	6966.6	6966.6	0.0
$AUCall$	7	7029.57	7029.57	0.0
$AUCall$	8	7110.67	7110.67	0.0
$AUCall$	9	8315.08	8315.08	0.0
$AUCall$	10	5620.89	5620.89	0.0
Rsq	1	0.786077	0.786077	0.0
Rsq	2	0.992764	0.992764	0.0
Rsq	3	0.813589	0.813589	0.0
Rsq	4	0.918859	0.918859	0.0
Rsq	5	0.863677	0.863677	0.0
Rsq	6	0.950119	0.950119	0.0
Rsq	7	0.970312	0.970312	0.0

Parameter	Subject	Value	Reference	Difference
Rsq	8	0.947969	0.947969	0.0
Rsq	9	0.947538	0.947538	0.0
Rsq	10	0.879699	0.879699	0.0
$ARsq$	1	0.714769	0.714769	0.0
$ARsq$	2	0.990351	0.990351	0.0
$ARsq$	3	0.776307	0.776307	0.0
$ARsq$	4	0.837717	0.837717	0.0
$ARsq$	5	0.844202	0.844202	0.0
$ARsq$	6	0.925179	0.925179	0.0
$ARsq$	7	0.960416	0.960416	0.0
$ARsq$	8	0.921954	0.921954	0.0
$ARsq$	9	0.921307	0.921307	0.0
$ARsq$	10	0.867669	0.867669	0.0
Kel	1	0.00338474	0.00338474	0.0
Kel	2	0.0141063	0.0141063	0.0
Kel	3	0.00329143	0.00329143	0.0
Kel	4	0.00769534	0.00769534	0.0
Kel	5	0.00685799	0.00685799	0.0
Kel	6	0.00769228	0.00769228	0.0
Kel	7	0.012459	0.012459	0.0
Kel	8	0.00893008	0.00893008	0.0
Kel	9	0.00564586	0.00564586	0.0
Kel	10	0.0165438	0.0165438	0.0
HL	1	204.786	204.786	0.0
HL	2	49.1374	49.1374	0.0
HL	3	210.591	210.591	0.0
HL	4	90.0736	90.0736	0.0
HL	5	101.072	101.072	0.0
HL	6	90.1095	90.1095	0.0
HL	7	55.6345	55.6345	0.0
HL	8	77.6194	77.6194	0.0
HL	9	122.771	122.771	0.0
HL	10	41.8978	41.8978	0.0
$Clast_{pred}$	1	117.306	117.306	0.0
$Clast_{pred}$	2	82.5367	82.5367	0.0
$Clast_{pred}$	3	66.9311	66.9311	0.0
$Clast_{pred}$	4	100.768	100.768	0.0
$Clast_{pred}$	5	105.196	105.196	0.0
$Clast_{pred}$	6	71.9399	71.9399	0.0
$Clast_{pred}$	7	61.1727	61.1727	0.0
$Clast_{pred}$	8	75.6043	75.6043	0.0
$Clast_{pred}$	9	93.7618	93.7618	0.0
$Clast_{pred}$	10	39.4088	39.4088	0.0
$AUCinf$	1	42925.0	42925.0	0.0
$AUCinf$	2	16154.9	16154.9	0.0
$AUCinf$	3	26026.2	26026.2	0.0
$AUCinf$	4	22004.1	22004.1	0.0

Parameter	Subject	Value	Reference	Difference
$AUCinf$	5	25714.4	25714.4	0.0
$AUCinf$	6	16001.8	16001.8	0.0
$AUCinf$	7	11689.0	11689.0	0.0
$AUCinf$	8	15446.2	15446.2	0.0
$AUCinf$	9	24865.2	24865.2	0.0
$AUCinf$	10	8171.16	8171.16	0.0
$AUCpct$	1	77.6694	77.6694	0.0
$AUCpct$	2	37.405	37.405	0.0
$AUCpct$	3	79.2649	79.2649	0.0
$AUCpct$	4	57.6541	57.6541	0.0
$AUCpct$	5	62.8175	62.8175	0.0
$AUCpct$	6	56.4636	56.4636	0.0
$AUCpct$	7	39.8614	39.8614	0.0
$AUCpct$	8	53.9649	53.9649	0.0
$AUCpct$	9	66.5594	66.5594	0.0
$AUCpct$	10	31.2106	31.2106	0.0
$MRTtauinf$	1	302.403	302.403	0.0
$MRTtauinf$	2	75.5906	75.5906	0.0
$MRTtauinf$	3	312.721	312.721	0.0
$MRTtauinf$	4	148.341	148.341	0.0
$MRTtauinf$	5	172.093	172.093	0.0
$MRTtauinf$	6	130.191	130.191	0.0
$MRTtauinf$	7	91.9083	91.9083	0.0
$MRTtauinf$	8	161.574	161.574	0.0
$MRTtauinf$	9	176.305	176.305	0.0
$MRTtauinf$	10	70.2607	70.2607	0.0
$Cltau$	1	0.0718519	0.0718519	0.0
$Cltau$	2	0.0504145	0.0504145	0.0
$Cltau$	3	0.122406	0.122406	0.0
$Cltau$	4	0.070133	0.070133	0.0
$Cltau$	5	0.0690266	0.0690266	0.0
$Cltau$	6	0.0851065	0.0851065	0.0
$Cltau$	7	0.0835329	0.0835329	0.0
$Cltau$	8	0.10859	0.10859	0.0
$Cltau$	9	0.0732516	0.0732516	0.0
$Cltau$	10	0.0927567	0.0927567	0.0
$Vztau$	1	21.2282	21.2282	0.0
$Vztau$	2	3.57389	3.57389	0.0
$Vztau$	3	37.1892	37.1892	0.0
$Vztau$	4	9.11369	9.11369	0.0
$Vztau$	5	10.0651	10.0651	0.0
$Vztau$	6	11.0639	11.0639	0.0
$Vztau$	7	6.70465	6.70465	0.0
$Vztau$	8	12.1601	12.1601	0.0
$Vztau$	9	12.9744	12.9744	0.0
$Vztau$	10	5.60675	5.60675	0.0

4.3.4 Linear/Log Trapezoidal rule; Extravascular; Dosetime 0.0; Tau 12; Dose 120

Code:

```
setdosetime!(ds, DoseTime(dose = 120, time = 0.0, tau = 12))
nca!(ds, adm = :ev, calcm = :logt)
```

Table 5: Plasma data results, Linear/Log Trapezoidal rule, Extravascular

Parameter	Subject	Value	Reference	Difference
$Cmax$	1	190.869	190.869	0.0
$Cmax$	2	261.177	261.177	0.0
$Cmax$	3	105.345	105.345	0.0
$Cmax$	4	208.542	208.542	0.0
$Cmax$	5	169.334	169.334	0.0
$Cmax$	6	154.648	154.648	0.0
$Cmax$	7	153.254	153.254	0.0
$Cmax$	8	138.327	138.327	0.0
$Cmax$	9	167.347	167.347	0.0
$Cmax$	10	125.482	125.482	0.0
$Tmax$	1	1.0	1.0	0.0
$Tmax$	2	1.0	1.0	0.0
$Tmax$	3	1.5	1.5	0.0
$Tmax$	4	1.0	1.0	0.0
$Tmax$	5	4.0	4.0	0.0
$Tmax$	6	2.5	2.5	0.0
$Tmax$	7	2.5	2.5	0.0
$Tmax$	8	4.0	4.0	0.0
$Tmax$	9	3.0	3.0	0.0
$Tmax$	10	2.0	2.0	0.0
$Cdose$	1	0.0	0.0	0.0
$Cdose$	2	0.0	0.0	0.0
$Cdose$	3	0.0	0.0	0.0
$Cdose$	4	0.0	0.0	0.0
$Cdose$	5	0.0	0.0	0.0
$Cdose$	6	0.0	0.0	0.0
$Cdose$	7	0.0	0.0	0.0
$Cdose$	8	0.0	0.0	0.0
$Cdose$	9	0.0	0.0	0.0
$Cdose$	10	0.0	0.0	0.0
$Clast$	1	112.846	112.846	0.0
$Clast$	2	85.241	85.241	0.0
$Clast$	3	67.901	67.901	0.0
$Clast$	4	97.625	97.625	0.0
$Clast$	5	110.778	110.778	0.0
$Clast$	6	69.501	69.501	0.0
$Clast$	7	58.051	58.051	0.0
$Clast$	8	74.437	74.437	0.0

Parameter	Subject	Value	Reference	Difference
$Clast$	9	93.44	93.44	0.0
$Clast$	10	42.191	42.191	0.0
$AUClast$	1	9572.86	9572.86	0.0
$AUClast$	2	10054.0	10054.0	0.0
$AUClast$	3	5391.53	5391.53	0.0
$AUClast$	4	9296.22	9296.22	0.0
$AUClast$	5	9518.65	9518.65	0.0
$AUClast$	6	6948.58	6948.58	0.0
$AUClast$	7	6987.06	6987.06	0.0
$AUClast$	8	7064.78	7064.78	0.0
$AUClast$	9	8298.96	8298.96	0.0
$AUClast$	10	5485.65	5485.65	0.0
$AUCtau$	1	1668.36	1668.36	0.0
$AUCtau$	2	2379.57	2379.57	0.0
$AUCtau$	3	979.109	979.109	0.0
$AUCtau$	4	1709.79	1709.79	0.0
$AUCtau$	5	1738.24	1738.24	0.0
$AUCtau$	6	1408.16	1408.16	0.0
$AUCtau$	7	1432.02	1432.02	0.0
$AUCtau$	8	1080.02	1080.02	0.0
$AUCtau$	9	1630.98	1630.98	0.0
$AUCtau$	10	1292.83	1292.83	0.0
$AUMCtau$	1	9973.81	9973.81	0.0
$AUMCtau$	2	14631.1	14631.1	0.0
$AUMCtau$	3	6022.93	6022.93	0.0
$AUMCtau$	4	10308.0	10308.0	0.0
$AUMCtau$	5	11473.1	11473.1	0.0
$AUMCtau$	6	8471.1	8471.1	0.0
$AUMCtau$	7	8982.04	8982.04	0.0
$AUMCtau$	8	6271.74	6271.74	0.0
$AUMCtau$	9	10040.8	10040.8	0.0
$AUMCtau$	10	8361.79	8361.79	0.0
$AUCall$	1	9572.86	9572.86	0.0
$AUCall$	2	10054.0	10054.0	0.0
$AUCall$	3	5391.53	5391.53	0.0
$AUCall$	4	9296.22	9296.22	0.0
$AUCall$	5	9518.65	9518.65	0.0
$AUCall$	6	6948.58	6948.58	0.0
$AUCall$	7	6987.06	6987.06	0.0
$AUCall$	8	7064.78	7064.78	0.0
$AUCall$	9	8298.96	8298.96	0.0
$AUCall$	10	5485.65	5485.65	0.0
Rsq	1	0.786077	0.786077	0.0
Rsq	2	0.992764	0.992764	0.0
Rsq	3	0.813589	0.813589	0.0
Rsq	4	0.918859	0.918859	0.0
Rsq	5	0.85336	0.85336	0.0
Rsq	6	0.950119	0.950119	0.0

Parameter	Subject	Value	Reference	Difference
Rsq	7	0.970312	0.970312	0.0
Rsq	8	0.947969	0.947969	0.0
Rsq	9	0.947538	0.947538	0.0
Rsq	10	0.880923	0.880923	0.0
$ARsq$	1	0.714769	0.714769	0.0
$ARsq$	2	0.990351	0.990351	0.0
$ARsq$	3	0.776307	0.776307	0.0
$ARsq$	4	0.837717	0.837717	0.0
$ARsq$	5	0.82892	0.82892	0.0
$ARsq$	6	0.925179	0.925179	0.0
$ARsq$	7	0.960416	0.960416	0.0
$ARsq$	8	0.921954	0.921954	0.0
$ARsq$	9	0.921307	0.921307	0.0
$ARsq$	10	0.863912	0.863912	0.0
Kel	1	0.00338474	0.00338474	0.0
Kel	2	0.0141063	0.0141063	0.0
Kel	3	0.00329143	0.00329143	0.0
Kel	4	0.00769534	0.00769534	0.0
Kel	5	0.00681333	0.00681333	0.0
Kel	6	0.00769228	0.00769228	0.0
Kel	7	0.012459	0.012459	0.0
Kel	8	0.00893008	0.00893008	0.0
Kel	9	0.00564586	0.00564586	0.0
Kel	10	0.0171897	0.0171897	0.0
HL	1	204.786	204.786	0.0
HL	2	49.1374	49.1374	0.0
HL	3	210.591	210.591	0.0
HL	4	90.0736	90.0736	0.0
HL	5	101.734	101.734	0.0
HL	6	90.1095	90.1095	0.0
HL	7	55.6345	55.6345	0.0
HL	8	77.6194	77.6194	0.0
HL	9	122.771	122.771	0.0
HL	10	40.3233	40.3233	0.0
$Clast_{pred}$	1	117.306	117.306	0.0
$Clast_{pred}$	2	82.5367	82.5367	0.0
$Clast_{pred}$	3	66.9311	66.9311	0.0
$Clast_{pred}$	4	100.768	100.768	0.0
$Clast_{pred}$	5	105.298	105.298	0.0
$Clast_{pred}$	6	71.9399	71.9399	0.0
$Clast_{pred}$	7	61.1727	61.1727	0.0
$Clast_{pred}$	8	75.6043	75.6043	0.0
$Clast_{pred}$	9	93.7618	93.7618	0.0
$Clast_{pred}$	10	38.8109	38.8109	0.0
$AUCinf$	1	42912.5	42912.5	0.0
$AUCinf$	2	16096.8	16096.8	0.0
$AUCinf$	3	26021.2	26021.2	0.0

Parameter	Subject	Value	Reference	Difference
$AUCinf$	4	21982.5	21982.5	0.0
$AUCinf$	5	25777.7	25777.7	0.0
$AUCinf$	6	15983.7	15983.7	0.0
$AUCinf$	7	11646.4	11646.4	0.0
$AUCinf$	8	15400.3	15400.3	0.0
$AUCinf$	9	24849.1	24849.1	0.0
$AUCinf$	10	7940.08	7940.08	0.0
$AUCpct$	1	77.6921	77.6921	0.0
$AUCpct$	2	37.5401	37.5401	0.0
$AUCpct$	3	79.2802	79.2802	0.0
$AUCpct$	4	57.7107	57.7107	0.0
$AUCpct$	5	63.074	63.074	0.0
$AUCpct$	6	56.5272	56.5272	0.0
$AUCpct$	7	40.0069	40.0069	0.0
$AUCpct$	8	54.1257	54.1257	0.0
$AUCpct$	9	66.6026	66.6026	0.0
$AUCpct$	10	30.9119	30.9119	0.0
$MRTtauinf$	1	302.635	302.635	0.0
$MRTtauinf$	2	75.3237	75.3237	0.0
$MRTtauinf$	3	313.068	313.068	0.0
$MRTtauinf$	4	148.311	148.311	0.0
$MRTtauinf$	5	172.558	172.558	0.0
$MRTtauinf$	6	130.226	130.226	0.0
$MRTtauinf$	7	91.8667	91.8667	0.0
$MRTtauinf$	8	164.918	164.918	0.0
$MRTtauinf$	9	176.985	176.985	0.0
$MRTtauinf$	10	68.1676	68.1676	0.0
$Cltau$	1	0.0719271	0.0719271	0.0
$Cltau$	2	0.0504294	0.0504294	0.0
$Cltau$	3	0.12256	0.12256	0.0
$Cltau$	4	0.0701841	0.0701841	0.0
$Cltau$	5	0.0690354	0.0690354	0.0
$Cltau$	6	0.0852177	0.0852177	0.0
$Cltau$	7	0.0837976	0.0837976	0.0
$Cltau$	8	0.111109	0.111109	0.0
$Cltau$	9	0.0735756	0.0735756	0.0
$Cltau$	10	0.0928198	0.0928198	0.0
$Vztau$	1	21.2504	21.2504	0.0
$Vztau$	2	3.57495	3.57495	0.0
$Vztau$	3	37.2362	37.2362	0.0
$Vztau$	4	9.12034	9.12034	0.0
$Vztau$	5	10.1324	10.1324	0.0
$Vztau$	6	11.0783	11.0783	0.0
$Vztau$	7	6.72589	6.72589	0.0
$Vztau$	8	12.4421	12.4421	0.0
$Vztau$	9	13.0318	13.0318	0.0
$Vztau$	10	5.39972	5.39972	0.0

4.3.5 Urine data; Linear-trapezoidal rule; Extravascular; Dosetime 0.0; Dose 100

Code:

```
upkds = upkimport(upkdata, :st, :et, :conc, :vol, :subj;
dosetime =  MetidaNCA.DoseTime(dose = 100))
MetidaNCA.nca!(upkds)
```

Table 6: Urine data results

Parameter	Value	Reference	Difference
$AUCall$	17.125	17.125	0.0
$Prec$	16.0	16.0	0.0
$Tmax$	1.5	1.5	0.0
$Rlast$	0.333333	0.333333	0.0
AR	16.0	16.0	0.0
$ARsq$	0.810983	0.810983	0.0
HL	5.15526	5.15526	0.0
$AUClast$	17.125	17.125	0.0
$AUCinf$	19.6042	19.6042	0.0
Vol	11.0	11.0	0.0
$AUCpct$	12.6461	12.6461	0.0
Kel	0.134454	0.134454	0.0
$Maxrate$	4.0	4.0	0.0
Rsq	0.905492	0.905492	0.0

4.3.6 Pharmacodynamics data; Linear-trapezoidal rule

Code:

```
pd =  MetidaNCA.pdimport(pddata, :time, :obs;
bl = 3.0, th = 1.5, id = Dict(:subj => 1))
pdres = MetidaNCA.nca!(pd)
```

Table 7: Pharmacodynamics data results

Parameter	Value	Reference	Difference
$Tmax$	5.0	5.0	0.0
$TBBL$	5.51905	5.51905	0.0
$TIMEBTW$	2.28095	2.28095	0.0
$AUCBTW$	6.92619	6.92619	0.0
$AUCBBL$	8.73571	8.73571	0.0
$TBTH$	3.2381	3.2381	0.0
$AUCNETT$	12.15	12.15	0.0
$Rmax$	8.0	8.0	0.0
$AUCABL$	7.38571	7.38571	0.0
$AUCATH$	13.9595	13.9595	0.0
$TATH$	5.7619	5.7619	0.0
$AUCNETB$	−1.35	−1.35	0.0
$AUCBTH$	1.80952	1.80952	0.0
$TABL$	3.48095	3.48095	0.0

5 Glossary

- Installation qualification (IQ) - Establishing confidence that process equipment and ancillary systems are compliant with appropriate codes and approved design intentions, and that manufacturer's recommendations are suitably considered.
- Operational qualification (OQ) Establishing confidence that process equipment and sub-systems are capable of consistently operating within established limits and tolerances.
- Product performance qualification (PQ) - Establishing confidence through appropriate testing that the finished product produced by a specified process meets all release requirements for functionality and safety.
- Repository - GitHub repository: https://github.com/PharmCat/MetidaNCA.jl
- Master branch - main branch on GitHub (link).
- Current machine - pc that used for validation report generating.

6 Reference

- General Principles of Software Validation; Final Guidance for Industry and FDA Staff
- Guidance for Industry Process Validation: General Principles and Practices
- Glossary of Computer System Software Development Terminology

7 Appendix 1

7.0.1 Testing PK dataset.

Subject	Formulation	Time	Concentration
1	T	0.0	0.0
1	T	0.5	178.949
1	T	1.0	190.869
1	T	1.5	164.927
1	T	2.0	139.962
1	T	2.5	129.59
1	T	3.0	131.369
1	T	4.0	150.854
1	T	5.0	121.239
1	T	6.0	139.229
1	T	8.0	128.52
1	T	10.0	143.243
1	T	12.0	144.964
1	T	24.0	133.16
1	T	48.0	137.271
1	T	72.0	112.846
2	R	0.0	0.0
2	R	0.5	62.222
2	R	1.0	261.177
2	R	1.5	234.063
2	R	2.0	234.091
2	R	2.5	222.881
2	R	3.0	213.896
2	R	4.0	196.026
2	R	5.0	199.634
2	R	6.0	196.037
2	R	8.0	213.352
2	R	10.0	200.088
2	R	12.0	196.035
2	R	24.0	160.338
2	R	48.0	110.28
2	R	72.0	85.241
3	R	0.0	0.0
3	R	0.5	49.849
3	R	1.0	77.367
3	R	1.5	105.345
3	R	2.0	100.943
3	R	2.5	72.746
3	R	3.0	69.985
3	R	4.0	93.565
3	R	5.0	91.981
3	R	6.0	82.71
3	R	8.0	84.205

3	R	10.0	85.342
3	R	12.0	76.027
3	R	24.0	81.259
3	R	48.0	70.107
3	R	72.0	67.901
4	R	0.0	0.0
4	R	0.5	52.421
4	R	1.0	208.542
4	R	1.5	188.923
4	R	2.0	165.177
4	R	2.5	146.996
4	R	3.0	152.701
4	R	4.0	154.345
4	R	5.0	128.398
4	R	6.0	149.807
4	R	8.0	151.066
4	R	10.0	136.819
4	R	12.0	132.257
4	R	24.0	141.247
4	R	48.0	129.138
4	R	72.0	97.625
5	T	0.0	0.0
5	T	0.5	0.0
5	T	1.0	9.545
5	T	1.5	153.964
5	T	2.0	152.34
5	T	2.5	151.452
5	T	3.0	161.312
5	T	4.0	169.334
5	T	5.0	162.907
5	T	6.0	166.651
5	T	8.0	168.668
5	T	10.0	155.103
5	T	12.0	154.066
5	T	24.0	162.974
5	T	48.0	109.814
5	T	72.0	110.778
6	T	0.0	0.0
6	T	0.5	57.882
6	T	1.0	100.498
6	T	1.5	138.651
6	T	2.0	147.287
6	T	2.5	154.648
6	T	3.0	122.316
6	T	4.0	132.857
6	T	5.0	126.067
6	T	6.0	140.466
6	T	8.0	115.542
6	T	10.0	102.16

6	T	12.0	113.751
6	T	24.0	101.049
6	T	48.0	92.55
6	T	72.0	69.501
7	R	0.0	0.0
7	R	0.5	19.95
7	R	1.0	128.405
7	R	1.5	136.807
7	R	2.0	113.109
7	R	2.5	153.254
7	R	3.0	123.606
7	R	4.0	142.655
7	R	5.0	112.347
7	R	6.0	139.919
7	R	8.0	105.513
7	R	10.0	134.408
7	R	12.0	123.37
7	R	24.0	110.511
7	R	48.0	90.291
7	R	72.0	58.051
8	R	0.0	0.0
8	R	0.5	136.91
8	R	1.0	126.646
8	R	1.5	118.5
8	R	2.0	134.926
8	R	2.5	113.213
8	R	3.0	130.896
8	R	4.0	138.327
8	R	5.0	22.724
8	R	6.0	53.774
8	R	8.0	55.107
8	R	10.0	102.871
8	R	12.0	134.133
8	R	24.0	108.021
8	R	48.0	98.466
8	R	72.0	74.437
9	T	0.0	0.0
9	T	0.5	113.362
9	T	1.0	128.273
9	T	1.5	125.395
9	T	2.0	146.933
9	T	2.5	140.559
9	T	3.0	167.347
9	T	4.0	157.504
9	T	5.0	141.35
9	T	6.0	140.282
9	T	8.0	105.438
9	T	10.0	164.843
9	T	12.0	135.58

9	T	24.0	117.125
9	T	48.0	109.745
9	T	72.0	93.44
10	R	0.0	0.0
10	R	0.5	13.634
10	R	1.0	62.561
10	R	1.5	112.655
10	R	2.0	125.482
10	R	2.5	116.255
10	R	3.0	112.674
10	R	4.0	116.986
10	R	5.0	119.81
10	R	6.0	107.557
10	R	8.0	120.479
10	R	10.0	124.171
10	R	12.0	106.476
10	R	24.0	116.508
10	R	48.0	45.204
10	R	72.0	42.191

7.0.2 Testing urine PK dataset.

subj	conc	st	et	vol
1	1	0	1	1
1	2	1	2	2
1	2	2	6	3
1	1	6	12	3
1	1	12	18	2

7.0.3 Testing PD dataset.

subj	time	obs
1	0.0	0
1	1.0	1
1	2.0	4
1	2.5	7
1	3.0	5
1	3.3	4
1	3.6	3
1	4.0	2
1	5.0	8
1	6.0	1
1	7.0	2
1	8.0	1
1	9.0	1

8 Appendix 2

8.0.1 Reference output.

Avialible at https://github.com/PharmCat/MetidaNCA.jl/tree/main/docs/src/pdf.

See Appendix 2.1.pdf,

Appendix 2.2.pdf,

Appendix 2.3.pdf,

Appendix 2.4.pdf,

Appendix 2.5.pdf.