MetidaNCA validation report

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Contents

Introduction and package description

Non-compartment anlysis software.

See documentation:

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

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.

Requirements

- Julia 1.5.* (or higher) installed
- Julia packages from dependence list installed (see Project.toml)

Developer software life cycle

- Development stage
- Testing procedures development
- Performing testing procedures on local machine
- Push to master 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)

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

Build support

Tier 1

- julia-version: 1.5, 1.6
- julia-arch: x64
- os: ubuntu-18.04, macos-10.15, windows-2019

Installation

System information

- Julia version: v“1.6.3”
- Current machine: “x86_64-pc-linux-gnu”

Installation method

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

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

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: “0.2.0”

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.

Coverage

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

- Coverage goal: >= 90.0%

Data

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

Testing results

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

```
Test Summary:                                                | Pass  Total
   Simple test                                               |   11     11
Test Summary:                                                | Pass  Total
  #1 Linear trapezoidal, Dose 100, Dosetime 0, no tau        |   18     18
Test Summary:                                                | Pass  Total
  #2 Linear up Log down, Dose 100, Dosetime 0.25, tau 9      |   17     17
Test Summary:                                                | Pass  Total
```

```
  #3 Linear trapezoidal, IV, Dose 120, Dosetime 0.0, tau 12 |   17     17
Test Summary:                                               | Pass  Total
  Linear up Log down, Dose 120, Dosetime 0, tau 12          |   17     17
Test Summary:                                               | Pass  Total
  Log trapezoidal ATM, Dose 120, Dosetime 0, tau 12         |    5      5
Test Summary:                                               | Pass  Total
  Linear up Log down ATM, Dose 120, Dosetime 0, tau 12      |    4      4
Test Summary:                                               | Pass  Total
  Linear trapezoidal, Dose 100, Dosetime 2.0, tau 10        |   15     15
Test Summary:                                               | Pass  Total
  Linear trapezoidal, Dose 100, Dosetime 0.0, tau 100       |   15     15
Test Summary:                                               | Pass  Total
  Linear up Log down, Dose 100, Dosetime 0.25, tau 9 IV     |    1      1
Test Summary:                                               | Pass  Total
  Linear trapezoidal, Dose 100, Dosetime 0, no tau AUCall   |    1      1
Test Summary:                                               | Pass  Total
  set-get*! tests                                           |   17     17
Test Summary:                                               | Pass  Total
  applylimitrule!                                           |   11     11
Test Summary:                                               | Pass  Total
  kel                                                       |    2      2
Test Summary:                                               | Pass  Total
  Output                                                    |    3      3
Test Summary:                                               | Pass  Total
  Urine PK                                                  |    1      1
```

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.

Parameter's names description

Name String	Description String
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 |
'------------'-------------------------------------'
```

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)
```

```
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	Concentrtion	AUC	AUC (cumulate)	AUMC	AUMC (cumulate)	Info
0.0	0.0	0.0	0.0	0.0	0.0	D
0.5	178.949	44.7373	44.7373	22.3686	22.3686	
1.0	190.869	92.4545	137.192	70.0859	92.4545	
1.5	164.927	88.949	226.141	109.565	202.019	
2.0	139.962	76.2223	302.363	131.829	333.848	
2.5	129.59	67.388	369.751	150.975	484.823	
3.0	131.369	65.2398	434.991	179.52	664.343	
4.0	150.854	141.112	576.102	498.762	1163.1	
5.0	121.239	136.047	712.149	604.806	1767.91	
6.0	139.229	130.234	842.383	720.784	2488.69	
8.0	128.52	267.749	1110.13	1863.53	4352.23	
10.0	143.243	271.763	1381.89	2460.59	6812.82	E
12.0	144.964	288.207	1670.1	3172.0	9984.82	E
24.0	133.16	1668.74	3338.85	29612.4	39597.3	E
48.0	137.271	3245.17	6584.02	1.17418e5	1.57015e5	E

72.0	112.846	3001.4	9585.42	176567.0	3.33582e5	E

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

Pharmacokinetic subject NCA result

Keys	Values
Symbol	Float64
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

15 rows omitted

Results

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

Code:

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

Cmax

Subject	Value	Reference	Difference
1	190.869	190.869	0.0
2	261.177	261.177	0.0
3	105.345	105.345	0.0
4	208.542	208.542	0.0
5	169.334	169.334	0.0
6	154.648	154.648	0.0
7	153.254	153.254	0.0
8	138.327	138.327	0.0
9	167.347	167.347	0.0
10	125.482	125.482	0.0

Tmax

Subject	Value	Reference	Difference
1	1.0	1.0	0.0
2	1.0	1.0	0.0
3	1.5	1.5	0.0
4	1.0	1.0	0.0
5	4.0	4.0	0.0
6	2.5	2.5	0.0
7	2.5	2.5	0.0
8	4.0	4.0	0.0
9	3.0	3.0	0.0
10	2.0	2.0	0.0

Cdose

Subject	Value	Reference	Difference
1	0.0	0.0	0.0
2	0.0	0.0	0.0
3	0.0	0.0	0.0
4	0.0	0.0	0.0
5	0.0	0.0	0.0
6	0.0	0.0	0.0
7	0.0	0.0	0.0
8	0.0	0.0	0.0
9	0.0	0.0	0.0

Subject	Value	Reference	Difference
10	0.0	0.0	0.0

Clast

Subject	Value	Reference	Difference
1	112.846	112.846	0.0
2	85.241	85.241	0.0
3	67.901	67.901	0.0
4	97.625	97.625	0.0
5	110.778	110.778	0.0
6	69.501	69.501	0.0
7	58.051	58.051	0.0
8	74.437	74.437	0.0
9	93.44	93.44	0.0
10	42.191	42.191	0.0

AUClast

Subject	Value	Reference	Difference
1	9585.42	9585.42	0.0
2	10112.2	10112.2	0.0
3	5396.55	5396.55	0.0
4	9317.84	9317.84	0.0
5	9561.26	9561.26	0.0
6	6966.6	6966.6	0.0
7	7029.57	7029.57	0.0
8	7110.67	7110.67	0.0
9	8315.08	8315.08	0.0
10	5620.89	5620.89	0.0

AUMClast

Subject	Value	Reference	Difference
1	333582.0	333582.0	0.0
2	298701.0	298701.0	0.0
3	186032.0	186032.0	0.0
4	313956.0	313956.0	0.0
5	315182.0	315182.0	0.0
6	226977.0	226977.0	0.0
7	219798.0	219798.0	0.0
8	240526.0	240526.0	0.0
9	277614.0	277614.0	0.0
10	154893.0	154893.0	0.0

AUCall

Subject	Value	Reference	Difference
1	9585.42	9585.42	0.0
2	10112.2	10112.2	0.0
3	5396.55	5396.55	0.0
4	9317.84	9317.84	0.0
5	9561.26	9561.26	0.0
6	6966.6	6966.6	0.0
7	7029.57	7029.57	0.0
8	7110.67	7110.67	0.0
9	8315.08	8315.08	0.0
10	5620.89	5620.89	0.0

Rsq

Subject	Value	Reference	Difference
1	0.786077	0.786077	0.0
2	0.992764	0.992764	0.0
3	0.813589	0.813589	0.0
4	0.918859	0.918859	0.0
5	0.85336	0.85336	0.0
6	0.950119	0.950119	0.0
7	0.970312	0.970312	0.0
8	0.947969	0.947969	0.0
9	0.947538	0.947538	0.0
10	0.880923	0.880923	0.0

ARsq

Subject	Value	Reference	Difference
1	0.714769	0.714769	0.0
2	0.990351	0.990351	0.0
3	0.776307	0.776307	0.0
4	0.837717	0.837717	0.0
5	0.82892	0.82892	0.0
6	0.925179	0.925179	0.0
7	0.960416	0.960416	0.0
8	0.921954	0.921954	0.0
9	0.921307	0.921307	0.0
10	0.863912	0.863912	0.0

Kel

Subject	Value	Reference	Difference
1	0.00338474	0.00338474	0.0
2	0.0141063	0.0141063	0.0
3	0.00329143	0.00329143	0.0
4	0.00769534	0.00769534	0.0
5	0.00681333	0.00681333	0.0
6	0.00769228	0.00769228	0.0
7	0.012459	0.012459	0.0
8	0.00893008	0.00893008	0.0
9	0.00564586	0.00564586	0.0
10	0.0171897	0.0171897	0.0

HL

Subject	Value	Reference	Difference
1	204.786	204.786	0.0
2	49.1374	49.1374	0.0
3	210.591	210.591	0.0
4	90.0736	90.0736	0.0
5	101.734	101.734	0.0
6	90.1095	90.1095	0.0
7	55.6345	55.6345	0.0
8	77.6194	77.6194	0.0
9	122.771	122.771	0.0
10	40.3233	40.3233	0.0

Clast_pred

Subject	Value	Reference	Difference
1	117.306	117.306	0.0
2	82.5367	82.5367	0.0
3	66.9311	66.9311	0.0
4	100.768	100.768	0.0
5	105.298	105.298	0.0
6	71.9399	71.9399	0.0
7	61.1727	61.1727	0.0
8	75.6043	75.6043	0.0
9	93.7618	93.7618	0.0
10	38.8109	38.8109	0.0

AUCinf

Subject	Value	Reference	Difference
1	42925.0	42925.0	0.0
2	16154.9	16154.9	0.0
3	26026.2	26026.2	0.0

Subject	Value	Reference	Difference
4	22004.1	22004.1	0.0
5	25820.3	25820.3	0.0
6	16001.8	16001.8	0.0
7	11689.0	11689.0	0.0
8	15446.2	15446.2	0.0
9	24865.2	24865.2	0.0
10	8075.32	8075.32	0.0

AUCpct

Subject	Value	Reference	Difference
1	77.6694	77.6694	0.0
2	37.405	37.405	0.0
3	79.2649	79.2649	0.0
4	57.6541	57.6541	0.0
5	62.97	62.97	0.0
6	56.4636	56.4636	0.0
7	39.8614	39.8614	0.0
8	53.9649	53.9649	0.0
9	66.5594	66.5594	0.0
10	30.3942	30.3942	0.0

MRTlast

Subject	Value	Reference	Difference
1	34.801	34.801	0.0
2	29.5388	29.5388	0.0
3	34.4724	34.4724	0.0
4	33.6941	33.6941	0.0
5	32.9644	32.9644	0.0
6	32.5808	32.5808	0.0
7	31.2676	31.2676	0.0
8	33.8261	33.8261	0.0
9	33.3868	33.3868	0.0
10	27.5567	27.5567	0.0

MRTinf

Subject	Value	Reference	Difference
1	293.162	293.162	0.0
2	71.9379	71.9379	0.0
3	305.041	305.041	0.0
4	130.7	130.7	0.0
5	149.967	149.967	0.0
6	128.241	128.241	0.0

Subject	Value	Reference	Difference
7	79.4983	79.4983	0.0
8	114.857	114.857	0.0
9	176.978	176.978	0.0
10	58.7464	58.7464	0.0

Clinf

Subject	Value	Reference	Difference
1	0.00232964	0.00232964	0.0
2	0.00619006	0.00619006	0.0
3	0.00384228	0.00384228	0.0
4	0.00454461	0.00454461	0.0
5	0.00387293	0.00387293	0.0
6	0.00624931	0.00624931	0.0
7	0.00855509	0.00855509	0.0
8	0.00647408	0.00647408	0.0
9	0.00402168	0.00402168	0.0
10	0.0123834	0.0123834	0.0

Vzinf

Subject	Value	Reference	Difference
1	0.688278	0.688278	0.0
2	0.438815	0.438815	0.0
3	1.16736	1.16736	0.0
4	0.590566	0.590566	0.0
5	0.568434	0.568434	0.0
6	0.812414	0.812414	0.0
7	0.686662	0.686662	0.0
8	0.724974	0.724974	0.0
9	0.712323	0.712323	0.0
10	0.720395	0.720395	0.0

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)
```

Cmax

Subject	Value	Reference	Difference
1	190.869	190.869	0.0
2	261.177	261.177	0.0
3	105.345	105.345	0.0
4	208.542	208.542	0.0
5	169.334	169.334	0.0
6	154.648	154.648	0.0
7	153.254	153.254	0.0
8	138.327	138.327	0.0
9	167.347	167.347	0.0
10	125.482	125.482	0.0

Tmax

Subject	Value	Reference	Difference
1	1.0	1.0	0.0
2	1.0	1.0	0.0
3	1.5	1.5	0.0
4	1.0	1.0	0.0
5	4.0	4.0	0.0
6	2.5	2.5	0.0
7	2.5	2.5	0.0
8	4.0	4.0	0.0
9	3.0	3.0	0.0
10	2.0	2.0	0.0

Cdose

Subject	Value	Reference	Difference
1	121.239	121.239	0.0
2	62.222	62.222	0.0
3	49.849	49.849	0.0
4	52.421	52.421	0.0
5	0.0	0.0	0.0
6	57.882	57.882	0.0
7	19.95	19.95	0.0
8	22.724	22.724	0.0
9	105.438	105.438	0.0

Subject	Value	Reference	Difference
10	13.634	13.634	0.0

Clast

Subject	Value	Reference	Difference
1	112.846	112.846	0.0
2	85.241	85.241	0.0
3	67.901	67.901	0.0
4	97.625	97.625	0.0
5	110.778	110.778	0.0
6	69.501	69.501	0.0
7	58.051	58.051	0.0
8	74.437	74.437	0.0
9	93.44	93.44	0.0
10	42.191	42.191	0.0

AUClast

Subject	Value	Reference	Difference
1	9566.6	9566.6	0.0
2	10054.3	10054.3	0.0
3	5392.46	5392.46	0.0
4	9297.1	9297.1	0.0
5	9519.18	9519.18	0.0
6	6948.99	6948.99	0.0
7	6988.77	6988.77	0.0
8	7058.82	7058.82	0.0
9	8302.37	8302.37	0.0
10	5486.84	5486.84	0.0

AUCtau

Subject	Value	Reference	Difference
1	1268.28	1268.28	0.0
2	1831.82	1831.82	0.0
3	754.649	754.649	0.0
4	1336.48	1336.48	0.0
5	1310.9	1310.9	0.0
6	1114.24	1114.24	0.0
7	1079.37	1079.37	0.0
8	766.62	766.62	0.0
9	1219.63	1219.63	0.0
10	970.306	970.306	0.0

AUMCtau

Subject	Value	Reference	Difference
1	5477.2	5477.2	0.0
2	8367.57	8367.57	0.0
3	3455.35	3455.35	0.0
4	6014.65	6014.65	0.0
5	6609.79	6609.79	0.0
6	5064.72	5064.72	0.0
7	4976.96	4976.96	0.0
8	2863.01	2863.01	0.0
9	5386.88	5386.88	0.0
10	4713.48	4713.48	0.0

AUCall

Subject	Value	Reference	Difference
1	9566.6	9566.6	0.0
2	10054.3	10054.3	0.0
3	5392.46	5392.46	0.0
4	9297.1	9297.1	0.0
5	9519.18	9519.18	0.0
6	6948.99	6948.99	0.0
7	6988.77	6988.77	0.0
8	7058.82	7058.82	0.0
9	8302.37	8302.37	0.0
10	5486.84	5486.84	0.0

Rsq

Subject	Value	Reference	Difference
1	0.786077	0.786077	0.0
2	0.992764	0.992764	0.0
3	0.813589	0.813589	0.0
4	0.918859	0.918859	0.0
5	0.85336	0.85336	0.0
6	0.950119	0.950119	0.0
7	0.970312	0.970312	0.0
8	0.947969	0.947969	0.0
9	0.947538	0.947538	0.0
10	0.880923	0.880923	0.0

ARsq

Subject	Value	Reference	Difference
1	0.714769	0.714769	0.0
2	0.990351	0.990351	0.0
3	0.776307	0.776307	0.0
4	0.837717	0.837717	0.0
5	0.82892	0.82892	0.0
6	0.925179	0.925179	0.0
7	0.960416	0.960416	0.0
8	0.921954	0.921954	0.0
9	0.921307	0.921307	0.0
10	0.863912	0.863912	0.0

Kel

Subject	Value	Reference	Difference
1	0.00338474	0.00338474	0.0
2	0.0141063	0.0141063	0.0
3	0.00329143	0.00329143	0.0
4	0.00769534	0.00769534	0.0
5	0.00681333	0.00681333	0.0
6	0.00769228	0.00769228	0.0
7	0.012459	0.012459	0.0
8	0.00893008	0.00893008	0.0
9	0.00564586	0.00564586	0.0
10	0.0171897	0.0171897	0.0

HL

Subject	Value	Reference	Difference
1	204.786	204.786	0.0
2	49.1374	49.1374	0.0
3	210.591	210.591	0.0
4	90.0736	90.0736	0.0
5	101.734	101.734	0.0
6	90.1095	90.1095	0.0
7	55.6345	55.6345	0.0
8	77.6194	77.6194	0.0
9	122.771	122.771	0.0
10	40.3233	40.3233	0.0

Clast_pred

Subject	Value	Reference	Difference
1	117.306	117.306	0.0
2	82.5367	82.5367	0.0
3	66.9311	66.9311	0.0

Subject	Value	Reference	Difference
4	100.768	100.768	0.0
5	105.298	105.298	0.0
6	71.9399	71.9399	0.0
7	61.1727	61.1727	0.0
8	75.6043	75.6043	0.0
9	93.7618	93.7618	0.0
10	38.8109	38.8109	0.0

AUCinf

Subject	Value	Reference	Difference
1	42906.2	42906.2	0.0
2	16097.0	16097.0	0.0
3	26022.1	26022.1	0.0
4	21983.3	21983.3	0.0
5	25778.2	25778.2	0.0
6	15984.1	15984.1	0.0
7	11648.2	11648.2	0.0
8	15394.4	15394.4	0.0
9	24852.5	24852.5	0.0
10	7941.27	7941.27	0.0

AUCpct

Subject	Value	Reference	Difference
1	77.7035	77.7035	0.0
2	37.5395	37.5395	0.0
3	79.2774	79.2774	0.0
4	57.7084	57.7084	0.0
5	63.0727	63.0727	0.0
6	56.5258	56.5258	0.0
7	40.001	40.001	0.0
8	54.1467	54.1467	0.0
9	66.5935	66.5935	0.0
10	30.9073	30.9073	0.0

MRTtauinf

Subject	Value	Reference	Difference
1	299.792	299.792	0.0
2	74.655	74.655	0.0
3	305.92	305.92	0.0
4	143.538	143.538	0.0
5	173.022	173.022	0.0
6	124.653	124.653	0.0

Subject	Value	Reference	Difference
7	92.7359	92.7359	0.0
8	175.462	175.462	0.0
9	178.811	178.811	0.0
10	69.5163	69.5163	0.0

Cltau

Subject	Value	Reference	Difference
1	0.0788472	0.0788472	0.0
2	0.0545905	0.0545905	0.0
3	0.132512	0.132512	0.0
4	0.0748234	0.0748234	0.0
5	0.0762832	0.0762832	0.0
6	0.0897472	0.0897472	0.0
7	0.0926469	0.0926469	0.0
8	0.130443	0.130443	0.0
9	0.081992	0.081992	0.0
10	0.10306	0.10306	0.0

Vztau

Subject	Value	Reference	Difference
1	23.2949	23.2949	0.0
2	3.86993	3.86993	0.0
3	40.2597	40.2597	0.0
4	9.7232	9.7232	0.0
5	11.1962	11.1962	0.0
6	11.6672	11.6672	0.0
7	7.43617	7.43617	0.0
8	14.6071	14.6071	0.0
9	14.5225	14.5225	0.0
10	5.99545	5.99545	0.0

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)
```

Cmax

Subject	Value	Reference	Difference
1	190.869	190.869	0.0
2	261.177	261.177	0.0
3	105.345	105.345	0.0
4	208.542	208.542	0.0
5	169.334	169.334	0.0
6	154.648	154.648	0.0
7	153.254	153.254	0.0
8	138.327	138.327	0.0
9	167.347	167.347	0.0
10	125.482	125.482	0.0

Tmax

Subject	Value	Reference	Difference
1	1.0	1.0	0.0
2	1.0	1.0	0.0
3	1.5	1.5	0.0
4	1.0	1.0	0.0
5	4.0	4.0	0.0
6	2.5	2.5	0.0
7	2.5	2.5	0.0
8	4.0	4.0	0.0
9	3.0	3.0	0.0
10	2.0	2.0	0.0

Cdose

Subject	Value	Reference	Difference
1	0.0	0.0	0.0
2	0.0	0.0	0.0
3	0.0	0.0	0.0
4	0.0	0.0	0.0
5	0.0	0.0	0.0
6	0.0	0.0	0.0
7	0.0	0.0	0.0
8	0.0	0.0	0.0
9	0.0	0.0	0.0

Subject	Value	Reference	Difference
10	0.0	0.0	0.0

Clast

Subject	Value	Reference	Difference
1	112.846	112.846	0.0
2	85.241	85.241	0.0
3	67.901	67.901	0.0
4	97.625	97.625	0.0
5	110.778	110.778	0.0
6	69.501	69.501	0.0
7	58.051	58.051	0.0
8	74.437	74.437	0.0
9	93.44	93.44	0.0
10	42.191	42.191	0.0

AUClast

Subject	Value	Reference	Difference
1	9585.42	9585.42	0.0
2	10112.2	10112.2	0.0
3	5396.55	5396.55	0.0
4	9317.84	9317.84	0.0
5	9561.26	9561.26	0.0
6	6966.6	6966.6	0.0
7	7029.57	7029.57	0.0
8	7110.67	7110.67	0.0
9	8315.08	8315.08	0.0
10	5620.89	5620.89	0.0

AUCtau

Subject	Value	Reference	Difference
1	1670.1	1670.1	0.0
2	2380.27	2380.27	0.0
3	980.346	980.346	0.0
4	1711.04	1711.04	0.0
5	1738.46	1738.46	0.0
6	1410.0	1410.0	0.0
7	1436.56	1436.56	0.0
8	1105.07	1105.07	0.0
9	1638.19	1638.19	0.0
10	1293.71	1293.71	0.0

AUMCtau

Subject	Value	Reference	Difference
1	9984.82	9984.82	0.0
2	14630.1	14630.1	0.0
3	6024.5	6024.5	0.0
4	10299.7	10299.7	0.0
5	11466.1	11466.1	0.0
6	8467.36	8467.36	0.0
7	9003.02	9003.02	0.0
8	6457.01	6457.01	0.0
9	10095.8	10095.8	0.0
10	8367.3	8367.3	0.0

AUCall

Subject	Value	Reference	Difference
1	9585.42	9585.42	0.0
2	10112.2	10112.2	0.0
3	5396.55	5396.55	0.0
4	9317.84	9317.84	0.0
5	9561.26	9561.26	0.0
6	6966.6	6966.6	0.0
7	7029.57	7029.57	0.0
8	7110.67	7110.67	0.0
9	8315.08	8315.08	0.0
10	5620.89	5620.89	0.0

Rsq

Subject	Value	Reference	Difference
1	0.786077	0.786077	0.0
2	0.992764	0.992764	0.0
3	0.813589	0.813589	0.0
4	0.918859	0.918859	0.0
5	0.863677	0.863677	0.0
6	0.950119	0.950119	0.0
7	0.970312	0.970312	0.0
8	0.947969	0.947969	0.0
9	0.947538	0.947538	0.0
10	0.879699	0.879699	0.0

ARsq

Subject	Value	Reference	Difference
1	0.714769	0.714769	0.0
2	0.990351	0.990351	0.0
3	0.776307	0.776307	0.0
4	0.837717	0.837717	0.0
5	0.844202	0.844202	0.0
6	0.925179	0.925179	0.0
7	0.960416	0.960416	0.0
8	0.921954	0.921954	0.0
9	0.921307	0.921307	0.0
10	0.867669	0.867669	0.0

Kel

Subject	Value	Reference	Difference
1	0.00338474	0.00338474	0.0
2	0.0141063	0.0141063	0.0
3	0.00329143	0.00329143	0.0
4	0.00769534	0.00769534	0.0
5	0.00685799	0.00685799	0.0
6	0.00769228	0.00769228	0.0
7	0.012459	0.012459	0.0
8	0.00893008	0.00893008	0.0
9	0.00564586	0.00564586	0.0
10	0.0165438	0.0165438	0.0

HL

Subject	Value	Reference	Difference
1	204.786	204.786	0.0
2	49.1374	49.1374	0.0
3	210.591	210.591	0.0
4	90.0736	90.0736	0.0
5	101.072	101.072	0.0
6	90.1095	90.1095	0.0
7	55.6345	55.6345	0.0
8	77.6194	77.6194	0.0
9	122.771	122.771	0.0
10	41.8978	41.8978	0.0

Clast_pred

Subject	Value	Reference	Difference
1	117.306	117.306	0.0
2	82.5367	82.5367	0.0
3	66.9311	66.9311	0.0

Subject	Value	Reference	Difference
4	100.768	100.768	0.0
5	105.196	105.196	0.0
6	71.9399	71.9399	0.0
7	61.1727	61.1727	0.0
8	75.6043	75.6043	0.0
9	93.7618	93.7618	0.0
10	39.4088	39.4088	0.0

AUCinf

Subject	Value	Reference	Difference
1	42925.0	42925.0	0.0
2	16154.9	16154.9	0.0
3	26026.2	26026.2	0.0
4	22004.1	22004.1	0.0
5	25714.4	25714.4	0.0
6	16001.8	16001.8	0.0
7	11689.0	11689.0	0.0
8	15446.2	15446.2	0.0
9	24865.2	24865.2	0.0
10	8171.16	8171.16	0.0

AUCpct

Subject	Value	Reference	Difference
1	77.6694	77.6694	0.0
2	37.405	37.405	0.0
3	79.2649	79.2649	0.0
4	57.6541	57.6541	0.0
5	62.8175	62.8175	0.0
6	56.4636	56.4636	0.0
7	39.8614	39.8614	0.0
8	53.9649	53.9649	0.0
9	66.5594	66.5594	0.0
10	31.2106	31.2106	0.0

MRTtauinf

Subject	Value	Reference	Difference
1	302.403	302.403	0.0
2	75.5906	75.5906	0.0
3	312.721	312.721	0.0
4	148.341	148.341	0.0
5	172.093	172.093	0.0
6	130.191	130.191	0.0

Subject	Value	Reference	Difference
7	91.9083	91.9083	0.0
8	161.574	161.574	0.0
9	176.305	176.305	0.0
10	70.2607	70.2607	0.0

Cltau

Subject	Value	Reference	Difference
1	0.0718519	0.0718519	0.0
2	0.0504145	0.0504145	0.0
3	0.122406	0.122406	0.0
4	0.070133	0.070133	0.0
5	0.0690266	0.0690266	0.0
6	0.0851065	0.0851065	0.0
7	0.0835329	0.0835329	0.0
8	0.10859	0.10859	0.0
9	0.0732516	0.0732516	0.0
10	0.0927567	0.0927567	0.0

Vztau

Subject	Value	Reference	Difference
1	21.2282	21.2282	0.0
2	3.57389	3.57389	0.0
3	37.1892	37.1892	0.0
4	9.11369	9.11369	0.0
5	10.0651	10.0651	0.0
6	11.0639	11.0639	0.0
7	6.70465	6.70465	0.0
8	12.1601	12.1601	0.0
9	12.9744	12.9744	0.0
10	5.60675	5.60675	0.0

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.

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

Appendix 1

Testing 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

Appendix 2

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.