

R Scripts to Streamline Non-Compartmental Analysis (NCA):

A Data Programmer's Dream



Table of contents

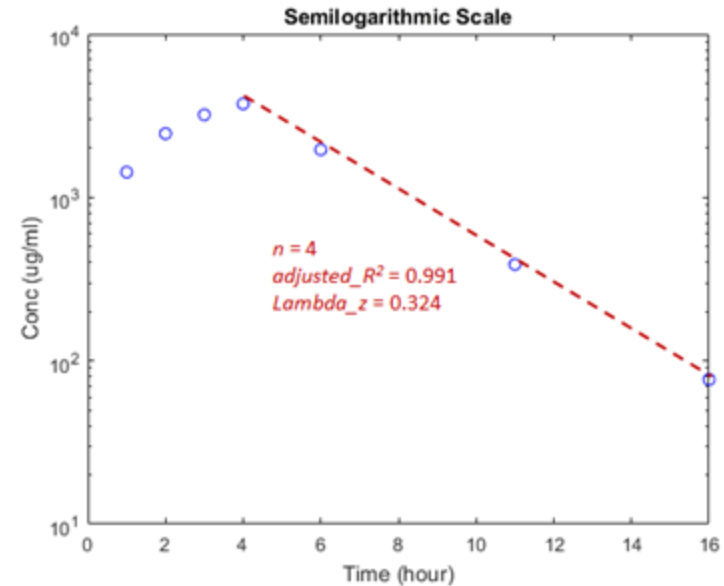
- Introduction
- Current landscape
- Project purpose
- Future horizon
- aNCA Demo
- Call for actions

Introduction

Introduction

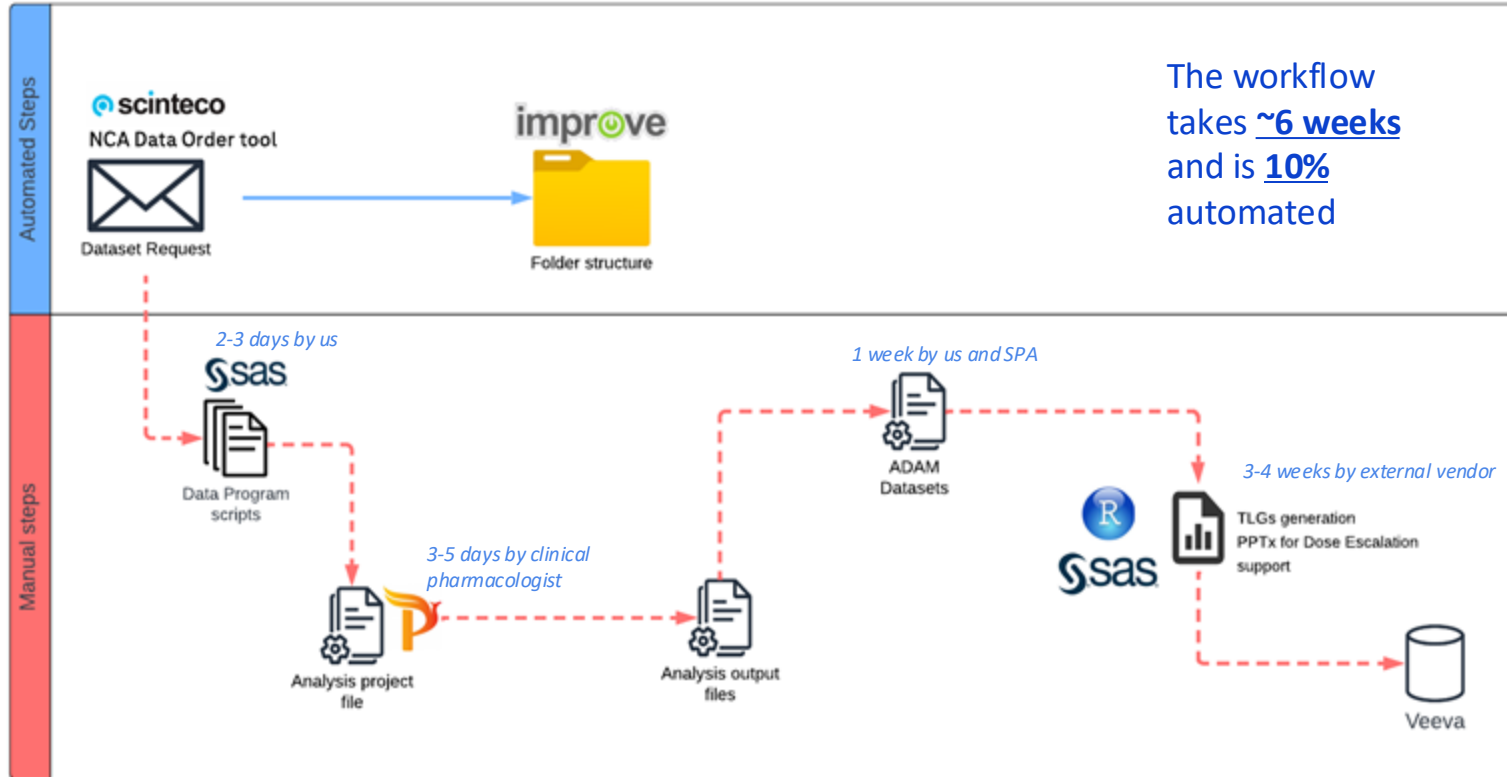
What is a Non-Compartmental Analysis (NCA)?

- **Patient Sample Collection:**
Patients visit the Clinical Research Organization (CRO) for blood sample collection at specific times after dosing.
- **Sample Processing & Shipment:**
Blood samples are processed (plasma/serum) and shipped to bioanalytical labs.
- **Bioanalysis:**
Drug concentrations are measured using techniques like LC-MS to generate concentration-time data.
- **Data Delivery & NCA:**
The concentration data is analyzed through NCA to calculate key PK parameters (AUC, C_{max}, t_{1/2}, CL, V_d).
- **Regulatory Use:**
NCA results inform dose-exposure relationships and are used for regulatory submissions in bioequivalence studies.



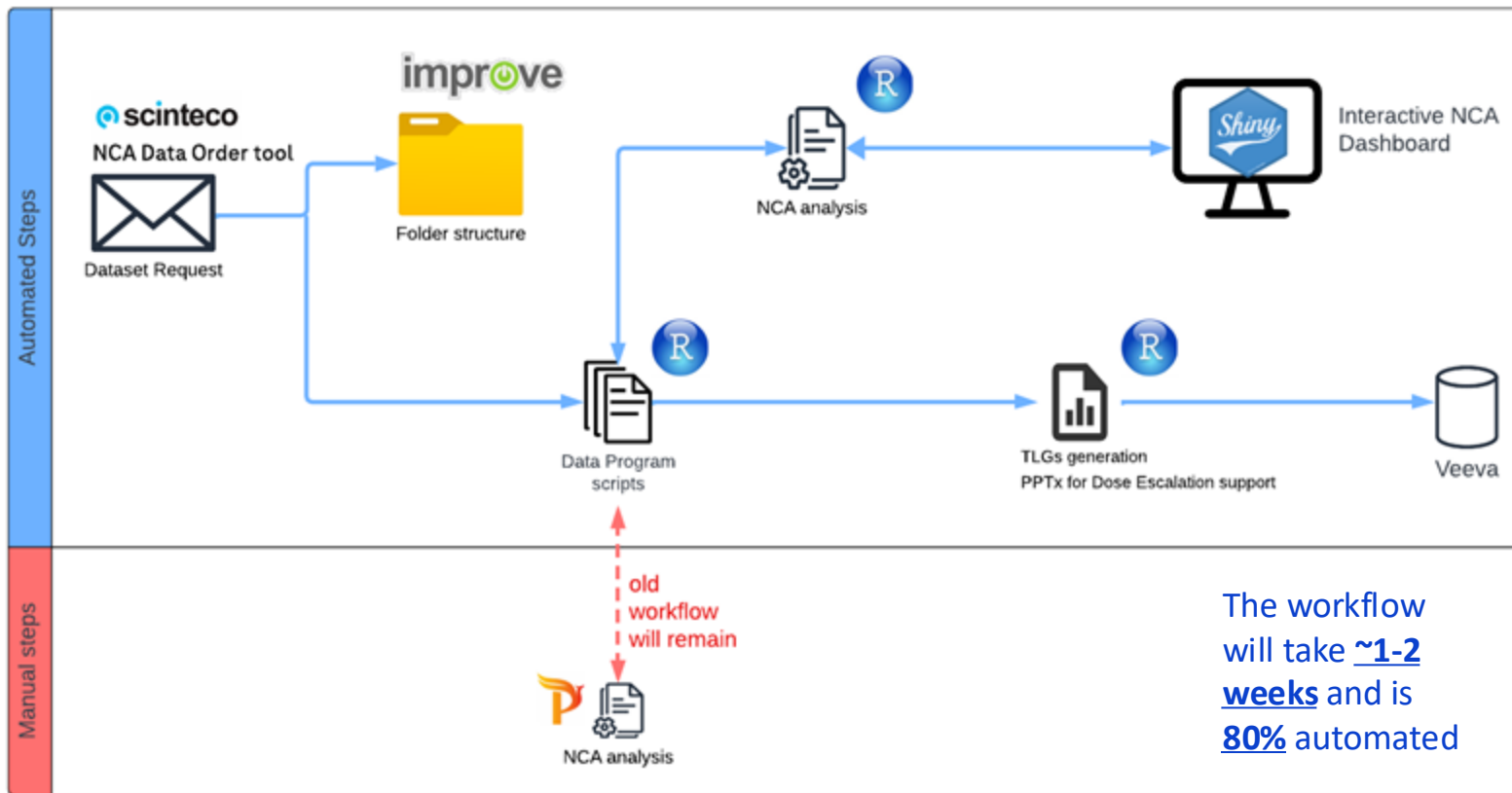
Current landscape

aNCA - Current situation



Future Horizon

aNCA - Future Horizon



Users
expected: 50-80%

Users
expected: 50-20%

Project purpose

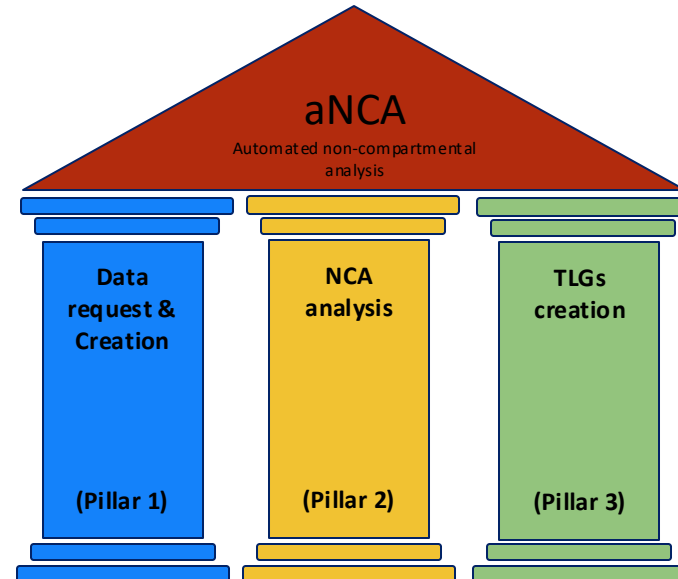
Project Overview



Project purpose

High level Product Vision

- Automate and streamline the E2E NCA process from pre clinical AND clinical
- Open up potential for “reverse translation” as data structures are harmonized
- More independence from external software providers
- Consists in 3 main Pillars
 - Dataset request and automated data creation
 - Automated Analysis
 - Automated outputs creation (CSR, dose escalation,...)
- Boost data quality and increase output creation efficiency
- Speed-up NCAs while keeping control on analysis settings and access



aNCA Demo

aNCA Demo



Call for actions

Working Open Source: Pharmaverse*

- **Join us** in advancing Open-Source Pharma for the community!
<https://github.com/pharmaverse/aNCA>
- **Opportunity to learn from each other** and advance together
- **Sharing ideas**, different perspectives and concerns from our different expertise
- **Do not hesitate to reach out** anytime for any code explanation, detail or development questions, either by GitHub or email/chat or Slack Channel



Login and Select File Path

Browse ADPC... CSV rds

Select the study type

☒ SAD☐ MAD

Add Filter

Select Column: Condition:

USUBJID

==

Value:

Submit

Remove Filter

MATRIX

Visit.Number

Visit.name

Planned.Study

Date.Time.c

Planned.Tin

Planned.Tin

Time.Point.

clinical Data

CSV

Clinical Data Summary (CSV)

Show 10 entries

Search:

	USUBJID	Reference.ID	ANALYTE	CONC	Numeric.Result.Finding.In.Standard.Units	CONCUNIT	MATRIX	Visit.Number	Visit.name	Planned
1	11101	EP928522F08	DummyRO	0	0.0004085	ug/mL	SERUM	1	Cycle 1 Day 1	
2	11101	EP928530F01	DummyRO	7.58	7.58	ug/mL	SERUM	1	Cycle 1 Day 1	
3	11101	EP928531F01	DummyRO	8.5	8.5	ug/mL	SERUM	1	Cycle 1 Day 1	
4	11101	EP928532F01	DummyRO	8.66	8.66	ug/mL	SERUM	1	Cycle 1 Day 1	
5	11101	EP928529F01	DummyRO	7.03	7.03	ug/mL	SERUM	2	Cycle 1 Day 2	
6	11101	EP928528F01	DummyRO	3.78	3.78	ug/mL	SERUM	4	Cycle 1 Day 4	
7	11101	EP928501F13	DummyRO	0.0063	0.0063	ug/mL	SERUM	999	Discontinuation Visit	
8	11101	EP433426G11	DummyRO	0	0.0004085	ug/mL	SERUM	997	Safety Follow Up	
9	11101	EP304624H16	DummyRO	0	0.0004085	ug/mL	SERUM	201	Cycle 2 Day 1	
10	11101	EP306095H01	DummyRO	7.28	7.28	ug/mL	SERUM	201	Cycle 2 Day 1	

Showing 1 to 10 of 538 entries

Previous

1

2

3

4

5

...

54

Next

Data Selection

Settings

Slope Selector

Exclusions

Upload Settings

 No file selected

Choose the analyte :

DummyRO

Show 10 entries

Search:

ATAFD	NTAFD	TIMEUNIT	ACONC	CONCUNIT	LLOQ	ADM	ADUR	NDUR	DOSE	DOSEUNIT	AGE	RACE	SEX	TAU
-0.17	0	Hours	0	ug/mL	0	Infusion	1.5	1.5	35	mg	52	WHITE	M	
1.5	0.5	Hours	7.58	ug/mL	0	Infusion	1.5	1.5	35	mg	52	WHITE	M	
5	4	Hours	8.5	ug/mL	0	Infusion	1.5	1.5	35	mg	52	WHITE	M	
7.5	8	Hours	8.66	ug/mL	0	Infusion	1.5	1.5	35	mg	52	WHITE	M	
27.25	48	Hours	7.03	ug/mL	0	Infusion	1.5	1.5	35	mg	52	WHITE	M	
73.08	144	Hours	3.78	ug/mL	0	Infusion	1.5	1.5	35	mg	52	WHITE	M	
383.67		Hours	0.0063	ug/mL	0	Infusion	1.5	1.5	35	mg	52	WHITE	M	
2425.17		Hours	0	ug/mL	0	Infusion	1.5	1.5	35	mg	52	WHITE	M	
7750.58	504	Hours	0	ug/mL	0	Infusion	1.5	1.5	35	mg	52	WHITE	M	
7752.42	504.5	Hours	7.28	ug/mL	0	Infusion	1.5	1.5	35	mg	52	WHITE	M	

Showing 1 to 10 of 538 entries

Previous 1 2 3 4 5 ... 54 Next

Data Selection

Settings

Slope Selector

Exclusions

Choose the Dose Number:

1 2

Extrapolation Method:

LinearUp LogDown

☒ Select Partial AUC

+

-

Min:

0

Max:

24

Rule Sets:

☒ RSQADJ:

>=

0.7

☒

AUCPEO

<=

20

☒ SPAN:

>=

2

NCA Results

Slopes

Exclusions

Summary Tables

Save Project Settings

Select Parameters :

AILAMZ, AUCALL, AUCIFO, AUCIFOD, AL

Select All

Deselect All

Search:

LAMZHL	✓
LAMZICPT	✓
LAMZLL	✓
LAMZNPT	✓
LAMZUL	✓
MRTEVIFO	✓
MRTEVIFP	✓
MRTEVLST	✓
MRTIVIFO	✓
MRTIVIFP	✓
MRTIVLST	✓
R2	✓
R2ADJ	✓
R2flagged	✓
SPAN	✓
SPANflagged	✓
SWING	✓
SWINGTAU	✓
TLAG	✓
TLST	✓
TMAX	✓
TMIN	✓
VSSO	✓
VSSP	✓
VZFO	✓
VZFP	✓
VZFSS	✓
VZO	✓
VZP	✓
VZSS	✓

JND	ANALYTE	MATRIX	PROFILE	PROFTYPE	GROUP	GROUPN	GROUPU	TIMEUNIT	CONCUN
O	DummyRO	SERUM	1	SD	35	35	mg	HOURS	ug/mL
O	DummyRO	SERUM	2	SD	35	35	mg	HOURS	ug/mL
O	DummyRO	SERUM	1	SD	35	35	mg	HOURS	ug/mL
O	DummyRO	SERUM	2	SD	35	35	mg	HOURS	ug/mL
O	DummyRO	SERUM	1	SD	35	35	mg	HOURS	ug/mL
O	DummyRO	SERUM	2	SD	35	35	mg	HOURS	ug/mL
O	DummyRO	SERUM	1	SD	35	35	mg	HOURS	ug/mL
O	DummyRO	SERUM	2	SD	35	35	mg	HOURS	ug/mL
O	DummyRO	SERUM	1	SD	35	35	mg	HOURS	ug/mL
O	DummyRO	SERUM	1	SD	35	35	mg	HOURS	ug/mL

Plots per page:

2

Search Patient

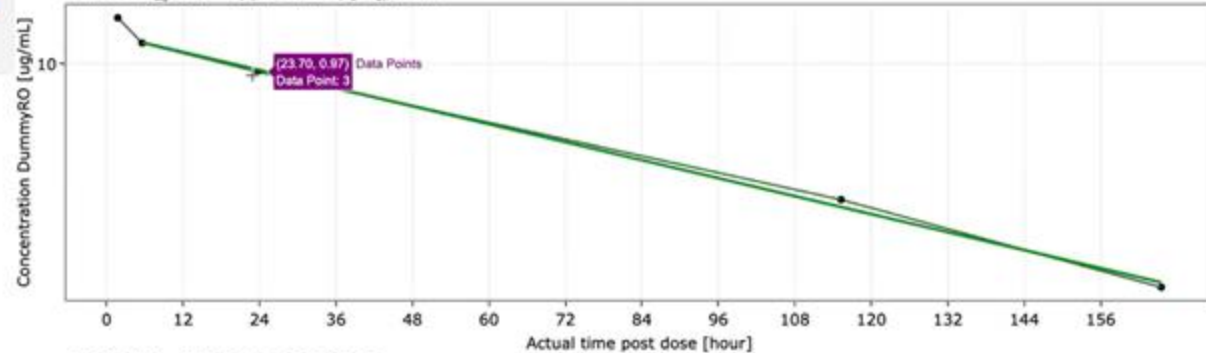
11102

Search

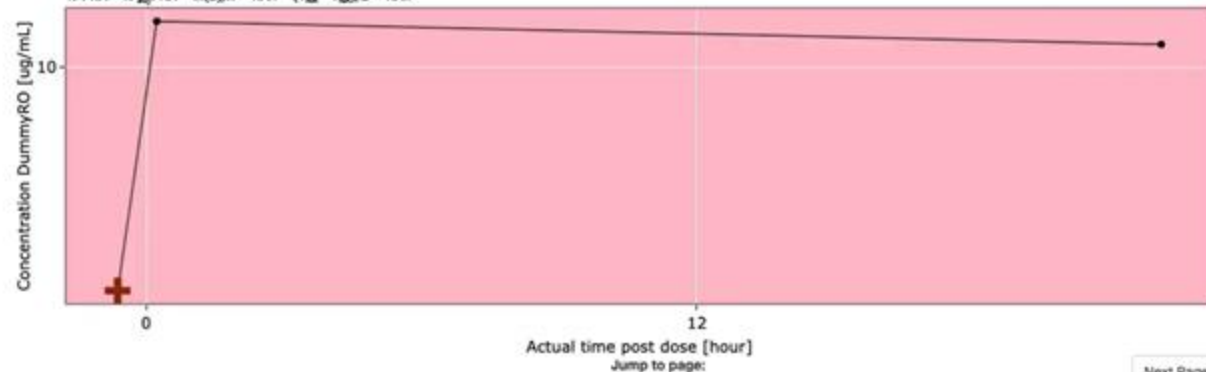
Reset



USUBJID: 11102, PROFILE: 1

 $R^2: 0.998$ $R^2_{adj}: 0.997$ $\ln(2)/\lambda = 53.7h$ $(T_1 - T_3)/2 = 80h$ 

USUBJID: 11102, PROFILE: 2

 $R^2: NA$ $R^2_{adj}: NA$ $\ln(2)/\lambda = NAh$ $(T_{obs} - T_{pred})/2 = NAh$ 

General Plotting

Dose Escalation

AutosideR

Individual Plots

Mean Plots

Choose the analyte :

DummyR0

Submit

Plots per page:

4



Specify the type of plot

Select the Plot type:

☒ Lin☐ Log

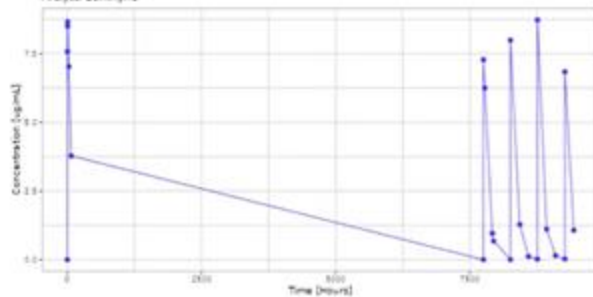
Choose the Timescale

☒ All Time☐ By Cycle

Choose the cycle :

1

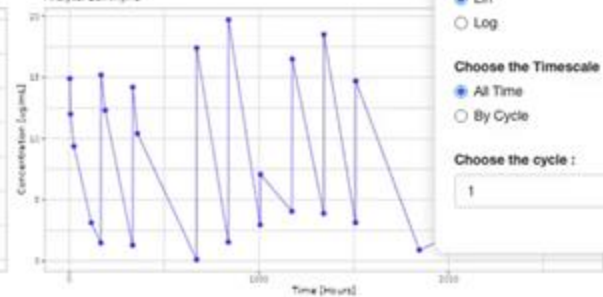
Plot of PK Concentration - Time Profile, by Patient: PK Population, XX00001

Subject: 11101
Analyte: DummyR0

DOSE → 11

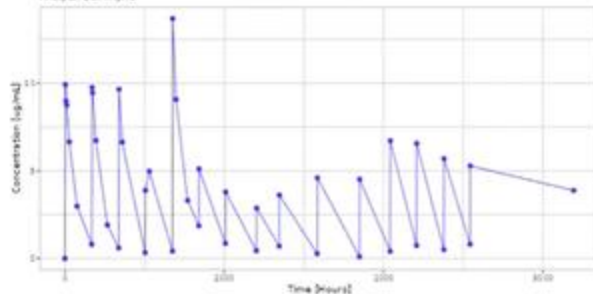
Showing 1 to 4 of 23 plots

Plot of PK Concentration - Time Profile, by Patient: PK Population, >

Subject: 11102
Analyte: DummyR0

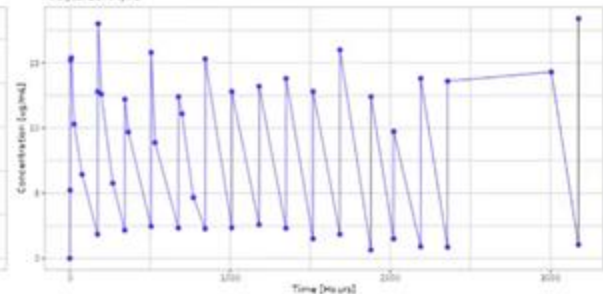
DOSE → 11

Plot of PK Concentration - Time Profile, by Patient: PK Population, XX00001

Subject: 11103
Analyte: DummyR0

DOSE → 11

Plot of PK Concentration - Time Profile, by Patient: PK Population, XX00001

Subject: 11104
Analyte: DummyR0

DOSE → 11