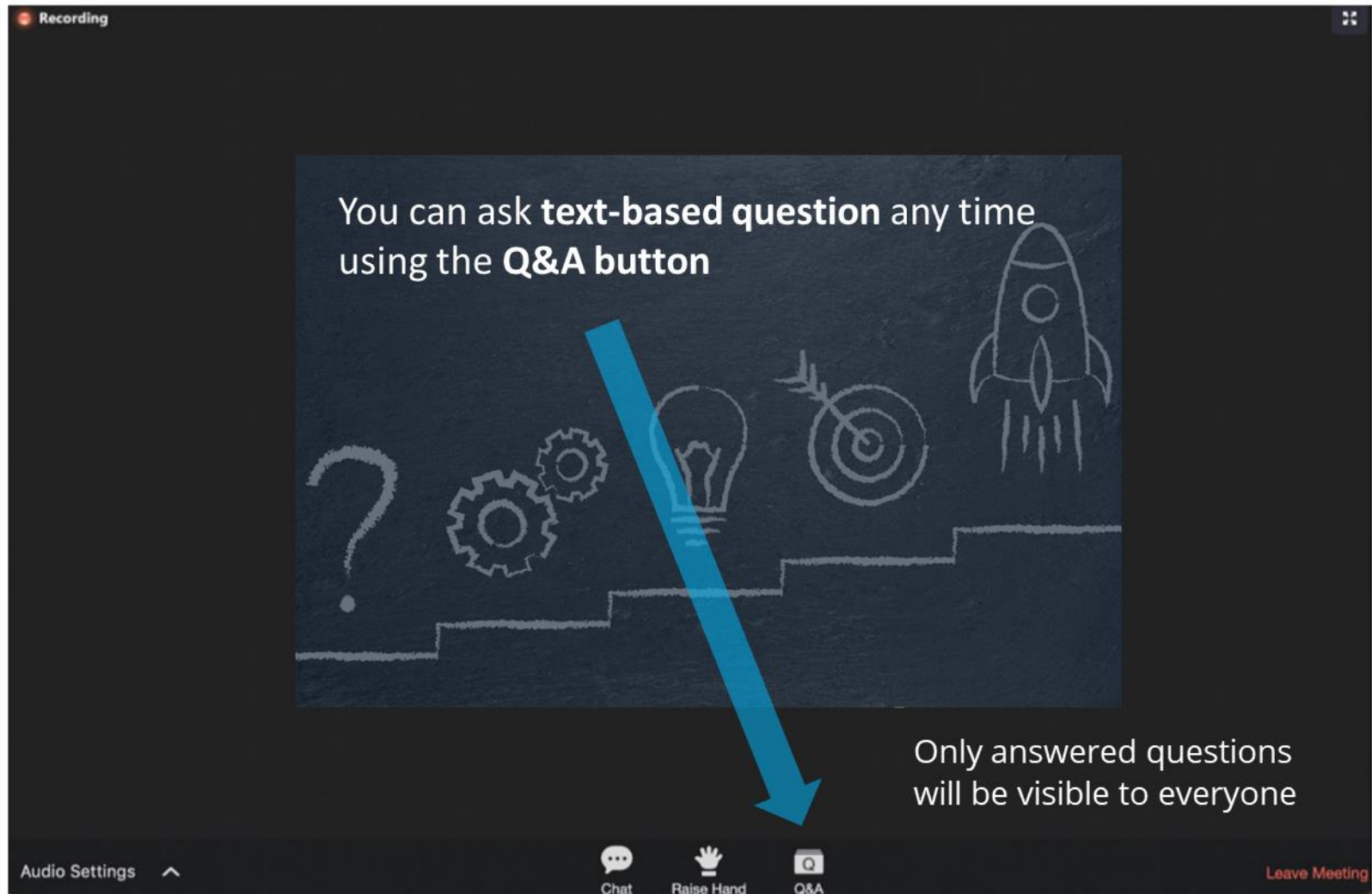


- The webinar starts at **2:00 pm Basel Time**  
**8:00 am East Coast Time**
- Everyone is placed on mute during the webinar
- Webinar material (including presentation) can be downloaded here:  
<https://training.intiquan.com/MIDDmodules/M2.2.zip>
- The webinar will be recorded
  - Recording will be made available on the following link:  
<https://training.intiquan.com/MIDDmodules/M2.2.mp4>
  - Recording available ~1 day after the webinar



# Q&A during Webinar



Recording

You can ask **text-based question** any time using the **Q&A button**

Only answered questions will be visible to everyone

Audio Settings ^

Chat Raise Hand Q&A

Leave Meeting

The screenshot shows a webinar interface with a dark background. At the top left, there is a 'Recording' indicator. The main content area features a chalkboard-style illustration with a sequence of icons: a question mark, two interlocking gears, a lightbulb, a target with an arrow, and a rocket. A large blue arrow points from the text 'Q&A button' to the 'Q&A' button in the bottom toolbar. The bottom toolbar includes 'Audio Settings', 'Chat', 'Raise Hand', 'Q&A', and 'Leave Meeting'.

# Module 2.4

## PKPD Modeling Workflow(s)

IntiQuan Webinar Series on efficient support of  
Model Informed Drug Development (MIDD)

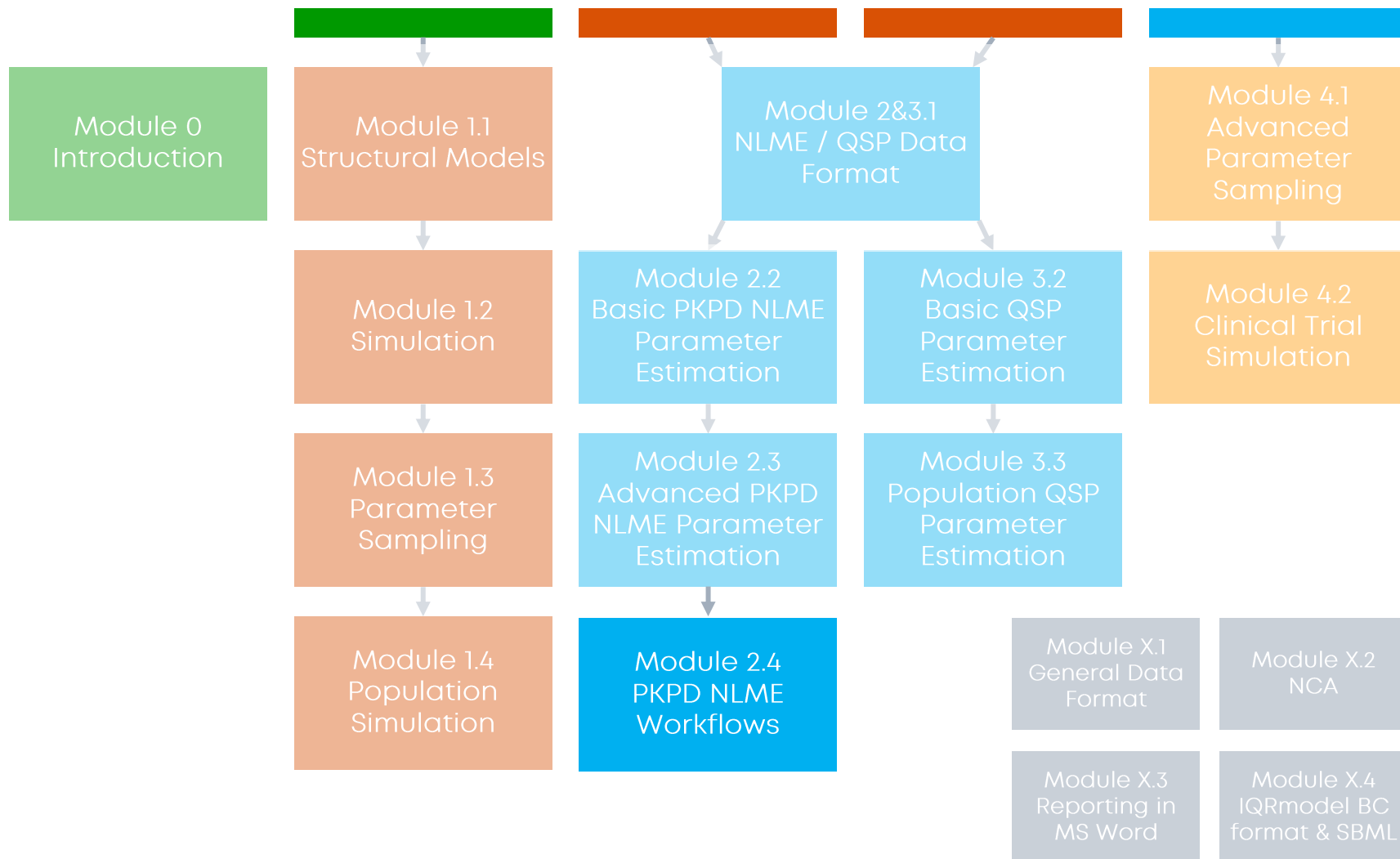
# Outline

1. Background
2. Example workflows
3. Special elements
4. Conclusions
5. Outlook webinar modules
6. Q&A

# Background

# Overview of Webinar Series by IntiQuan

IntiQuan Webinar Series on efficient support of Model Informed Drug Development (MIDD)



# Goals of this module

- **You will have seen examples on how to**
  - ✓ Set up complete workflows - from data to report
- **Giving you the possibility to use the approaches in own projects**

# Download of webinar material

- The Webinar material is available as a convenient download
- After installation of IQR Tools, simply type the following

```
library(IQRtools)  
install_MIDDmodule("2.4")
```

- Or download directly from:

```
https://training.intiquan.com/MIDDmodules/M2.4.zip
```

Modules 2.2, 2.3, & 2.4 require presence of NONMEM and/or MONOLIX on the system to fully run the examples

Convenient setup of IQR Tools options, including interfacing with NONMEM and MONOLIX on the system through the IQR Tools options setup:

```
library(IQRtools)
setup_IQRtools()
```

```
49 # UNIX setup
50 # -----
51 # Name of the NONMEM executable or shell script. Required calling syntax:
52 # "command controlfile outputfile"
53 # NONMEM Version 7.2/7.3/7.4 have been tested with IQR Tools.
54 .PATH_SYSTEM_NONMEM <- list(
55   # First entry is used as default version
56   NM743 = 'nmfe74'
57 )
58
59 # MacOS setup
60 # -----
61 # Name of the NONMEM executable or shell script. Required calling syntax:
62 # "command controlfile outputfile"
63 # NONMEM Version 7.2/7.3/7.4 have been tested with IQR Tools.
64 .PATH_SYSTEM_NONMEM <- list(
65   NM74 = "nmfe74"
66 )
67
68 # WINDOWS setup
69 # -----
70 # Path to NONMEM (Version 7.2/7.3/7.4 have been tested) batch files. The info
71 # is provided as a list. By default the first entry is used but the user can
72 # switch when calling the IQRnlmeProject function.
73 .PATH_SYSTEM_NONMEM <- list(
74   NM74 = "C:/nm74g64/run/nmfe74.bat"
75 )
```

**NONMEM7™**

The program for Nonlinear  
Mixed Effects Modeling



Parallel NONMEM runs handled by IQR Tools as well – can be set up in options as well.  
Requires a shell/batch script available on systems command line with the following calling syntax:

command NRCORES controlfile outputfile"

## IQdesktop

- Helps getting the complete environment set up in ~0 min
- Is freely available
- Requires admin rights on your computer (to install docker)
- *Bring your own NONMEM and/or MONOLIX licenses*
- ...

- More information:  
<https://iqdesktop.intiquan.com>

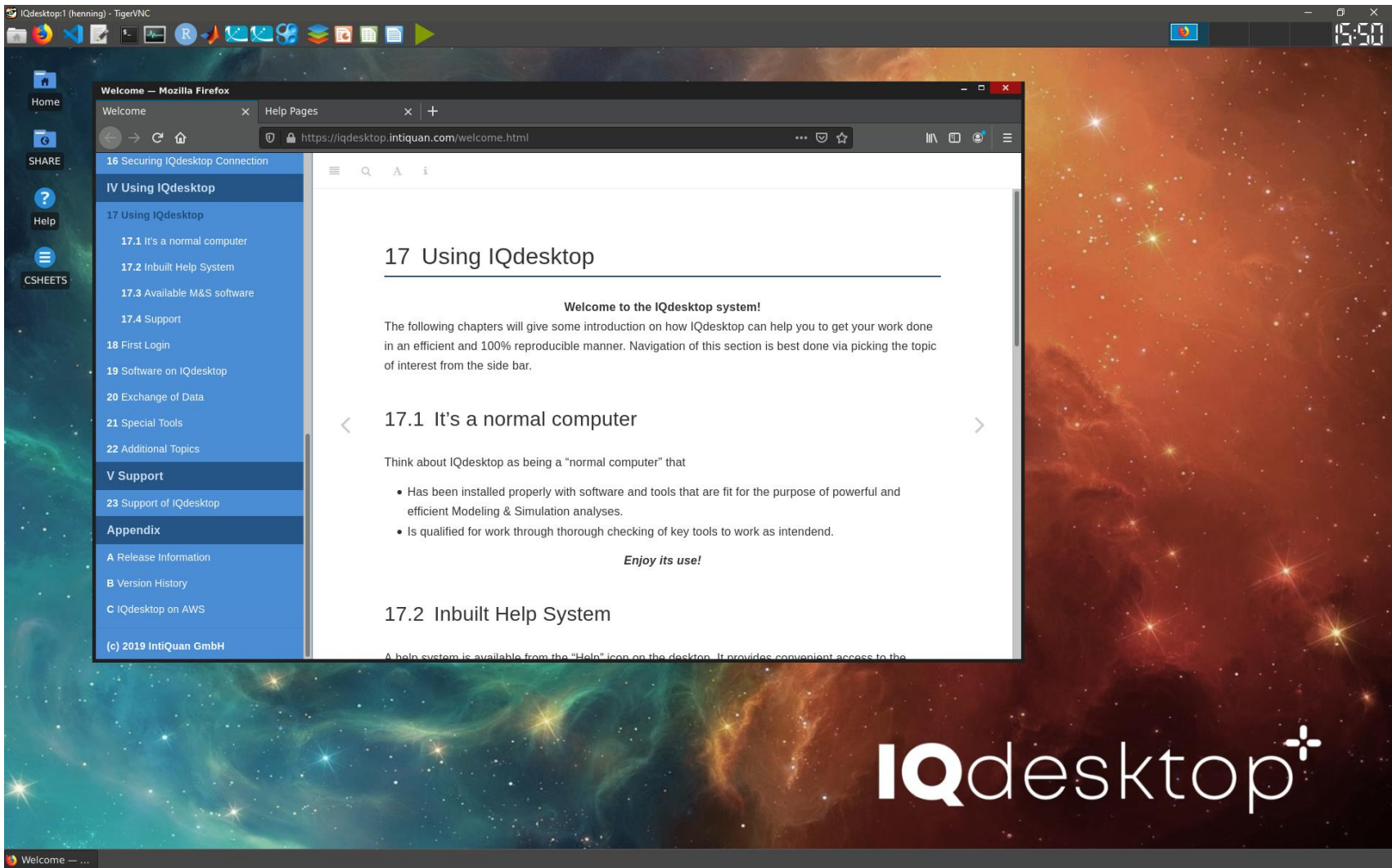
### ■ Installation guide

- [Windows](#)
- [macOS](#)
- [Linux](#)
- [Cloud](#)

[https://iqdesktop.intiquan.com/doc/IQDesktop\\_Installation\\_Windows.mp4](https://iqdesktop.intiquan.com/doc/IQDesktop_Installation_Windows.mp4)

## A.1 Release V2.1.1 - 30 April 2021

- **Image name:** `intiquan/iqdesktop:2.1.1`
- **Base system:** Ubuntu 18.04
- **Connections:** VNC, SSH (incl. screen)
- **Modeling & Simulation & specific Development Tools**
  - IQR Tools (Version 1.7.0)
  - IQnca (Version 1.0.0)
  - IQReport (Version 1.51)
  - IQSlides (Version 0.3.2)
  - R default (Version 3.6.3)
    - CRAN snapshot dated 2020-03-15
    - URL: <https://cran.intiquan.com/snapshot/2020-03-15>
  - R exploratory (Version 4.0.3)
    - CRAN snapshot dated 2020-12-21
    - URL: <https://cran.intiquan.com/snapshot/2020-12-21>
    - IQR Tools, IQnca, and IQSlides not installed on R 4.0.3
  - MATLAB (Version R2021A) + Simbiology and relevant toolboxes
  - NONMEM (Version 7.4.3)
  - NONMEM (Version 7.5.0)
  - MONOLIX (Version 2019R1)
  - MONOLIX (Version 2020R1)
  - CellDesigner (Version 4.4.2)
  - PsN (Version 5.0.0) (no gls and qa)
  - RHEM (Version 0.1.2)
  - Rstudio (Version 1.2.5042)
  - Jenkins 2.249.2 CI/CD server (including suggested plugins)
  - Population Isoboles R package (1.0.0)
- **Changes**
  - Update to MATLAB R2021A
  - Update to IQSlides 0.3.2



<https://iqdesktop.intiquan.com>

[https://iqdesktop.intiquan.com/doc/IQDesktop\\_Installation\\_Windows.mp4](https://iqdesktop.intiquan.com/doc/IQDesktop_Installation_Windows.mp4)

# Example workflows

# Population PK workflow - from data to report

- Functionality available in IQR Tools allows for implementation of full analysis workflows that are reproducible at any point in time
  - Reproducible conduct of a popPK
  - Fully scripted
  - From data preparation to final report
    - Fake data
    - Focus on workflow - not on completeness

The screenshot shows the SAS Universal Viewer interface. On the left, a tree view displays the workflow structure: 03\_workflows, 01\_PopPK\_Data2Report, Data, DataSource (highlighted), Models, Output, Report, and Scripts. On the right, a list of files is shown: dm.xpt, ex.xpt, lb.xpt, pc.xpt, and vs.xpt. Below the tree, a data table is displayed with columns: STUDYID, DOMAIN, USUBJID, PC380, PCTESTCD, PCTEST, PCORRES, PCORRESU, and PCSTRESC. The table contains 6 rows of data.



The screenshot shows the IQR Tools interface. On the left, a tree view displays the workflow structure: 03\_workflows, 01\_PopPK\_Data2Report, Data, DataSource, Models, Output, Report (highlighted), and Scripts. On the right, a list of files is shown: very\_basic\_report.docx and very\_basic\_report.rmd. Below the tree, a report preview is displayed. The report includes a table of model parameters, a table of model statistics, and a plot of predicted versus observed values.

PARAMETER	VALUE	SE	SD	COMMENT
CL	0.147	11.1%	-	Clearance (L/hour)
V1	2.17	8.88%	-	Central volume (L)
Q1	0.414	12.3%	-	Intercompartmental clearance (L/hour)
V1F	2.31	11.5%	-	Peripheral volume (L)

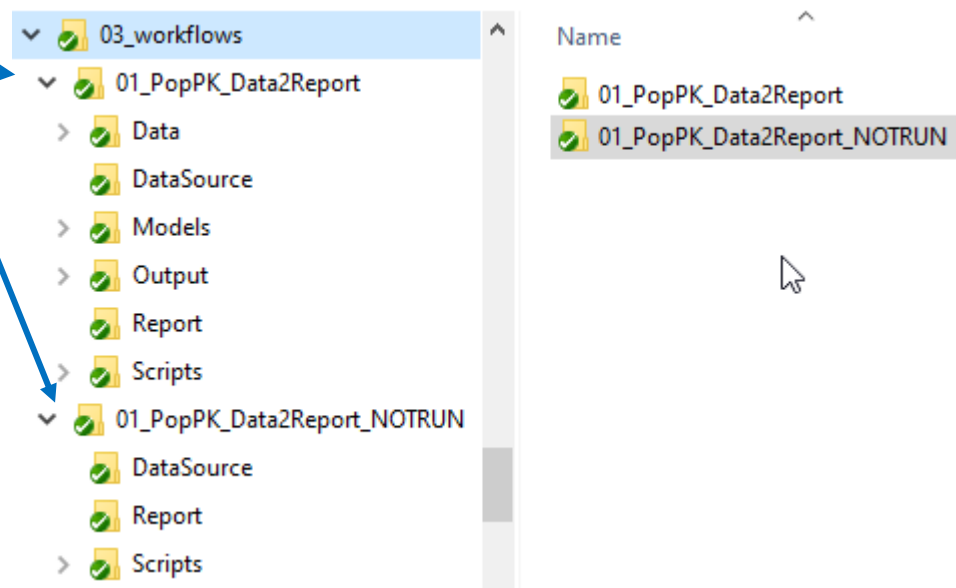
STATISTIC	VALUE	SE	SD	COMMENT
RMSE	0.283	21.8%	1.2%	Lognormal
RMSE(CV)	0.117	21.8%	0.3%	Lognormal
RMSE(CV)	0.147	21.8%	0.3%	Lognormal
RMSE(CV)	0.289	28.2%	11.2%	Lognormal

Figure 1 Prediction corrected VPC for final selected model  
Prediction-corrected Visual Predictive Check (VPC) - 95%  
Model: Output.FINALMODEL.SIS.FINALMODEL

# Population PK workflow - from data to report

- Example material contains the PopPK workflow twice

1. Fully executed
2. Only key files that need to be present to regenerate all results



Examples/03\_workflows

# Population PK workflow - from data to report

- "Base" material for the workflow analysis

## Source data

01\_PopPK\_Data2Report\_NOTRUN

- DataSource
- Report
- Scripts
  - dm.xpt
  - ex.xpt
  - lb.xpt
  - pc.xpt
  - vs.xpt
- Resources

## Scripts performing the analysis

01\_PopPK\_Data2Report\_NOTRUN

- DataSource
- Report
- Scripts
  - SCRIPT\_00\_RUNALL.R
  - SCRIPT\_01\_importData.R
  - SCRIPT\_02\_createNLMEdata.R
  - SCRIPT\_03\_exploreNLMEdata.R
  - SCRIPT\_10\_PK\_base.R
  - SCRIPT\_20\_PK\_covariate.R
  - SCRIPT\_25\_PK\_covariance.R
  - SCRIPT\_30\_FinalModel.R
  - SCRIPT\_40\_Comparison\_Tables.R
  - SCRIPT\_99\_report.R
- Resources

## Report in RMD (Markdown format)

01\_PopPK\_Data2Report\_NOTRUN

- DataSource
- Report
  - very\_basic\_report.rmd
- Scripts
- Resources

Conversion of RMD files to Word requires presence of IQReport (<https://iqreport.intiquan.com>)

```
!TAB[Demographics table - continuous,size:10](../Output/03_exploreNLMEdata/TAB01_summaryCovPF.txt)
!TAB[Demographics table - categorical,size:10](../Output/03_exploreNLMEdata/TAB02_summaryCatPF.txt)
!LANDSCAPE
!TAB[size:7](../Output/03_exploreNLMEdata/TAB03_summaryObsPF.txt)
Correlation of potential covariates are shown in Appendix @FIG(fig_contcor), @FIG(fig_catcor), and @FIG(fig_contcatcor).
!PORTRAIT

# Model Results
* All tested models shown in Appendix @TAB(taball)
* Key model results shown in @TAB(tabkey)
* Final selected model results shown in @TAB(tabfinal)
  * Prediction corrected VPC shown in @FIG(figvpc)
  * Diagnostics shown in @SEC(diagnostics)
  * Final model control file in Appendix @TEXT(txtcontrol)
  * Final model output file in Appendix @TEXT(txtoutput)

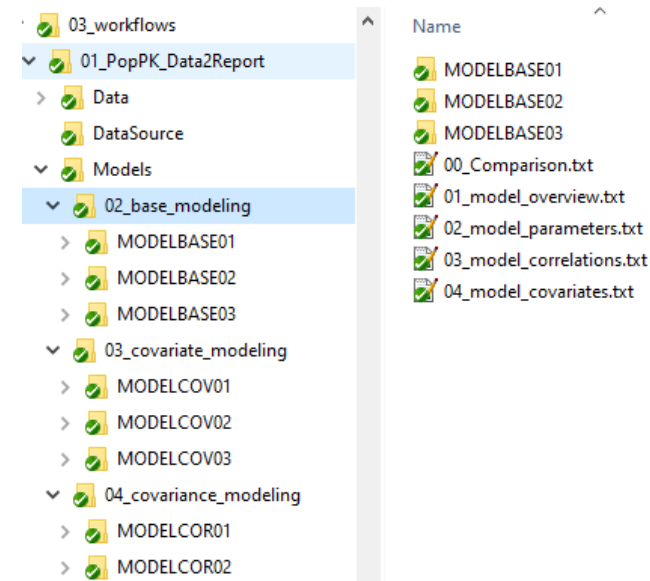
!TAB[Key model results,label:tabkey,size:10](../Output/FINALMODELS/TAB_01_comparison.txt)
!TAB[Final selected model,label:tabfinal,size:10](../Output/FINALMODELS/03_FINALMODEL/project_parameters_table.txt)
!FIG[Prediction corrected VPC for final selected model,label:figvpc](../Output/FINALMODELS/FIG001_poVPC_FINALMODEL_1.pdf)
!APPENDIX

# Data Specification {#dataspec}
!PDF[scale:90](../Data/01_dataNLME_PK/dataNLME_define.pdf)
!LANDSCAPE

# Data Programming
!TAB[Manually selected ignored observation records,label:data1,size:8](../Output/02_createNLMEdata/01_datacleaning/01_Man
```

# Advantages of workflow based analyses

- Full documentation of analysis
- 100% reproducible at any point in time
  - On the same system => ensured through use of virtualized computer systems (e.g. IQdesktop)
  - By any person (not only the initial analyst)
- Easy structuring of model development in folders
  - Base model
    - Base model
    - Covariate model
    - Covariance model
    - Etc.
- Full audit trail available
  - Through use of version control (e.g. git)
- Can be followed and reused with minor modifications



# Special elements

# Conclusions

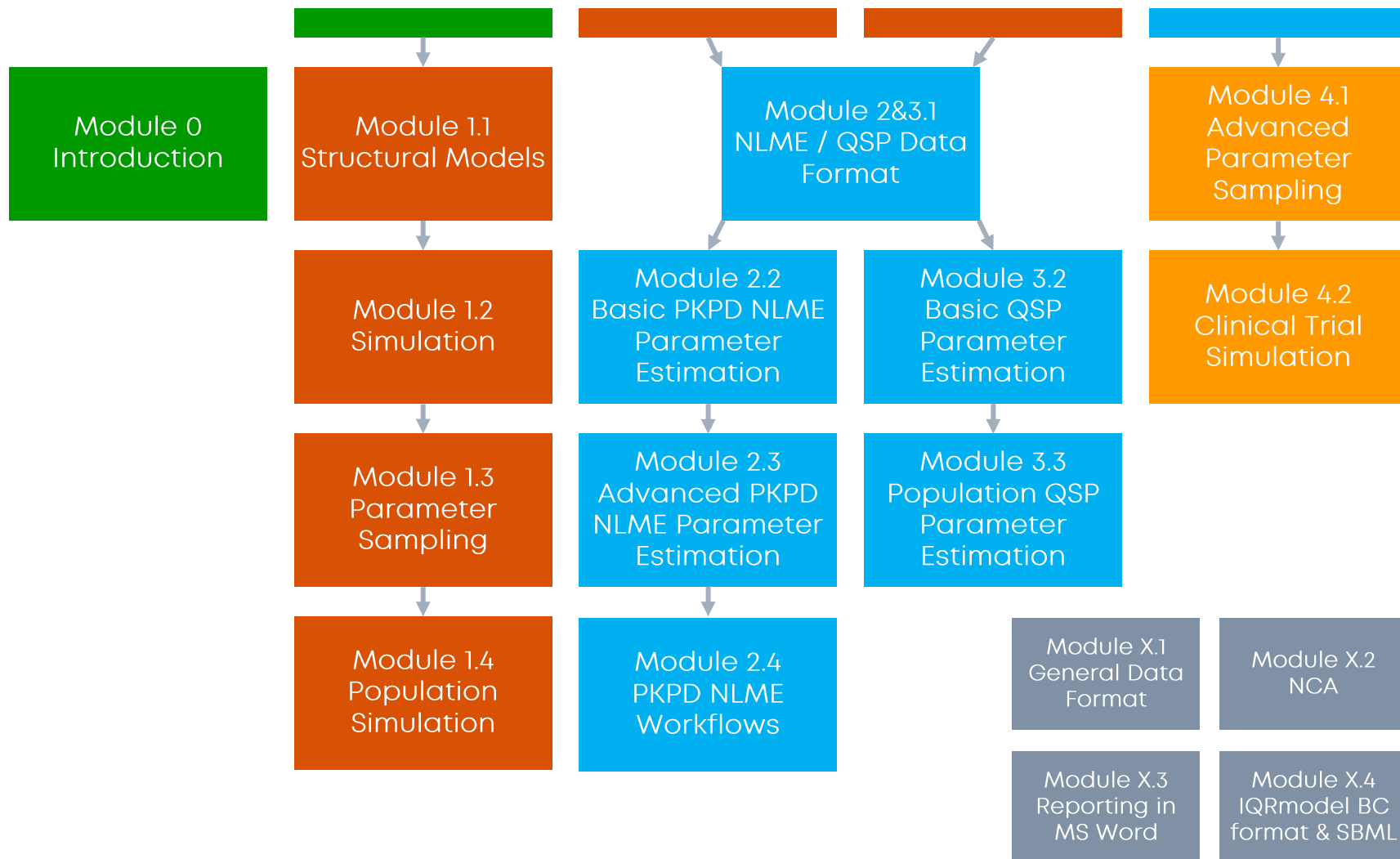
# Conclusions

- IQR Tools supports powerful script based set up of full analyses
  - From data to final report in Word
  - PK, PKPD, QSP, etc.
- High flexibility
- 100% reproducibility
- Adequate setup with version control ensures
  - Audit trail
  - Full analysis can be executed by anyone (not only by the initial analyst)

# Outlook webinar modules

# Overview of Webinar Series by IntiQuan

IntiQuan Webinar Series on efficient support of Model Informed Drug Development (MIDD)



# Q&A session

Thank  
You

# Contact information



IntiQuan GmbH  
Elisabethenstrasse 23  
4051 Basel  
Switzerland

Phone: +41 76 603 28 06  
E-mail: [info@intiquan.com](mailto:info@intiquan.com)  
Web: [www.intiquan.com](http://www.intiquan.com)