A DSL for Clinical Trial Design

CLARIO.

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Who is Clario.

We **support** Research Organization
in conducting **Clinical Trials**
to unlock better **evidence**

Research Organization

Pharmaceutical Company
Non-Profit Organization (Anti Cancer Fund)
Public Institution (University of Würzburg)

↔

Sponsoring and/or **conducting** clinical trials for
new **drug** development
medical device development
creation of international **standard** of care

Clinical Trial

Trial of **Drugs**

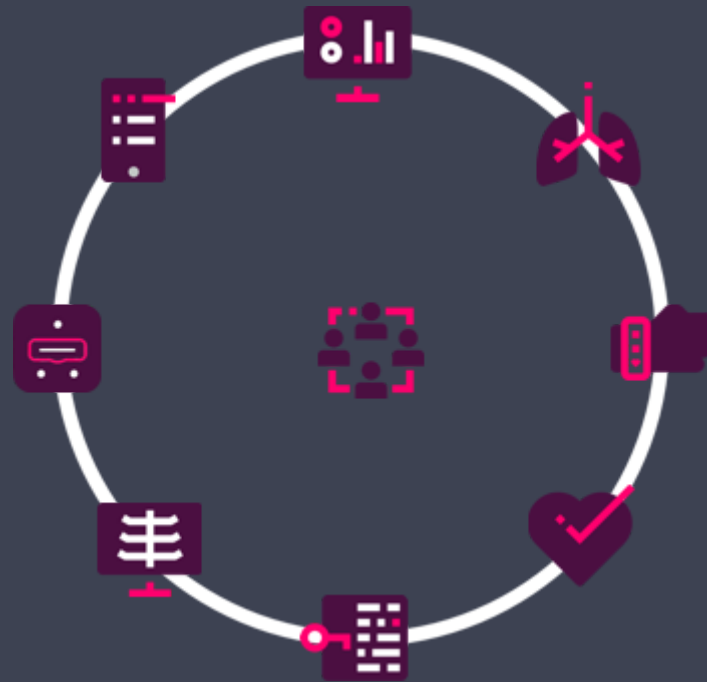Is that new drug safe? And Effective?

Trial of **Devices**

Is that new device safe? compliant to regulation?

Evidence

Evidence/proof of safety and efficacy
Based on data (**endpoints**)

Clinical Trial in 2023

Trend is more **endpoints**.
More **complex** protocol

Clinical Trial in 2023

Richer evidence is an opportunity seen as a greater risk.
Clario is flipping **complexity** into an **opportunity**.

How DSL is helping us?

- Express complex clinical trial protocol requirements (**less use of General Programming Language**)
- Increase quality by executing and testing the protocol during Study Build (**early testing**)

How DSL is helping us?

- Automate systems configurations (**configurable converters**)
- Automate documentation generations (**increase compliance**)

Form ACQ5 | for protocol D9180C00003

Allowed Roles:	site	Show Progress Bar?	☒
Long name:	Asthma Control Questionnaire	Include Audio Recording?	☐
Name on device:	<ACQ5>	Include in Daily Compliance Report?	☒
Name in backend:	ACQ5	Include in "By Visit" Completion Report?	☒
User languages:	Site	Device ID:	<ACQ5>
Source provider:	Clario	KRSU:	<ACQ5>

Data Definitions

timeseries item group ACQIG

Name	ID	Req	Type			Unit	Question		Default	Short Text	
Pain Level	field_10	required	codelist	0	Not painful	<none>	title [Edit]		<none>	<Pain Level>	■
				1	A little bit painful		text What is your pain level over the last d... [Edit]				
				2	Very painful [Format] ■						
Sleep	field_20	required	codelist	0	Sleep regularly	<none>	title [Edit]		<none>	<Sleep>	■
				1	Sleep lightly		text How did you sleep last night? [Edit]				
				2	Cannot sleep [Format] ■						
Mood	field_30	required	codelist	0	Good moood	<none>	title [Edit]		<none>	<Mood>	■
				1	Slightly demotivated		text How is your mood this morning [Edit]				
				2	Depressed [Format] ■						
ACQ5 Score Result Message	...	required	message			<none>	title [Edit]		...		■
							text Your Score is {{{ACQ5Score}}} [Edit]				

Calculated Values

```
ACQ5Score : integer range hard 0 .. 2 <not stored> = round avg ┌ ACQIG.PainLevel.value    half-up to 0 decs  [Edit]
                            soft <none>                          │ ACQIG.Mood.value
                                                                 └ ACQIG.Sleep.value     ■
```

Visualization Definitions

Visualization for Handheld **start screen** <first>

Allowed Roles: <none>

Screen	Layout	Repeating	Field	Widget	Question		Branch
Pain Level Screen	vertical		F ACQIG.PainLevel	⊞ Radio Button	title	<from data>	branch alt ACQIG.PainLevel. => MoodScreen
					text	<from data>	is(NotPainful)
							otherwise => SleepScreen
Sleep Screen	vertical		F ACQIG.Sleep	⊞ Radio Button	title	<from data>	next
					text	<from data>	
Mood Screen	vertical		F ACQIG.Mood	⊞ Radio Button	title	<from data>	next
					text	<from data>	
ACQ5 Score Result Message Screen	vertical		message representing ACQ5ScoreResultMessage		title	<same as data>	affidavit
					text	<same as data>	

V11
V12
V13
V14
V15
V16
Sessions
  Daily
  Weekly Diary
Tasks and Workflows
Forms
  InformedConsentSigned
  ElligibilityCriteria
  EQ_5D_5L
  CAT
  Spirometry
  IPAdministration
  ACQ5
Libraries

R Patient Session | Weekly Diary

Event ID: 20

Display Name: Weekly Diary
Display Name Targets: <none>

Short Name: <none>

Activities as unordered list:

Activity	Applicable if	Segments	Req/Opt
☑ CAT	subject.age >= 18	<all>	optional
☑ EQ_5D_5L	subject.age < 18	<all>	optional

First Scheduled: when Activation Completed + 6 days

  Then Repeats: weekly max <unlimited> times
                     until dispo Phase became PhaseCodelist.
                                                Follow_Up
                     except any other session/visit on same day
        Label: <numeric>

Scheduling Window: <on the day>
Time of Day: 17:00 - 23:00
Expires: within 5 hours

Segments: <no filters>
Ready Condition: [E] ElligibilityCriteria.ECIG.
                         ElligibilityCriteria2.is(Yes)

Options: <none>

Inspector

com.clario.designer.base.structure.ExpressionImplAnnotation

Description: Patient must be elligible tu run that session
Function Name: elligCheck
Placeholder: true
URL: http://127.0.0.1:63320/node?ref=r%3A48cda1d1-a8d0-4449-9dbf-3c00dc9eb7ba%280BERON%29%2F7432608320292518297
Attached to: ElligibilityCriteria(latest completed).ECIG.ElligibilityCriteria2.isOneOf(Yes) (org.iets3.core.expr.base.structure.DotExpression)

Git   Documentation   TODO   Terminal   Console   Messages

Dispositions

Phase [phase] : codelist

100	Pre-Screening	
110	Screening_01	
120	Screening_02	
130	Screening_03	
799	Screen-Failure	
200	Treatment	
300	Follow-Up	
899	EarlyDiscontinuation	
999	Deactivation	

Format

```
initially -> Pre_Screening

structured by current value

when Pre_Screening
  event Pre_ScreeningVisit completed  -> Screening_01
when Screening_01
  task ElligibilityCriteria completed and if ElligibilityCriteria.ECIG.  -> Treatment
                                            ElligibilityCriteria2.
                                            is(Yes)
  task ElligibilityCriteria completed and if ElligibilityCriteria.ECIG.  -> Screening_02
                                            ElligibilityCriteria2.
                                            is(No)

when Screening_02
  task ElligibilityCriteria completed and if ElligibilityCriteria.      -> Treatment
                                            ECIG.
                                            ElligibilityCriteria2
                                            .is(Yes)
  task ElligibilityCriteria completed and if ElligibilityCriteria.      -> Screen_Failure
                                            ECIG.
                                            ElligibilityCriteria2
                                            .is(No)

when Treatment
  event V16 completed  -> Follow_Up
```

5 Device Phases

This section provides the specifications of device phases used for managing when data are collected on the data capture devices for storage in the StudyWorks database for the project and for relating the data collection to clinical phases in the project.

Spec. ID	Description	Value(s)
5.0.1	Are there multiple initial device phases from "Add Patient" assignment form completion?	N
5.0.2	Description of triggers for initial Device Phases (If multiple)	N/A

5.1 Phase Mapping Table

Spec. ID	Report Label to Display	Device Label to Display	Master Device Phase(s) that Make Up the Report Phase	Phase Code
5.1.1	**Clario Default Report Label: Screening**			
5.1.1.1	Screening	Screening	Pre-Screening	100
5.1.1.2	Screening	Screening	Screening_01	110
5.1.1.3	Screening	Screening	Screening_02	120
5.1.1.4	Screening	Screening	Screening_03	130
5.1.2	**Clario Default Report Label: Treatment**			
5.1.2.1	Treatment	Treatment	Treatment	200
5.1.3	**Clario Default Report Label: Follow-up**			
5.1.3.1	Follow-up	Follow-up	Follow-Up	300
5.1.4	**Clario Default Report Label: Extension**			
5.1.5	**Clario Default Report Label: Inactive**			
5.1.6	**Clario Default Report Label: Deactivation**			
5.1.6.1	Deactivation	Deactivation	Screen-Failure	799
5.1.6.2	Deactivation	Deactivation	EarlyDiscontinuation	899
5.1.6.3	Deactivation	Deactivation	Deactivation	999

5.2 Phase Configuration

The table below contains the phases and phase transition information for all devices in the project and includes descriptions of interdevice dependencies.

Spec. ID	Protocol ID	Initial Phase	Initial Phase Code	New Phase	New Phase Code	Form	Trigger for Phase Change
5.2_100_110	D9180C00003_clone	Pre_Screening	100	Screening_01	110	N/A	Pre-Screening Visit completed
5.2_110_200	D9180C00003_clone	Screening_01	110	Treatment	200	ElligibilityCriteria	task ElligibilityCriteria completed and `ElligibilityCriteria(latest completed).ECIG.ElligibilityCriteria2.isOneOf(Yes)`
5.2_110_120	D9180C00003_clone	Screening_01	110	Screening_02	120	ElligibilityCriteria	task ElligibilityCriteria completed and `ElligibilityCriteria(latest completed).ECIG.ElligibilityCriteria2.isOneOf(No)`
5.2_120_200	D9180C00003_clone	Screening_02	120	Treatment	200	ElligibilityCriteria	task ElligibilityCriteria completed and `ElligibilityCriteria(latest completed).ECIG.ElligibilityCriteria2.isOneOf(Yes)`

Project

Protocol

MyTestProtocol | StudyEvents | Sessions | Phases | Skippable | MyTestProtocol_SpecificationsConfiguration

- MyTestProtocol
  - General
    - Metadata
    - Demographics
    - Segments
    - Disposition Variables
    - Signatures
    - Site ID
    - Subject ID
    - Specifications Configuration
      - V0.1
      - V1.0
      - V2.0
      - V2.1
  - Visits & Sessions
    - StudyEvents
      - Container with Conditions
      - V1

Initial Setup: <none>

check timeline [ok]

```
Chart Configuration
ROWS                    COLUMNS
show dispo       ☒     days 1 .. 23
show events      ☒     mode Whenever something changes, min. one per day
show tasks       ☐
show reminders   ☐
```

requirement VS1 is ready

description

```
day 1    A    event is ready Unscheduled_optional_
         E    set dispo Phase = PhaseCodelist.Treatment
         A    event is ready VS1
         A    not event is ready VS2_canBeSkipped_
         A    not event is ready VS3
         A    not event is ready VS4_canBeSkipped_
         A    not event is ready VS5
day 2    H    complete event VS1
```

Browser

	1		2		3		4		5		6		7		8		9		10		11		12		13		14	
	00 00 (1)	23 59 (2)	00 00 (3)	23 59 (4)	00 00 (5)	23 59 (6)	00 00 (7)	23 59 (8)	00 00 (9)	23 59 (10)	00 00 (11)	23 59 (12)	00 00 (13)	23 59 (14)	00 00 (15)	23 59 (16)	00 00 (17)	23 59 (18)	00 00 (19)	23 59 (20)	00 00 (21)	23 59 (22)	00 00 (23)	23 59 (24)	00 00 (25)	23 59 (26)	00 00 (27)	23 59 (28)	00 00 (29)
[D] Phase (1)	Treatment	Treatment	Treatment	Treatment	Treatment	Treatment	Treatment	Treatment	Treatment	Treatment	Treatment	Treatment	Treatment	Treatment	Treatment	Treatment	Treatment	Treatment	Treatment	Treatment	Treatment	Treatment	Treatment	Treatment	Treatment	Treatment	Treatment	Treatment	Treatment
[E] ContainerWithConditions (2)	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R
[E] V1 (3)																			R	M									
[E] Container (4)	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R
[E] V2 (5)																													
[E] V3 (6)																													
[E] V4 (7)																													
[E] TerminationVisit (8)	R	M	R	M	R	M	R	M	R	M	R	M	R	M	R	M	R	M	R	M	R	M	R	M	R	M	R	M	R
[E] Daily (9)																													
[E] Weekly (10)																													
[E] DailySession (11)																													
[E] VS1 (12)	R	M	C	C*	R	M	R	M	R	M	R	M	R	M	R	M	R	M	R	M	R	M	R	M	R	M	R	M	R
[E] Unscheduled_optional_ (13)	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R
[E] VS2_canBeSkipped_ (14)			R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R
[E] VS3 (15)			R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R
[E] VS4_canBeSkipped_ (16)																													
[E] VS5 (17)																													

What have we learned about the approach?

- Expressing and Testing protocols in 1 stop-shop is **reducing** risks ✅
- Allows greater **automation**, reduces burden on Teams ✅
- Development cycles can be very quick ✅

What have we learned about the approach?

- **Learning** curve is big for both the dev team the end users 🛑
- MPS as fat desktop client is restricting the **user experience** 🛑
- Interoperability with 3rd parties is **limited** 🛑

What do we need in the future?

- MPS as a web app
- Server side services
- Interoperability with non-DSL systems

Thank you!