# Interoperable digital protocols with HL7 FHIR

Cal Collins
Chief Technology Officer
OpenClinica LLC

# Topics

- Moving to a digital protocol
- FHIR Schedule of Activities (SoA)
- SoA-based Interoperability - Application at OpenClinica
- Using Standards in an AI-driven World

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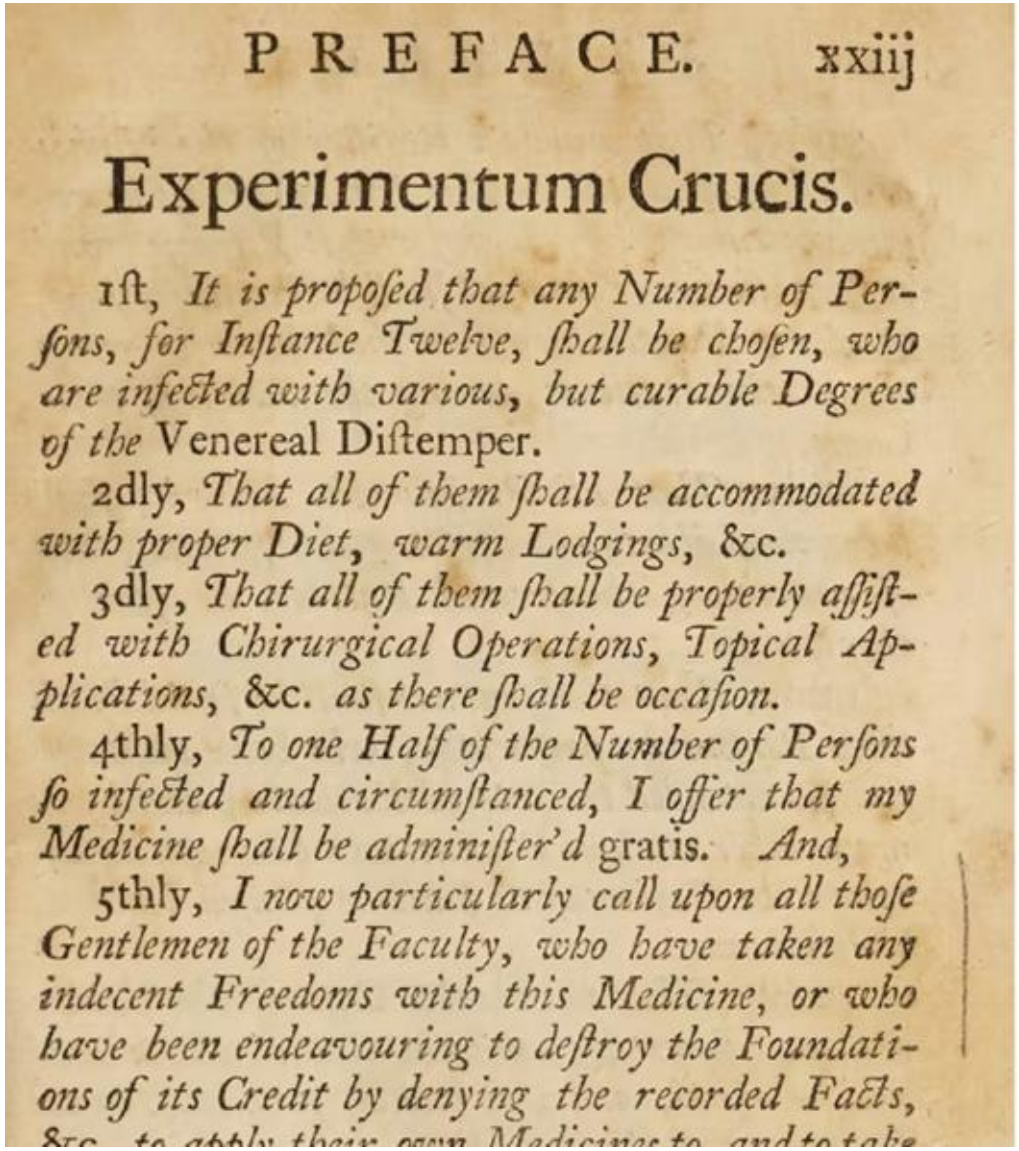
# Moving Towards a Digital Protocol

- The protocol - the core operational blueprint for a clinical trial - defines eligibility, procedures, visit schedules, endpoints, and data collection.
- Written as a Word document, it is readable by humans, interpreted by humans, and implemented by humans. Fundamentally the same as in the 1740s!
- Today, we take this document, manually interpret & implement separately across multiple systems and sites. This creates inefficiencies and inconsistencies.



PREFACE. xxiij

Experimentum Crucis.

1ſt, *It is propoſed that any Number of Perſons, for Inſtance Twelve, ſhall be choſen, who are infected with various, but curable Degrees of the* Venereal Diſtemper.

2dly, *That all of them ſhall be accommodated with proper Diet, warm Lodgings,* &c.

3dly, *That all of them ſhall be properly aſſiſted with Chirurgical Operations, Topical Applications,* &c. *as there ſhall be occaſion.*

4thly, *To one Half of the Number of Perſons ſo infected and circumſtanced, I offer that my Medicine ſhall be adminiſter'd* gratis. *And,*

5thly, *I now particularly call upon all thoſe Gentlemen of the Faculty, who have taken any indecent Freedoms with this Medicine, or who have been endeavouring to deſtroy the Foundations of its Credit by denying the recorded Facts,*

https://www.cnn.com/2025/01/18/science/first-clinical-trial-lessons

# Moving Towards a Digital Protocol

- The digital protocol is structured, readable and implementable in software.
- Not (inherently) readable by humans, interpreted by humans, and implemented by humans.
- We need both!

SOA EDC FHIR Response 2.json


```
{
    "resourceType": "Bundle",
    "type": "transaction",
    "entry": [
        {
            "resource": {
                "resourceType": "ActivityDefinition",
                "id": "informed-consent",
                "status": "draft",
                "description": "Informed consent procedure",
                "kind": "ServiceRequest",
                "code": {
                    "coding": [
                        {
                            "system": "http://snomed.info/sct",
                            "code": "371530004",
                            "display": "Clinical consultation report"
                        }
                    ],
                    "text": "Clinical consultation report"
                },
                "text": {
                    "status": "additional",
                    "div": "<div xmlns=\"http://www.w3.org/1999/xhtml\'
report</div>"
                }
            },
            "request": {
                "method": "POST",
                "url": "ActivityDefinition"
            }
        },
        {
            "resource": {
                "resourceType": "ActivityDefinition",
                "id": "inclusion-criteria",
                "status": "draft",
                "description": "Inclusion criteria",
                "kind": "ServiceRequest"
```

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# HL7 FHIR Schedule of Activities (SoA)

## What is FHIR SoA?

- A standardized JSON representation of a study's planned visits, interventions, assessments, and tasks.

## Why is FHIR SoA important?

- It enables consistent implementation across systems and sites
- Streamlined startup and implementation of amendments through automated EDC / eCOA / CTMS / eSource configuration
- Visit scheduling that's coordinated across systems and organizations
- Generating downstream datasets

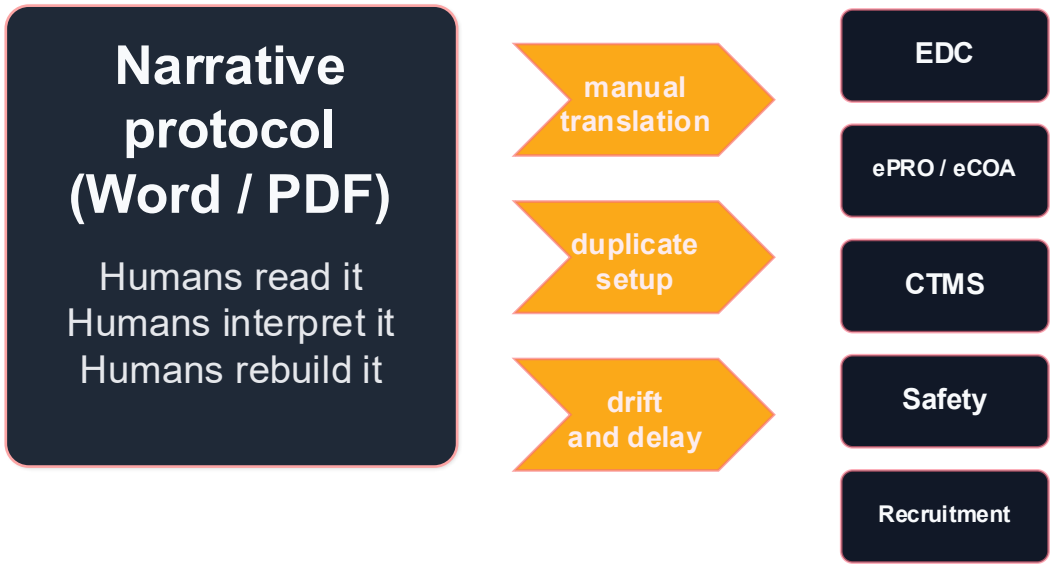
| Evaluation/ Procedure | Registration & Screening (Pre-randomization) | Paclitaxel Regimen (first 12 weeks) [a] | AC Regimen (last 12 weeks) | Pre-Surgery | Surgery | During 10 year Follow-up |
|---|---|---|---|---|---|---|
| Informed Consent | X | X (post-randomization) | | | | |
| Assess Eligibility | X | | | | | |
| Medical History | X | | | | | |
| Physical Exam | X | X | X | X | | X |
| Laboratory Blood Tests[b] | X | X | X[l] | X[l] | | X (30 days, 6 and 12 months post surgery if immunotherapy arms) |
| Pregnancy Test | X | X[p] | | | | X[p] (30 days post-surgery) |
| Investigational Agent-specific Laboratory and Assessment Tests | X | X | X | X[l] | | |
| Metastatic Evaluation[g] | X | | | | | |
| Breast MRI | X | X[e] (end of week 3 and end of week 6) | X[f] (before AC1 and before AC3) | X | | |
| ECHO/MUGA | X[c] | X[d, r] | X[d, r] | | | X[d, r] |
| ECG | X[j] | | | | | |
| Biopsy/Tissue Collection[k] | X | X[n] (end of week 12;end of 3 week for EOP) | | | X | |
| Study Blood Draw for Serum, Plasma, and Buffy Coat | X | X (end of week 3,end of 6 weeks and end of 12 weeks) | | X | | X (30 days post-surgery and annually for up to 10 years or at recurrence) |
| Clinical Assessment[h] | X | X | X | X | | X |
| Tumor Response[s] | | X | | X | | |
| Administration of Investigational Agent | | X | X | | | |
| Adverse Event Collection | | X | X | X | X | X |

| Evaluation/ Procedure | Registration & Screening (Pre-randomization) | Paclitaxel Regimen (first 12 weeks) [a] | AC Regimen (last 12 weeks) | Pre-Surgery | Surgery | During 10 year Follow-up |
|---|---|---|---|---|---|---|
| | | | | | | (30 days, 6 and 12 months post-surgery) |
| Ultrasound of the axilla[i] | | X (end of week 12) | | | | |
| Optional Biopsy of Suspicious Node[i] | | X (end of week 12) | | | | |
| GGT test | X[m] | | | | | |
| Free T4 test[o] | X | X | X | | | X (30 days, 6 months and 12 months post- surgery) |
| Urine pregnancy[p] | X | X | | | | X (30 days post- |

# The Clinical Research Protocol Problem

A protocol is still treated like a document, even though it really needs to function like infrastructure.

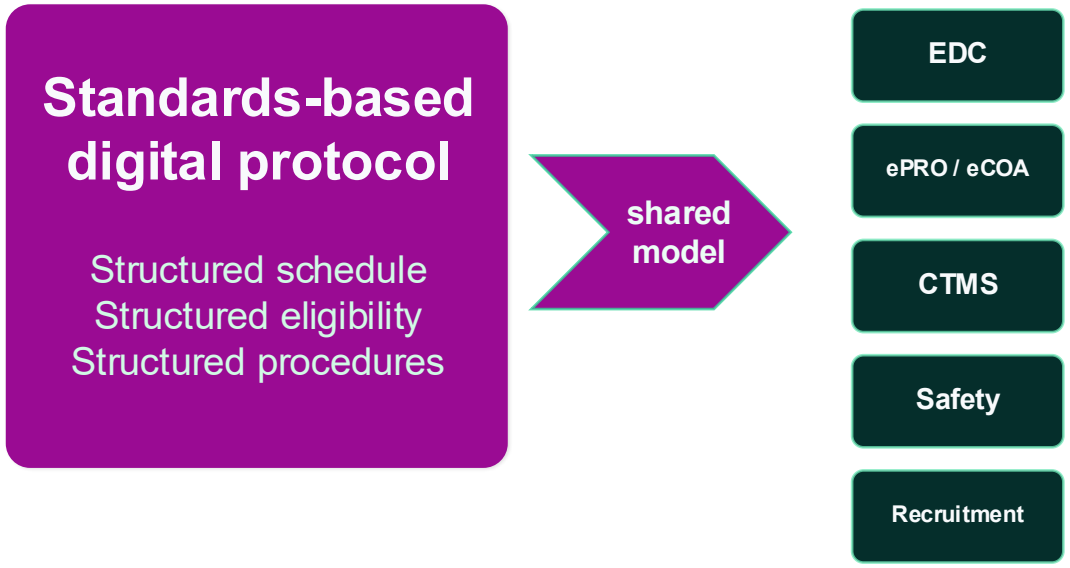
## TODAY




**Every system rebuilds the study from the same text.**

Result: interpretation risk, repeated configuration work, slower startup and harder amendments.

## WITH STANDARDS-BASED DIGITAL PROTOCOLS




**One structured protocol can configure many connected systems.**

Result: a shared source of truth, cleaner interoperability, faster startup, and faster change propagation.

*The protocol should move from something people reinterpret into something the ecosystem can execute.*

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# About OpenClinica

## Integrated, self-service eClinical toolset

### Electronic Data Capture
OpenClinica Core

### Dashboards & Reporting
OpenClinica Insight

### eCOA
OpenClinica Participate

### eConsent
OpenClinica Consent

### Participant Recruitment
OpenClinica Recruit

### Randomization & Supply
OpenClinica Randomize

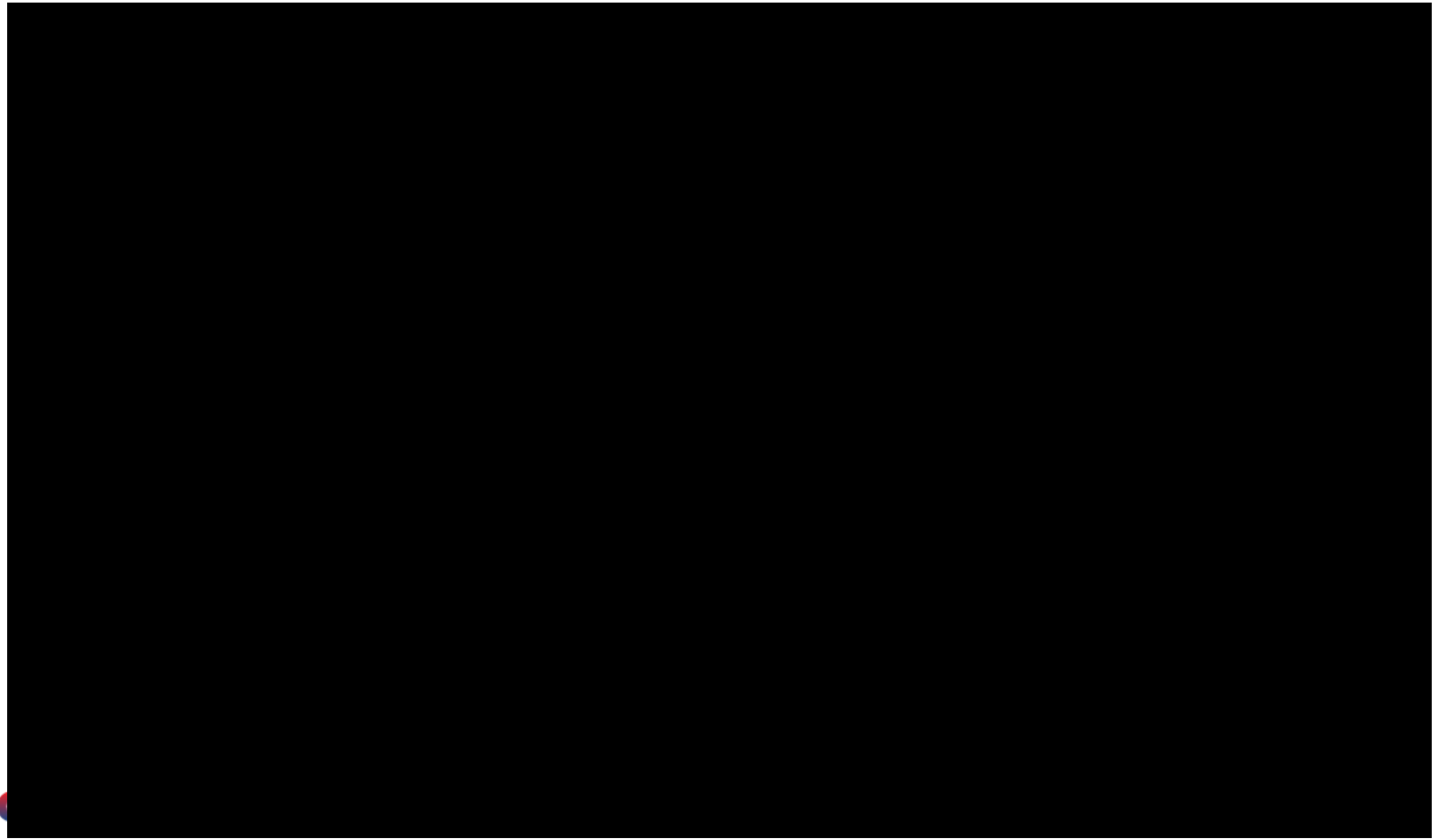
### Medical Coding
OpenClinica Code

### EHR eSource
OpenClinica Unite

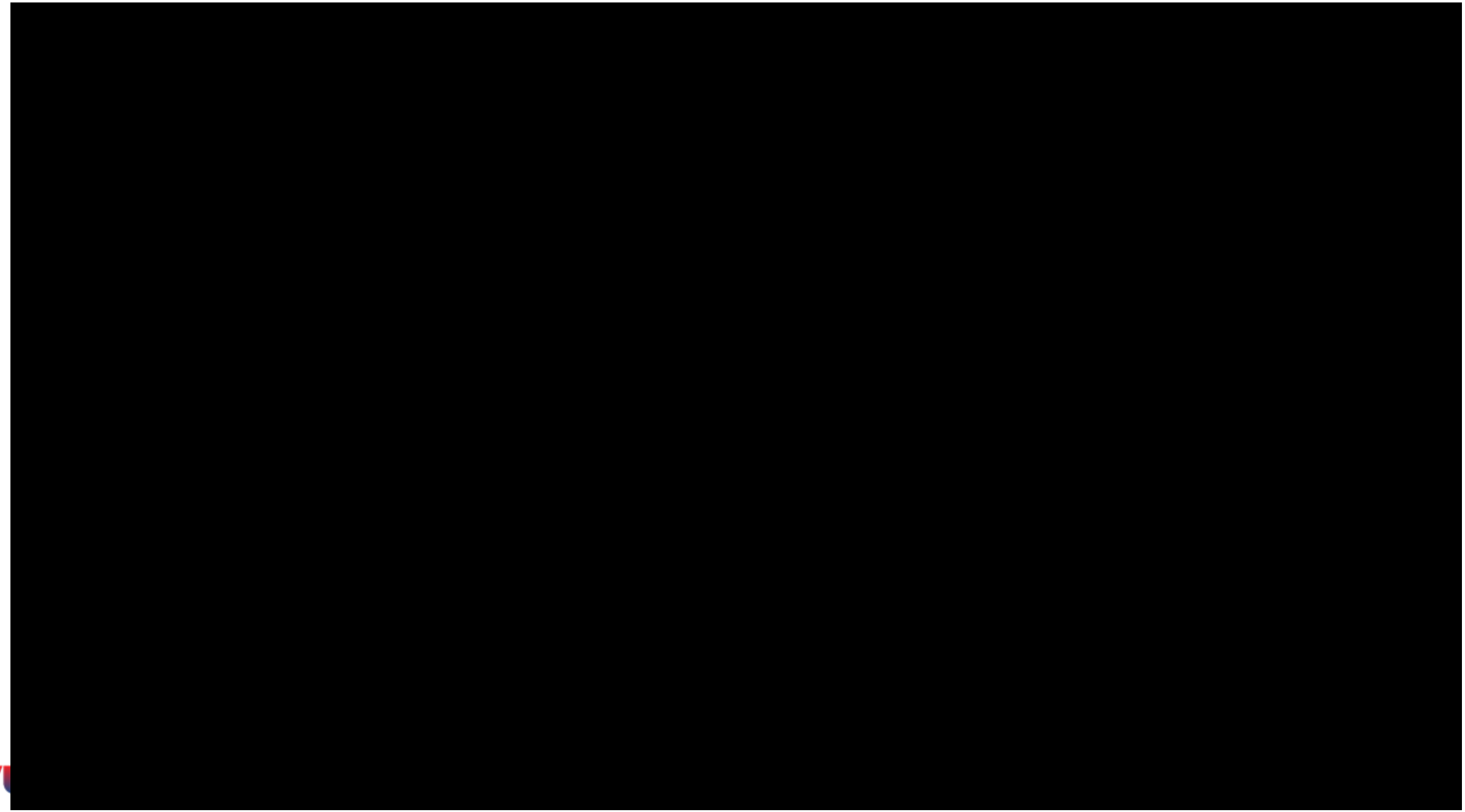


OpenClinica

# Import Study SoA into EDC Designer



# EHR to EDC | SoA-based Transfer OpenClinica



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# Using Standards in an AI-driven World

- Digital protocol standards (ICH M11, USDM, FHIR SoA) are rapidly moving forward in maturity, awareness, and support
- The huge benefits come once there is widespread adoption. But this takes time!
- We need to keep protocols human authored and accessible - document-centric approaches do this well.
- The combination of generative AI plus open standards such as FHIR SoA is highly compelling.

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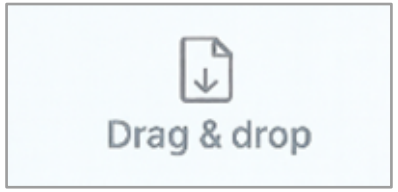
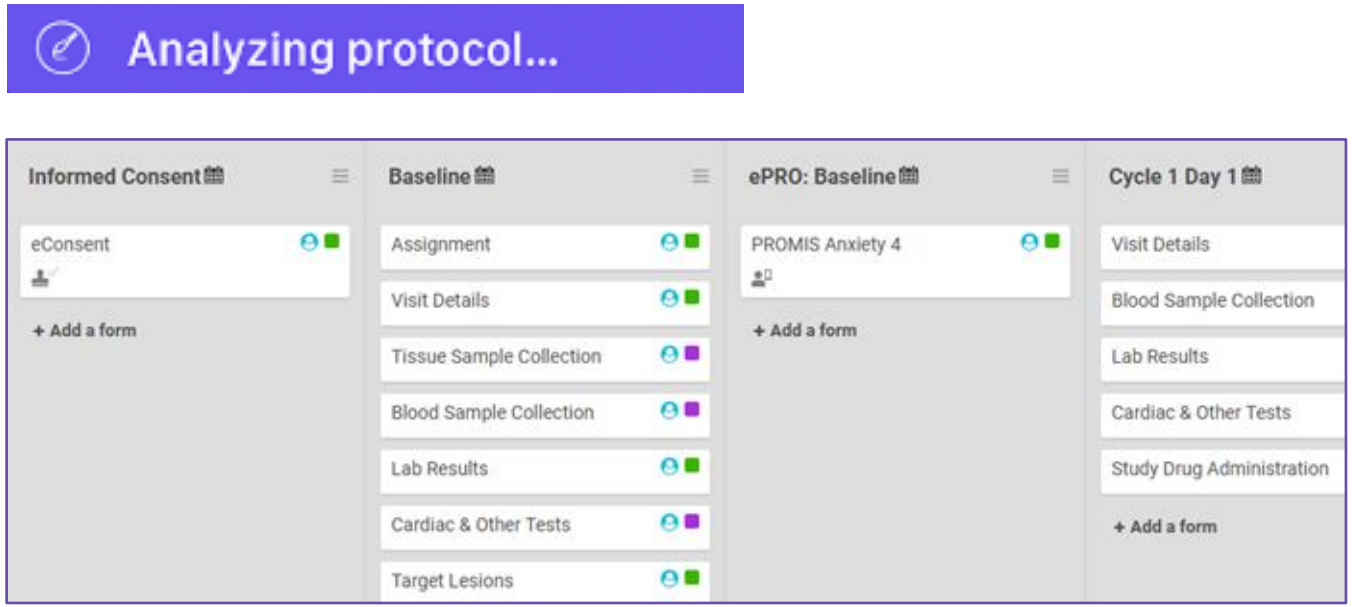
# AI: Transform Protocols into OpenClinica Studies

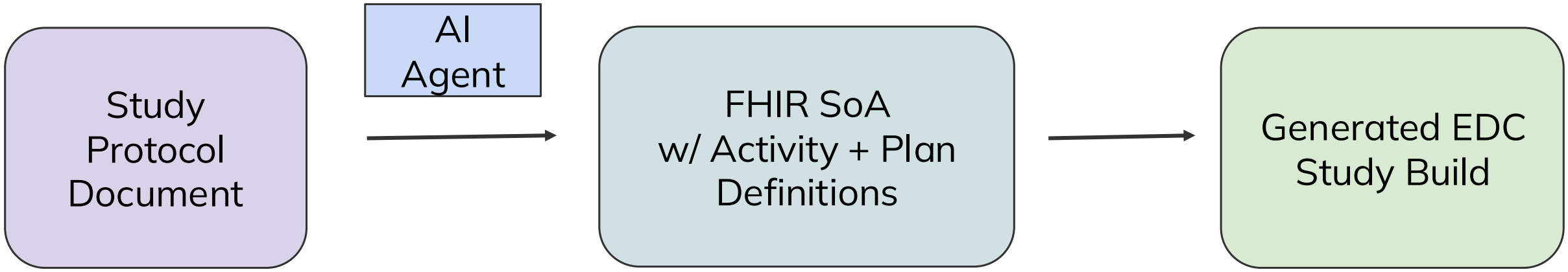
*From PDF protocol to live Study Build - in minutes*




1. Upload a study protocol into OpenClinica
2. The OC AI Protocol Agent reads, structures, and generates a Study Board - fully mapped to OC standards



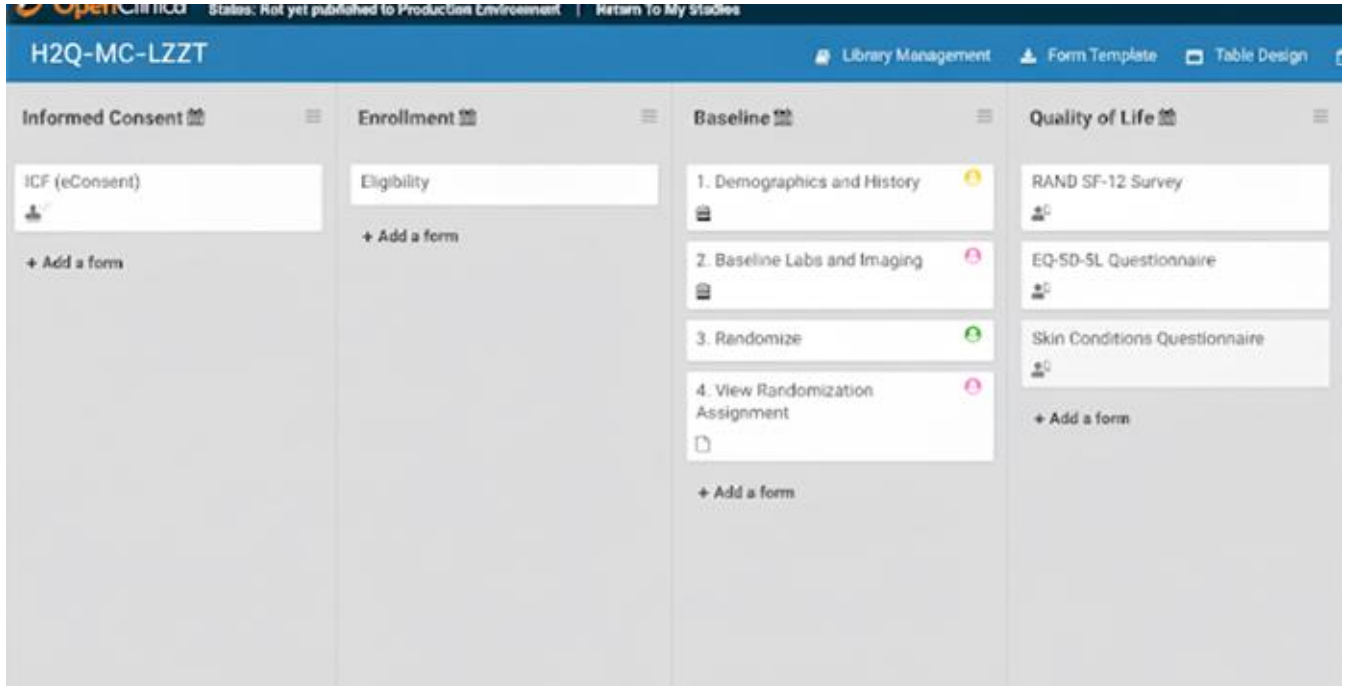
## Goal: Leverage HL7 FHIR Formatting tools to move straight from Visit Schedules to Study Builds.



# A Protocol AI Agent that generates Event / Form Cards in Study Designer directly from an imported Study Protocol

**Protocol Attachment LZZT.1**
**Schedule of Events for Protocol H2Q-MC-LZZT(c)**

| | VISIT | 1 | 2 | 3 | 4 | 5 | | 7 | 8 |
|---|---|---|---|---|---|---|---|---|---|
| ACTIVITY | WEEK | -2 | -3 | 0 | 2 | 4 | | 6 | 8 |
| Informed consent | | X | | | | | | | |
| Patient number assigned | | X | | | | | | | |
| Hachinski ≤4 | | X | | | | | | | |
| MMSE 10-23 | | X | | | | | | | |
| Physical examination | | X | | | | | | | |
| Medical History | | X | | | | | | | |
| Habits | | X | | | | | | | |
| Chest x-ray | | X | | | | | | | |
| Apo E genotyping | | | | | X | | | | |
| Patient randomized | | | | X | | | | | |
| Vital signs/Temperature | | X | X | X | X | X | | X | X |
| Ambulatory ECG placed | | | X | | | | | | |
| Ambulatory ECG removed | | | | X | | | | | |
| ECG | | X | | | X | X | | X | X |



## High accuracy vs gold standard

| Study | Average Specificity | Average Sensitivity | FHIR Bundle Validity |
|---|---|---|---|
| A | 80.64% | 92.85% | 100% |
| B | 99.38% | 99.00% | 100% |
| C | 100.00% | 92.00% | 100% |

We evaluated the syntactic and structural similarity of automatically generated visit schedules to their respective protocol-defined gold standards, assessed model reproducibility across five independent runs, and identify systematic deviations in event or assessment extraction.

FHIR (Fast Healthcare Interoperability Resources) standard is used internally to define the study structure. This is the same open standard used for OpenClinica Unite EHR->EDC integration. Combining AI with this open standard is a significant accelerant for producing accurate study definitions.

**Studies**:

**A**: Multicenter interventional trial evaluating scheduled assessments across multiple study parts (A and B).

**B**: Long-term follow-up study for participants receiving therapy, focusing on continued monitoring of safety and efficacy outcomes.

**C**: Prospective, observational product study designed to assess real-world outcomes and data collection patterns following treatment.

# Open Standards are a Key Accelerant for AI

## Where a publicly documented standard exists for your use case, use it if at all possible!

**HL7 FHIR (Fast Healthcare Interoperability Resources):**

- Regulatory and developer support are unmatched in the industry.
- Uses JSON, a modern developer-friendly data standard.
- Permits flexible, atomic data sharing
- Data quality & consistency across sites
- ***Thoroughly documented in formal technical detail on the public web – LLMs already have expertise in the standard.***

# Thank You!

Cal Collins
Chief Technology Officer
OpenClinica LLC
ccollins@openclinica.com