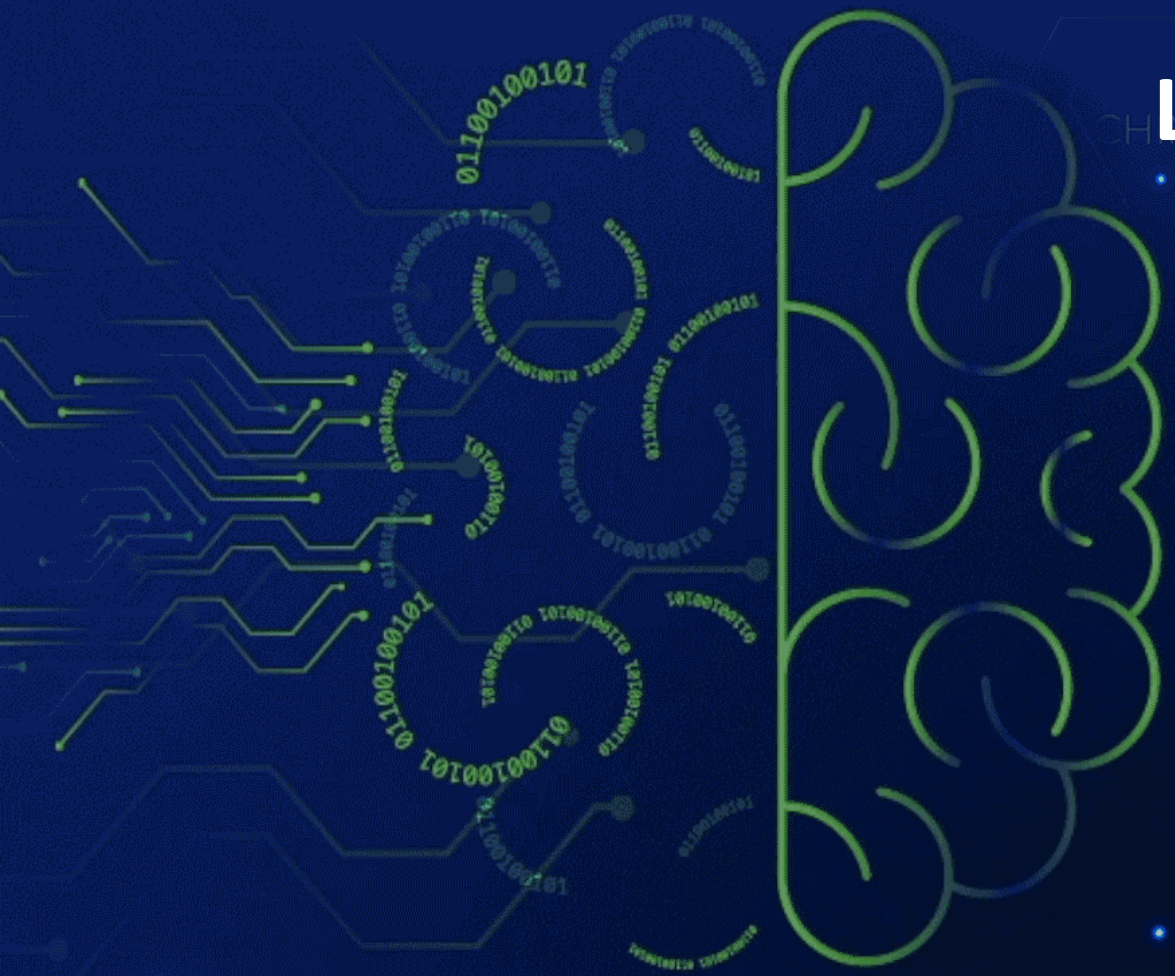

Being Best in Class Accelerating Clinical Trials by Leveraging Metadata to Reduce Database Build Time

RALPH RUSSO

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Being Best in Class – Accelerating Clinical Trials by Leveraging Metadata to Reduce Database Build Time

Session Chai: Ralph Russo – Pfizer

Speaker 1: Alain Monroy – Pfizer

Leveraging Automations and Production Metadata to Expedite Study Build

Speaker 2: Ian Fleming – Medidata Solutions

Using graph-based metadata structures to drive next-generation clinical data management

Speaker 3: Stephen Benham – Formedix

How metadata automation accelerates clinical trials, and was leveraged to expedite COVID-19 trials

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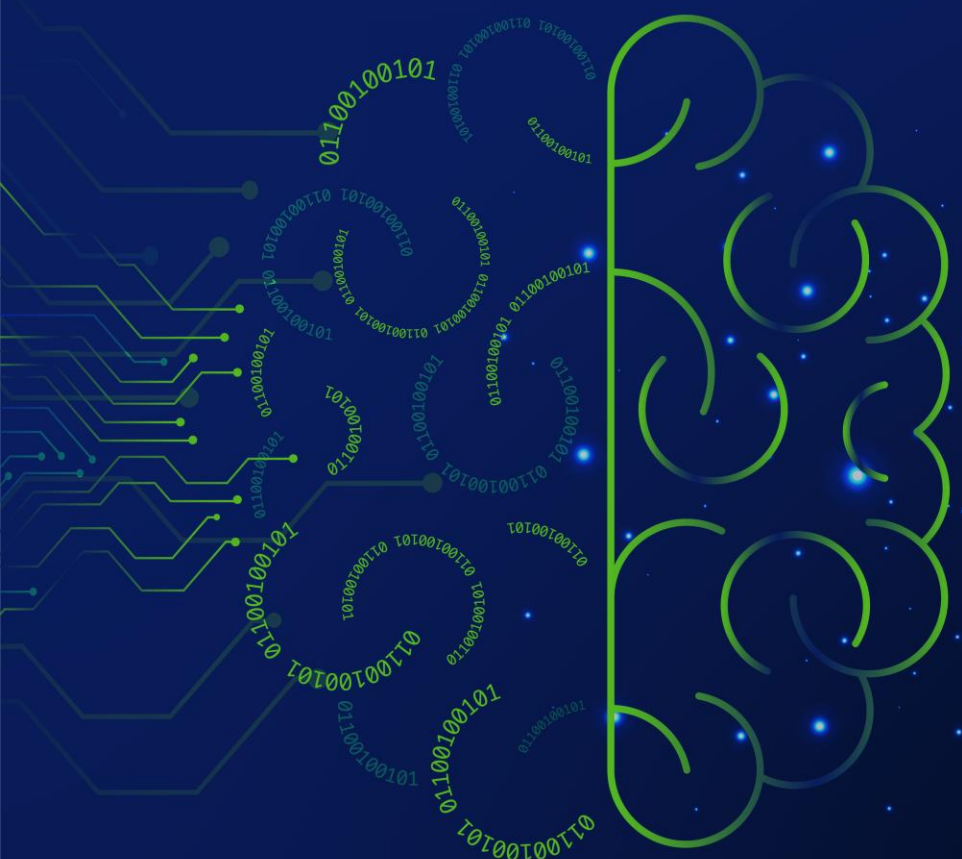
Leveraging Automations and Production Metadata to Expedite Study Build

Alain Monroy - Pfizer



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Topics

- EDC Study Build – Current Paradigm
- Present Challenges
- Redefining the Journey Ahead
  - 1- Automated study builds using Time and Events spec
  - 2- Mining metadata from production studies
  - 3- Harmonizing protocol design and Standards EDC objects

EDC Study Build – Current Paradigm

- Specs manually developed based on protocol requirements
- Study build done manually based on those specs
- New/change to Standards objects are identified during both spec and study build process

Present Challenges

Discordance between protocols and existing Standards

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Present Challenges

Manual, time-consuming work to create specs. Requires several team meetings to confirm details of what is needed; back-and-forth discussions on metadata content; easy to miss details

Present Challenges

- Manual study design and programming based on specs
- Development of new standard objects needed in the study might contribute to build delays
- Manual work on specs and study build decreases quality and pushes timelines out

Redefining The Journey Ahead

At Pfizer, we are closing the gaps with below 3-step approach:

1. Automated study builds using Time and Events spec
2. Mining metadata from production studies
3. Full alignment of protocol design and Standards EDC objects

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1- Automated study builds using Time and Events spec

Based on the study Time and Events specs, automatically generate:

- Study visits
- Standards forms and corresponding Standards edit checks added within those visits
- Copies of Standards forms and edit checks also included in those visits following correct sequence
- Some Standards dynamics

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1- Automated study builds using Time and Events spec

Benefits:

a. Full time and events build programmatically
b. Visits listed in sequence as indicated in the protocol and so are the forms within each of those visits.
c. Standards forms needed in the study and corresponding edit checks inserted automatically
d. Copies of Standards forms needed in the study also create programmatically along with corresponding edit checks
e. Standards dynamics generated via automation
f. Process can be used repetitive during prototyping until the study reaches UAT (this is due to CDMS limitation)

Overall Evaluation:

- Significantly reduces the programming activity since a great part is done automatically
- Not too difficult to implement. Main prerequisites would be only to have robust Standards and T&E specs in a format that allows to be read programmatically.

Challenges not addressed yet:

- T&E and CRF Specs still done fully manual
- Design and programming work within forms and fields continues fully manual

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Automation Demo

Demo Part 1: View here

Demo Part 2: View here

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Demo Part 1: View here

Demo Part 2: View here

2- Mining metadata from production studies

- Metadata mining uses production studies metadata to identified design trends within same TAs.
- Applies a scale (0-100) to fields and field responses indicating their probability to be used in specific TA.

2- Mining metadata from production studies

Benefits:

- This approach utilizes the similarities of studies from the same TA to 'predict' CRF content/design
- Reduces programming work even further by making more accurate predictions of fields and fields choices to be used (less deletion operations)
- CRF spec could be partially created in this case.

Overall Evaluation:

- Reduces programming activities further through content prediction
- Not too difficult to implement since additional requirement would be to have access to production studies metadata and compile them

Challenges not addressed yet:

- T&E still done fully manual
- CRF Specs partially automated, but still requires significant design work.
- Design and programming work within forms and fields reduced, but great part still manual.

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3- Harmonizing protocol design and Standards EDC objects

Protocol visits, forms and even fields terminology coming from and controlled at Standards level.

3- Harmonizing protocol design and Standards EDC objects

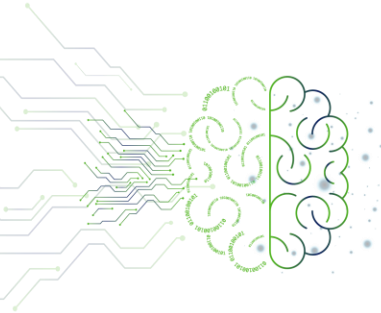
Benefits:

- Lists the visits and forms available to include in the protocol which uniquely correspond to actual visits and forms in Standards
- Early identification of new objects to be added to Standards.
- Full automation of T&E specs
- Almost full automation of CRF specs
- Close to full automation of CRF design
- Reduction in the number of amendments

Overall Evaluation:

- Significantly more complex to implement; it requires full alignment of protocol and Standards
- Reduces programming activities to the minimum since protocol and Standards objects are associated since the early protocol stage
- More accurate than utilizing AIs. No prediction to be made; objects mentioned in the protocol mapped to Standards.

Q&A



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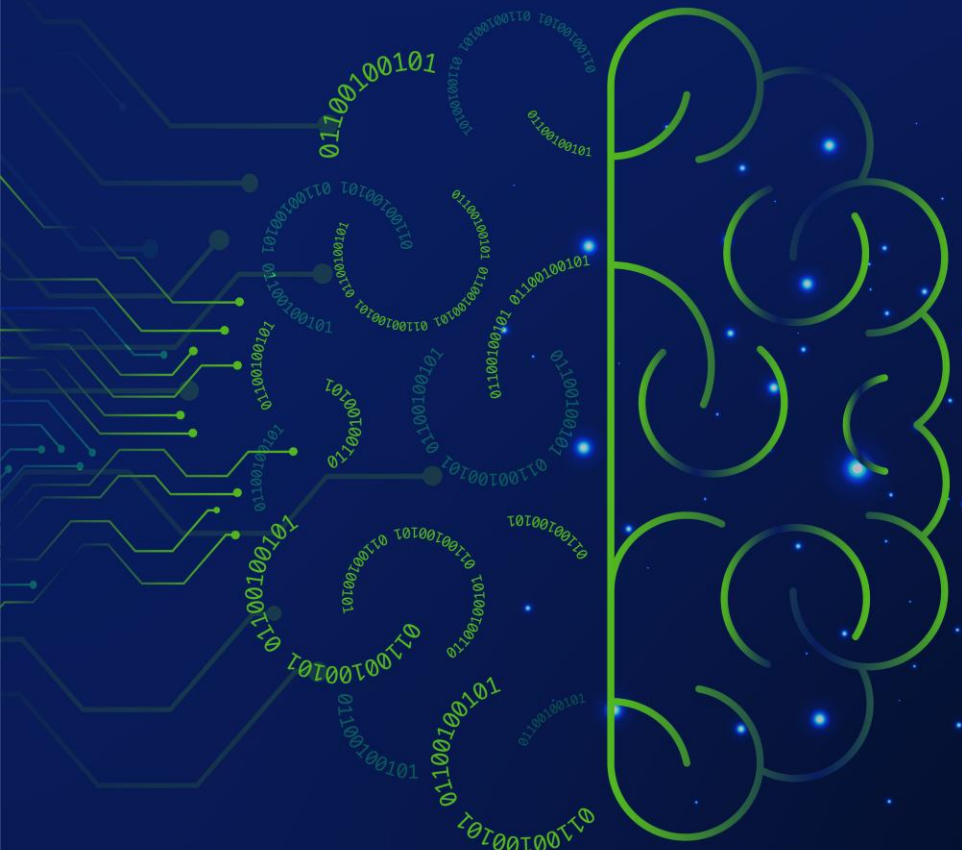
Using graph-based metadata structures to drive next-generation clinical data management

Ian Fleming- Medidata Solutions



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Why Data Shapes?

Design → Collection → Tabulation → Analysis

Each step in the process has its own set of tools and own metadata representation

Based on graphs

- Dimensionality is fit-to-purpose
- Easy to construct and evolve

Data shapes can provide a persistent set of metadata throughout the study

What is a Data Shape?

A set of **technical constraints** that defines the relationships and value level details for a collection of data

Can be considered a **micro-schema**

Aligned with **activities** or "data to be collected" as defined in the protocol

Conceptual/ logical model

- Physical model details can be added

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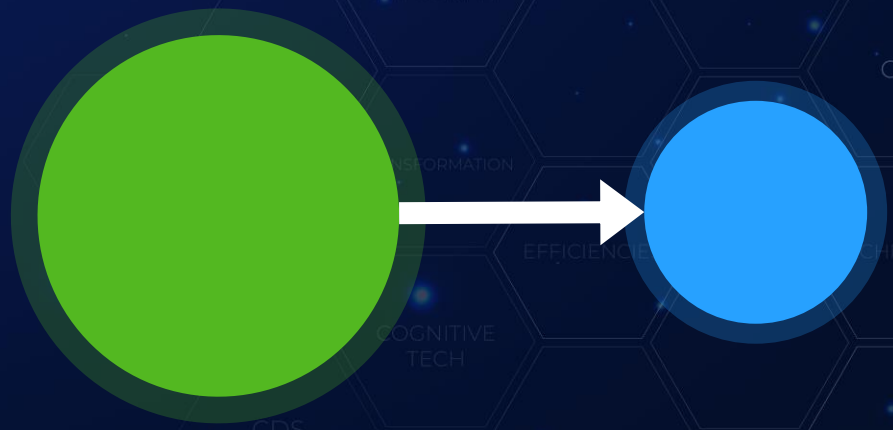
Constraint Types

Property/relationship
- cardinality
- object type

Value
- literal type
- Range
- Enumeration
- string
- language



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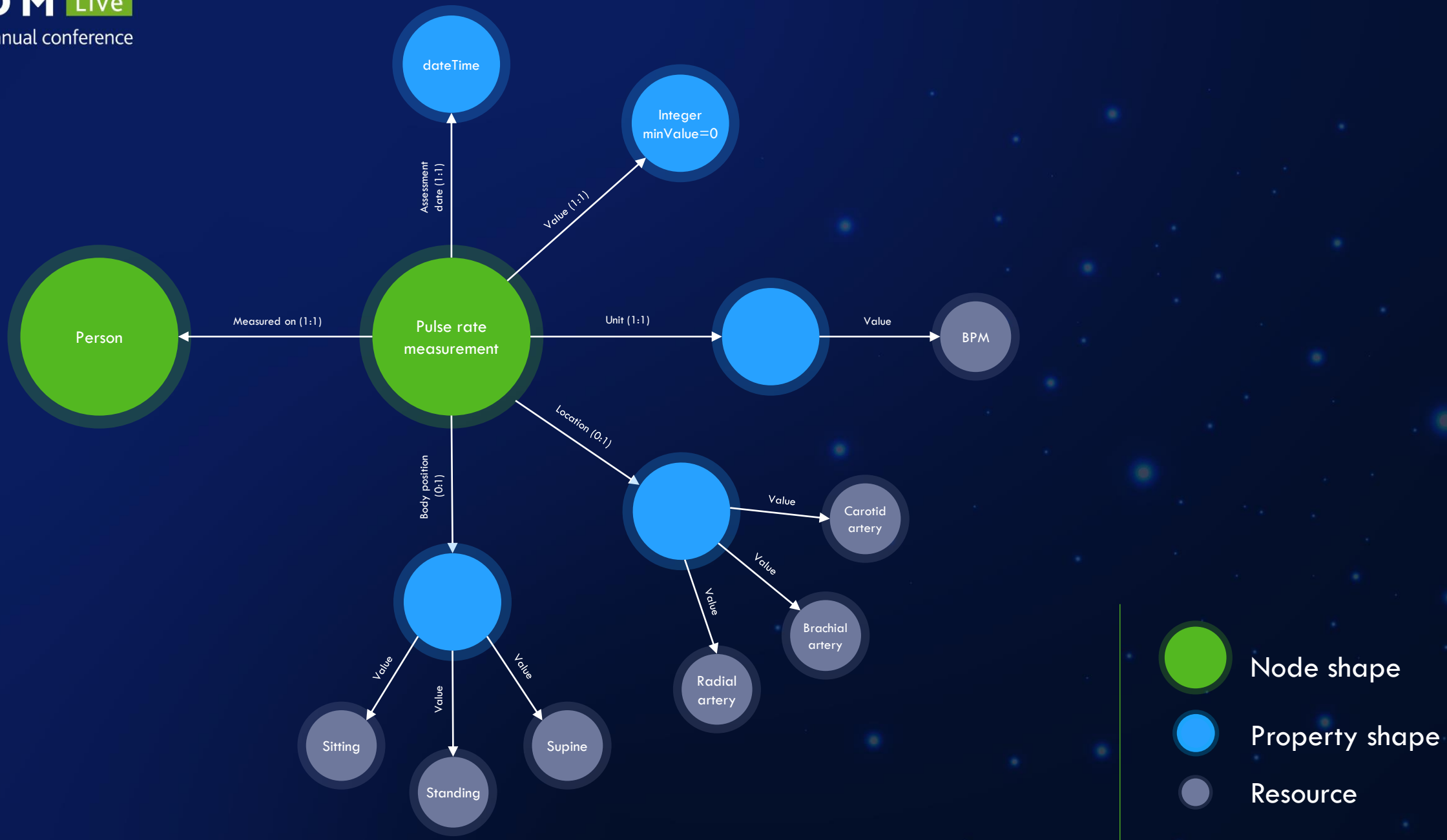

Shapes Constraints Language (SHACL)

A **W3C standard** for describing constraints for graph structures

Machine readable with **human readable** annotations for rich semantics

Based in **RDF**, the standard for the semantic web

FAIR by design

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Pulse Rate Measurement in SHACL Code

```
mds:PulseRateMeasurement a sh:NodeShape ;

    skos:prefLabel "Pulse rate measurement"@en ;
    sh:property
        mds:AssessmentDate ,
        mds:BodyPosition ,
        mds:AnatomicalLocation ,
        mds:PulseRateMeasurementValue ,
        mds:PulseRateMeasurementUnit .

mds:AssessmentDate a sh:PropertyShape ;
    skos:prefLabel "Assessment date"@en ;
    sh:path mdo:assessmentDate ;
    sh:datatype xsd:dateTime ;
    sh:minCount 1 ;
    sh:maxCount 1 .

mds:BodyPosition a sh:PropertyShape ;
    skos:prefLabel "Body position"@en ;
    sh:path mdo:bodyPosition ;
    sh:in ( ncit:C62167 ncit:C62166 ncit:C62122 ) .

mds:AnatomicalLocation a sh:PropertyShape ;
    skos:prefLabel "Location"@en ;
```

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Pulse Rate Measurement via GraphQL

```
{
    shape(uri:"mds:PulseRateMeasurement"){
        id
        labels {
            type
            text
        }
        properties {
            labels {
                type
                text
            }
            path {
                uri
            }
            datatype {
                uri
            }
            minCount
            maxCount
            maxExclusive {
                ...on Literal {
                    value
                }
            }
            in {
                ...on Resource {
                    uri
                }
            }
            hasValue {
                ...on Resource {
                    uri
                }
            }
        }
    }
}
```

Query


```
{
    "data": {
        "shape": {
            "id": "https://k.mdsol.com/s/PulseRateMeasurement",
            "labels": [
                {
                    "type": "preferred",
                    "text": "Pulse rate measurement"
                }
            ],
            "properties": [
                {
                    "labels": [
                        {
                            "type": "preferred",
                            "text": "Assessment date"
                        }
                    ],
                    "path": {
                        "uri": "https://k.mdsol.com/o/assessmentDate"
                    },
                    "datatype": {
                        "uri": "http://www.w3.org/2001/XMLSchema#dateTime"
                    },
                    "minCount": 1,
                    "maxCount": 1
                },
                {
                    "labels": [
                        {
                            "type": "preferred",
                            "text": "Body position"
                        }
                    ],
                    "path": {
                        "uri": "https://k.mdsol.com/o/bodyPosition"
                    },
                    "minCount": 0,
                    "maxCount": 1,
                    "in": [
```


Response

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Schema Mapping

We can generate physical models off of the shape syntax

Clinical Models

- EDC
- SDTM
- ADaM
- FHIR
- OMOP

Infrastructure

- GraphQL Schema
- Avro
- RDBMS DDL
- XML
- JSON

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EDC Mapping

Vital Signs 1

Form Not Done	
Assessment Date (dd/MMM/yyyy)	/ /
DAY	
Systolic Blood Pressure	
Systolic Blood Pressure Unit	MMHG
Diastolic Blood Pressure	
Diastolic Blood Pressure Unit	MMHG
Pulse	
Pulse Unit	BEATS/MIN
Body Position	

EDC Mapping as RDF/SHACL


```
mds:PulseRateMeasurement a sh:NodeShape ;

    mdo:mapping mdmap:PulseRate-EDC-Freebird .

mdmap:PulseRate-EDC-Freebird a mdo:ShapeMapping ;

    skos:prefLabel "Mapping from the pulse rate measurement shape to an EDC form" ;
    mdo:mappingReference <https://k.mdsol.com/d/freebird/edc/v2/> ;
    mdo:mappingTarget <https://k.mdsol.com/d/freebird/edc/v2/itemGroup/pulseRate> ;
    mdo:propertyMapping
        [
            mdo:property mds:AssessmentDate ;
            mdo:mappingTarget <https://k.mdsol.com/d/freebird/edc/v2/item/visitDate> ;
        ],
        [
            mdo:property mds:BodyPosition ;
            mdo:mappingTarget <https://k.mdsol.com/d/freebird/edc/v2/item/pulsePosition> ;
        ],
        [
            mdo:property mds:PulseRateMeasurementValue ;
            mdo:mappingTarget <https://k.mdsol.com/d/freebird/edc/v2/item/pulse> ;
        ],
        [
            mdo:property mds:PulseRateMeasurementUnit ;
            mdo:mappingTarget <https://k.mdsol.com/d/freebird/edc/v2/item/pulseUnit> ;
        ] .
```

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EDC Mapping as GraphQL

```
query{
    shape(uri:"mds:PulseRateMeasurement"){
        labels{
            text
        }
        mappings {
            reference
            propertyMappings {
                target
                property {
                    id
                }
            }
        }
    }
}
```

Query

```
{
    "data": {
        "shape": {
            "labels": [
                {
                    "text": "Pulse rate measurement"
                }
            ],
            "mappings": [
                {
                    "reference": "https://k.mdsol.com/d/freebird/edc/v2/",
                    "target": "https://k.mdsol.com/d/freebird/edc/v2/itemGroup/pulseRate",
                    "propertyMappings": [
                        {
                            "target": "https://k.mdsol.com/d/freebird/edc/v2/item/visitDate",
                            "property": {
                                "id": "https://k.mdsol.com/s/AssessmentDate"
                            }
                        },
                        {
                            "target": "https://k.mdsol.com/d/freebird/edc/v2/item/pulsePosition",
                            "property": {
                                "id": "https://k.mdsol.com/s/BodyPosition"
                            }
                        },
                        {
                            "target": "https://k.mdsol.com/d/freebird/edc/v2/item/pulse",
                            "property": {
                                "id": "https://k.mdsol.com/s/PulseRateMeasurementValue"
                            }
                        },
                        {
                            "target": "https://k.mdsol.com/d/freebird/edc/v2/item/pulseUnit",
                            "property": {
                                "id": "https://k.mdsol.com/s/PulseRateMeasurementUnit"
                            }
                        }
                    ]
                }
            ]
        }
    }
}
```

Response

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SDTM Mapping

USUBJID	VSDTC	VSORRES	VSORRESU	VSPOS
01-701-1015	5/7/14	68	mmHg	STANDING
01-701-1015	5/7/14	66	mmHg	STANDING
01-701-1015	5/21/14	67	mmHg	SUPINE
01-701-1015	5/21/14	65	mmHg	STANDING
01-701-1015	5/21/14	63	mmHg	STANDING
01-701-1015	6/18/14	63	mmHg	SUPINE
01-701-1015	6/18/14	57	mmHg	STANDING
01-701-1015	6/18/14	71	mmHg	STANDING
01-701-1015	7/2/14	61	mmHg	SUPINE
01-701-1015	7/2/14	59	mmHg	STANDING
01-701-1015	7/2/14	55	mmHg	STANDING
01-701-1015	12/26/13	58	IN	
01-701-1015	12/26/13	57	BEATS/MIN	SUPINE
01-701-1015	12/26/13	62	BEATS/MIN	STANDING
01-701-1015	12/26/13	65	BEATS/MIN	STANDING
01-701-1015	12/31/13	56	BEATS/MIN	SUPINE
01-701-1015	12/31/13	60	BEATS/MIN	STANDING
01-701-1015	12/31/13	57	BEATS/MIN	STANDING
01-701-1015	1/2/14	56	BEATS/MIN	SUPINE
01-701-1015	1/2/14	59	BEATS/MIN	STANDING
01-701-1015	1/2/14	59	BEATS/MIN	STANDING
01-701-1015	1/14/14	61	BEATS/MIN	SUPINE
01-701-1015	1/14/14	65	BEATS/MIN	STANDING
01-701-1015	1/14/14	61	BEATS/MIN	STANDING
01-701-1015	1/16/14	58	BEATS/MIN	SUPINE
01-701-1015	1/16/14	61	BEATS/MIN	STANDING
01-701-1015	1/16/14	62	BEATS/MIN	STANDING
01-701-1015	1/30/14	59	BEATS/MIN	SUPINE
01-701-1015	1/30/14	62	BEATS/MIN	STANDING
01-701-1015	1/30/14	59	BEATS/MIN	STANDING
01-701-1015	2/1/14	67	BEATS/MIN	SUPINE
01-701-1015	2/1/14	69	BEATS/MIN	STANDING
01-701-1015	2/1/14	65	BEATS/MIN	STANDING
01-701-1015	2/12/14	55	BEATS/MIN	SUPINE
01-701-1015	2/12/14	56	BEATS/MIN	STANDING
01-701-1015	2/12/14	57	BEATS/MIN	STANDING
01-701-1015	3/5/14	57	BEATS/MIN	SUPINE
01-701-1015	3/5/14	60	BEATS/MIN	STANDING
01-701-1015	3/5/14	57	BEATS/MIN	STANDING
01-701-1015	3/26/14	54	BEATS/MIN	SUPINE
01-701-1015	3/26/14	53	BEATS/MIN	STANDING
01-701-1015	3/26/14	52	BEATS/MIN	STANDING

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SDTM Mapping as RDF/SHACL


```
29  mds:PulseRateMeasurement a sh:NodeShape ;
30
31      mdo:mapping mdmap:PulseRate-SDTM33-Freebird .
32
33
34  mdmap:PulseRate-SDTM33-Freebird a mdo:ShapeMapping ;
35      mdo:mappingReference <https://k.mdsol.com/d/cdisc/dataTabulation/sdtmig/3-3> ;
36      mdo:mappingTarget <https://k.mdsol.com/d/cdisc/controlledTerminology/sdtmct/C66741.C49677> ;
37      mdo:propertyMapping
38          [
39              mdo:property mds:AssessmentDate ;
40              mdo:mappingTarget <https://k.mdsol.com/d/cdisc/dataTabulation/sdtmig/VS.VSDTC> ;
41          ],
42          [
43              mdo:property mds:BodyPosition ;
44              mdo:mappingTarget <https://k.mdsol.com/d/cdisc/dataTabulation/sdtmig/VS.VSPOS> ;
45          ],
46          [
47              mdo:property mds:PulseRateMeasurementUnit ;
48              mdo:mappingTarget <https://k.mdsol.com/d/cdisc/dataTabulation/sdtmig/VS.VSORRESU> ;
49          ],
50          [
51              mdo:property mds:PulseRateMeasurementValue ;
52              mdo:mappingTarget <https://k.mdsol.com/d/cdisc/dataTabulation/sdtmig/VS.VSORRES> ;
53          ] .
```

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SDTM Mapping via GraphQL

```
query{
    shape(uri:"mds:PulseRateMeasurement"){
        labels{
            text
        }
        mappings {
            reference
            propertyMappings {
                target
                property {
                    id
                }
            }
        }
    }
}
```

Query


```
{
    "data": {
        "shape": {
            "labels": [
                {
                    "text": "Pulse rate measurement"
                }
            ],
            "mappings": [
                {
                    "reference": "https://k.mdsol.com/d/cdisc/dataTabulation/sdtmig/3-3",
                    "target": "https://k.mdsol.com/d/cdisc/controlledTerminology/sdtmct/C66741.C49677",
                    "propertyMappings": [
                        {
                            "target": "https://k.mdsol.com/d/cdisc/dataTabulation/sdtmig/VS.VSDTC",
                            "property": {
                                "id": "https://k.mdsol.com/s/AssessmentDate"
                            }
                        },
                        {
                            "target": "https://k.mdsol.com/d/cdisc/dataTabulation/sdtmig/VS.VSPOS",
                            "property": {
                                "id": "https://k.mdsol.com/s/BodyPosition"
                            }
                        },
                        {
                            "target": "https://k.mdsol.com/d/cdisc/dataTabulation/sdtmig/VS.VSORRES",
                            "property": {
                                "id": "https://k.mdsol.com/s/PulseRateMeasurementValue"
                            }
                        },
                        {
                            "target": "https://k.mdsol.com/d/cdisc/dataTabulation/sdtmig/VS.VSORRESU",
                            "property": {
                                "id": "https://k.mdsol.com/s/PulseRateMeasurementUnit"
                            }
                        }
                    ]
                }
            ]
        }
    }
}
```


Response

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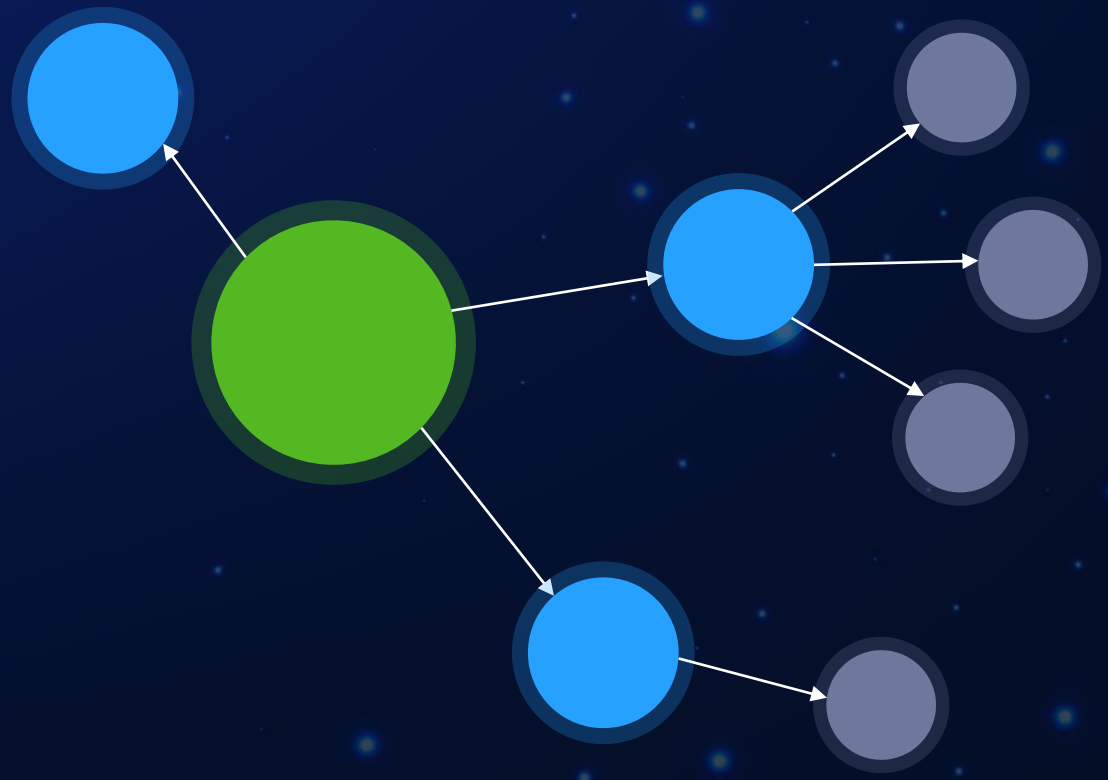
Analytics and Beyond

- Schema mapping to ADaM
- Automated Analysis Generation
- Integrated Quality Checks and Processing Logic
- Measurement specific Data Pipelines



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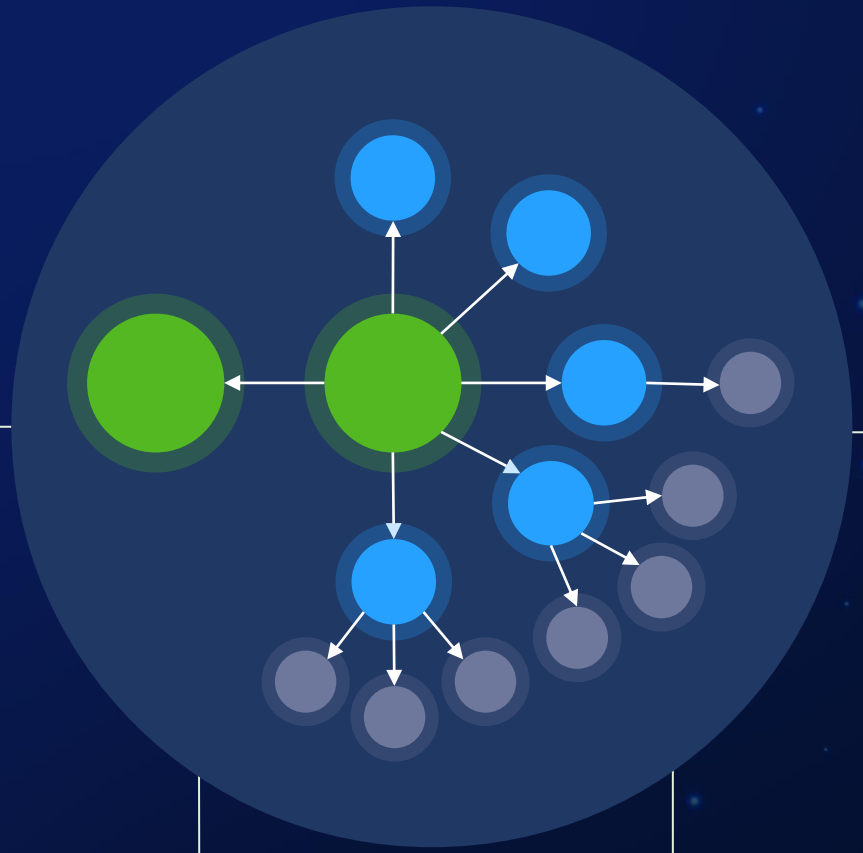


Design

Collection

Tabulation

Analysis

The Future of Working with Shapes

Libraries – RDF allows for the the construction of relevant collections

Easier to understand semantics will lead to **Democratization** to a broader user base

Versioning- DCAT and/or PAV ontologies provide robust versioning capabilities

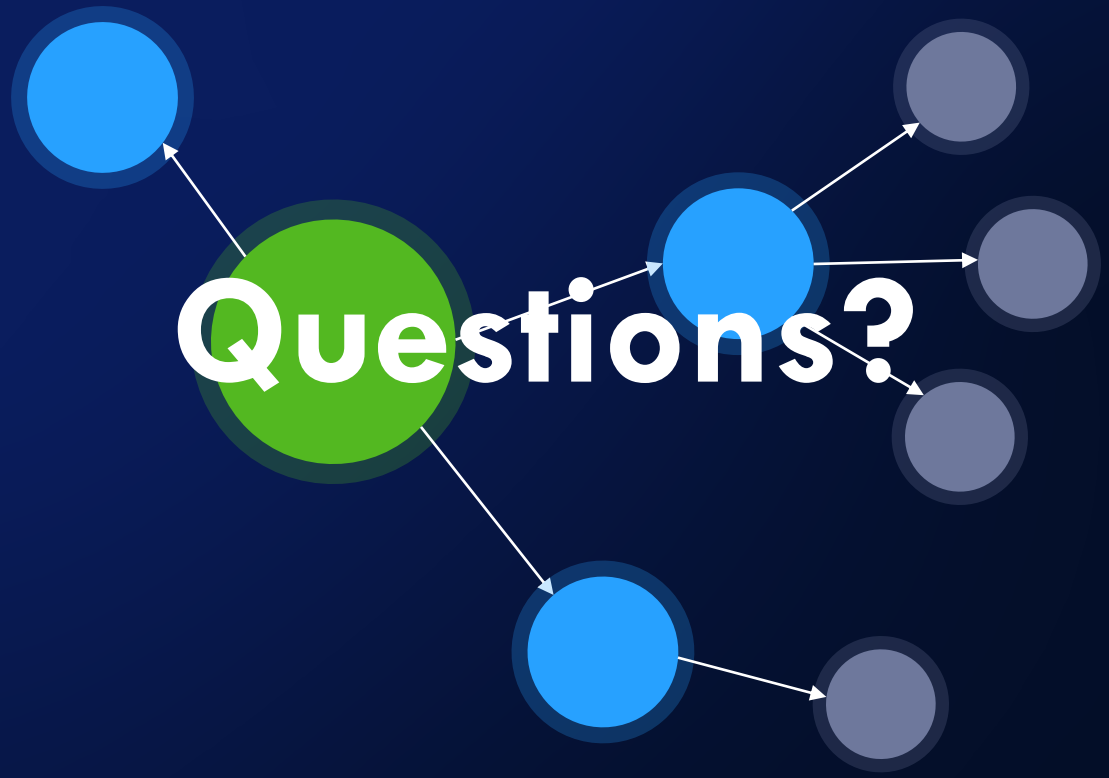
Enabling new and enhanced **User Experiences**

Ian Fleming

Director, Product Management

Data Platform

Semantics, Knowledge Graphs, GraphQL API



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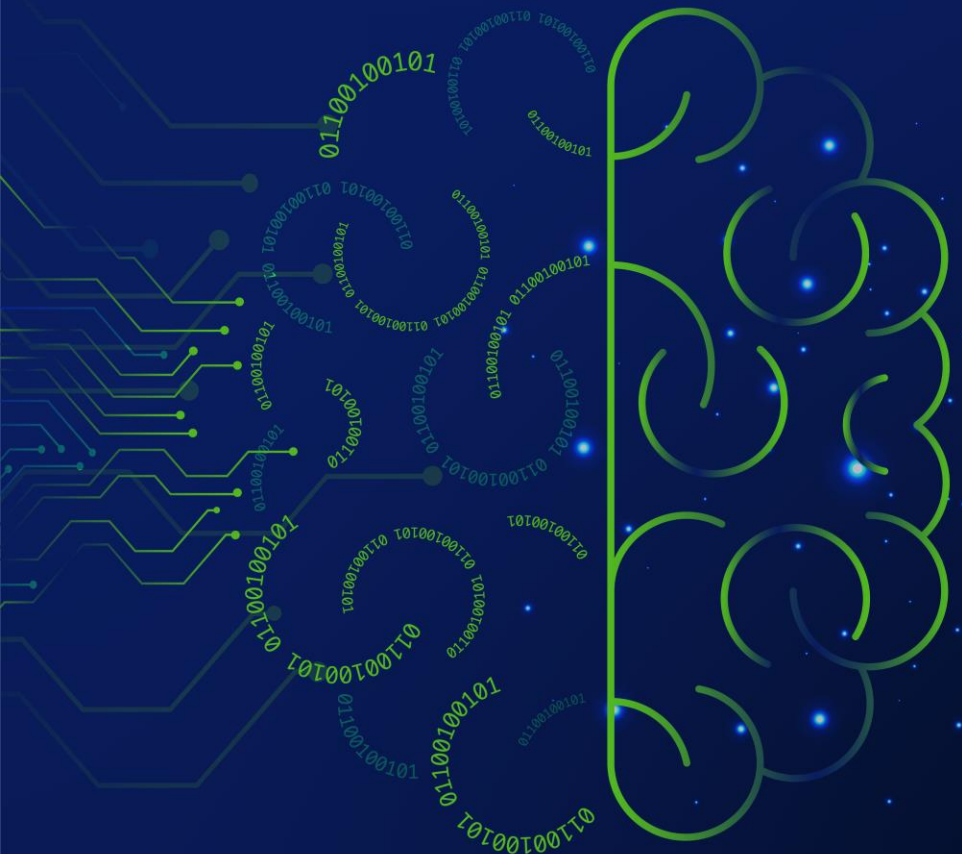
How metadata automation accelerates clinical trials, and was leveraged to expedite COVID-19 trials

Steven Benham | Formedix Booth 210



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Current challenges around metadata automation

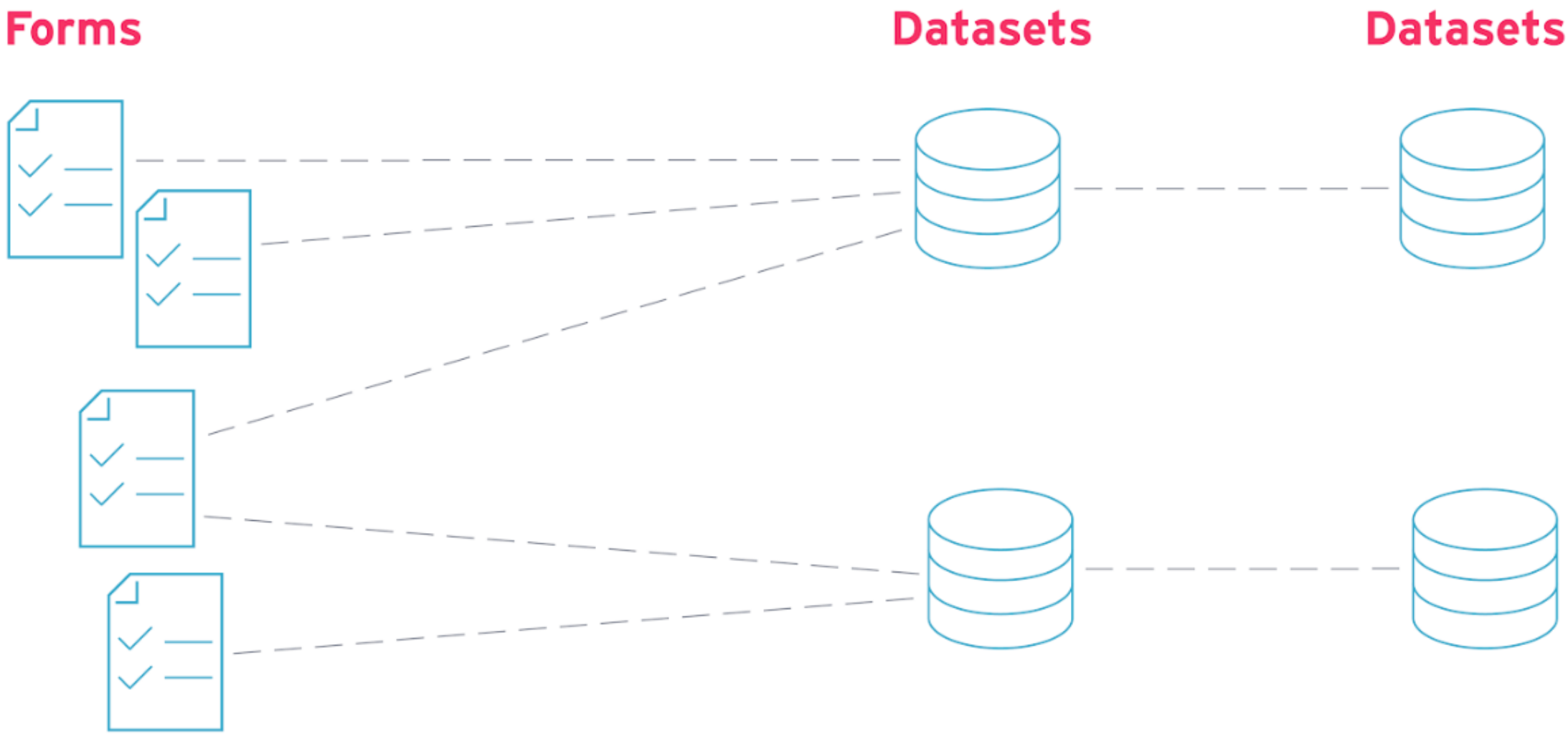
What impact can it have?

- Designing and building studies with no clear foundations and end-to-end approach.
- Changes not easily communicated to downstream activities.
- Increased costs and resources for study completion.
- Increased timelines on study submission.
- Patients waiting longer for lifesaving or life-changing treatments.

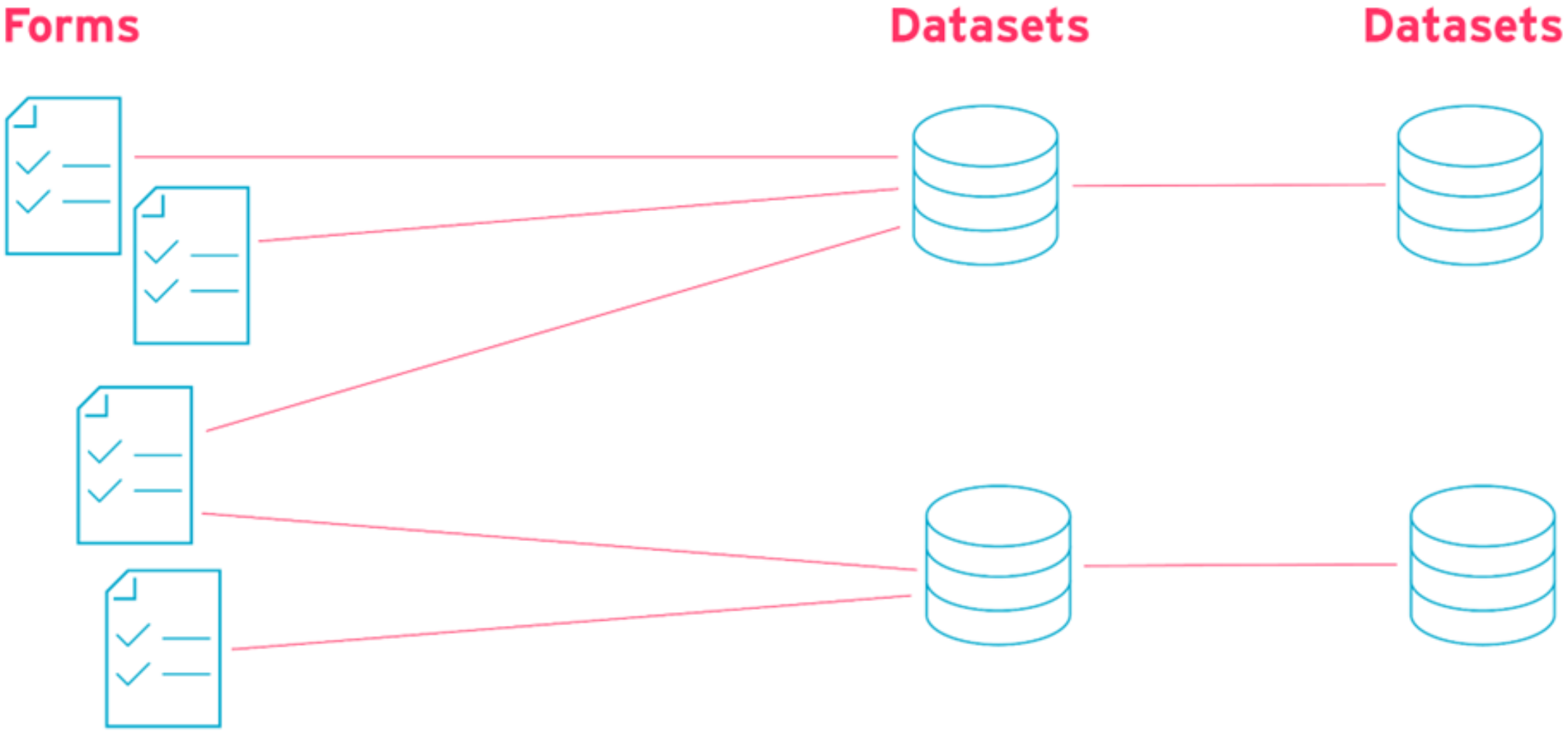
How we can improve things?

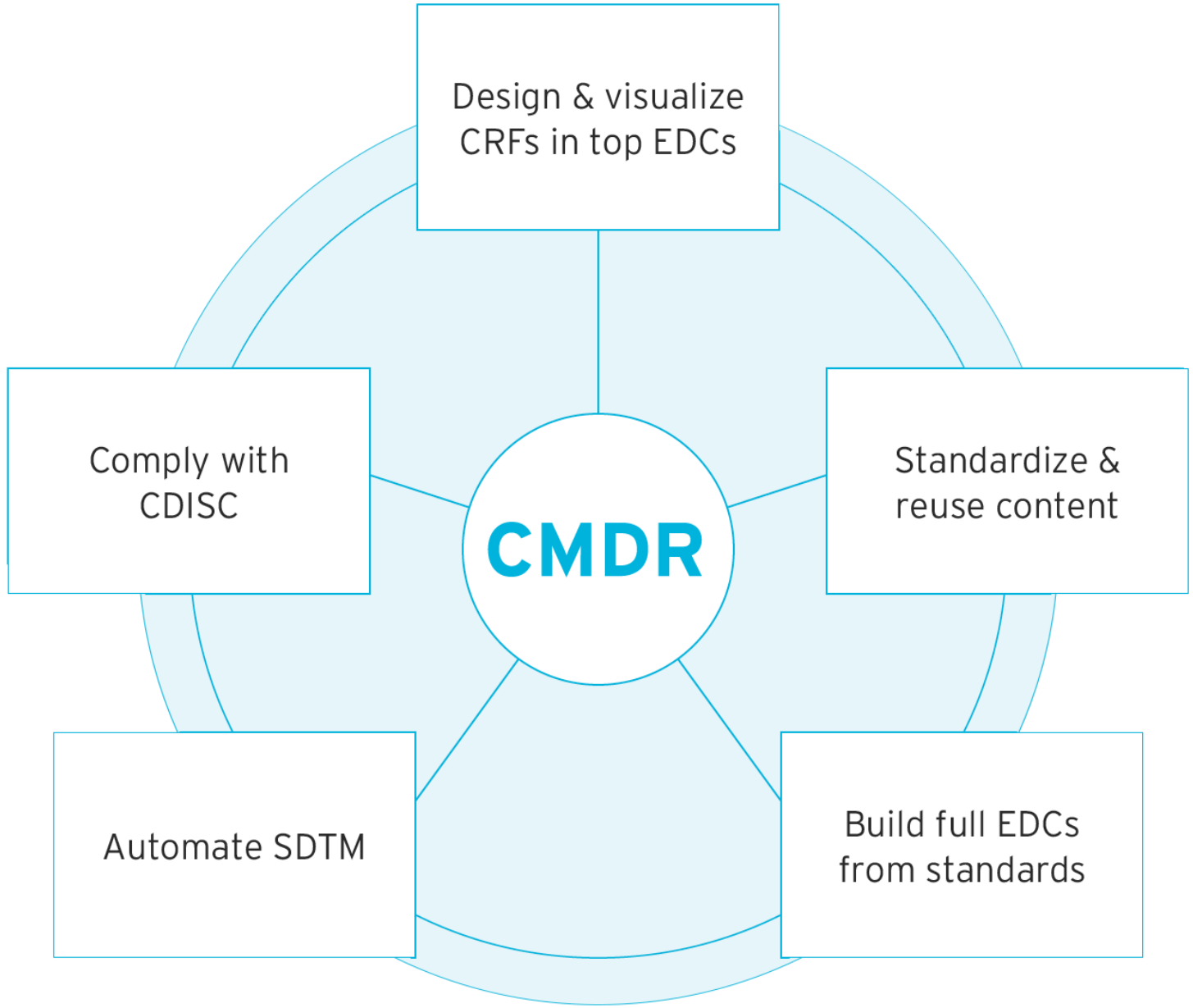
- Enhanced Metadata Management.
- Implement Standardization.
- Compliance.
- Automation.

End-to-end standards



End-to-end standards




Design & visualize CRFs in top EDCs
Comply with CDISC
CMDR
Standardize & reuse content
Automate SDTM
Build full EDCs from standards

Standardization in trials

Establish approved metadata content…

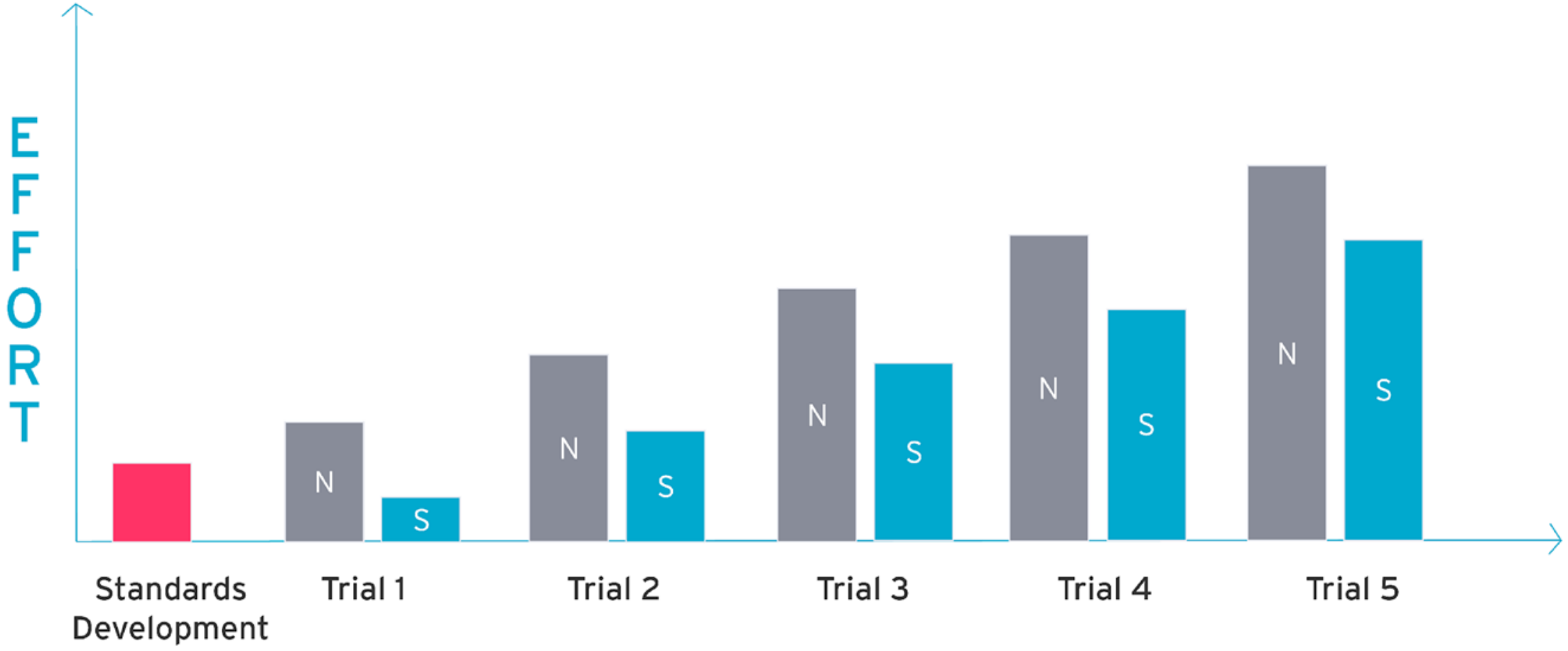
Standardizing metadata provides pre-approved content for reuse across future studies. This equates to time savings, and better data quality and consistency. Plus, it's easier for stakeholders to find the latest approved content.

Flexible management of organizational standards

For end-to-end studies:

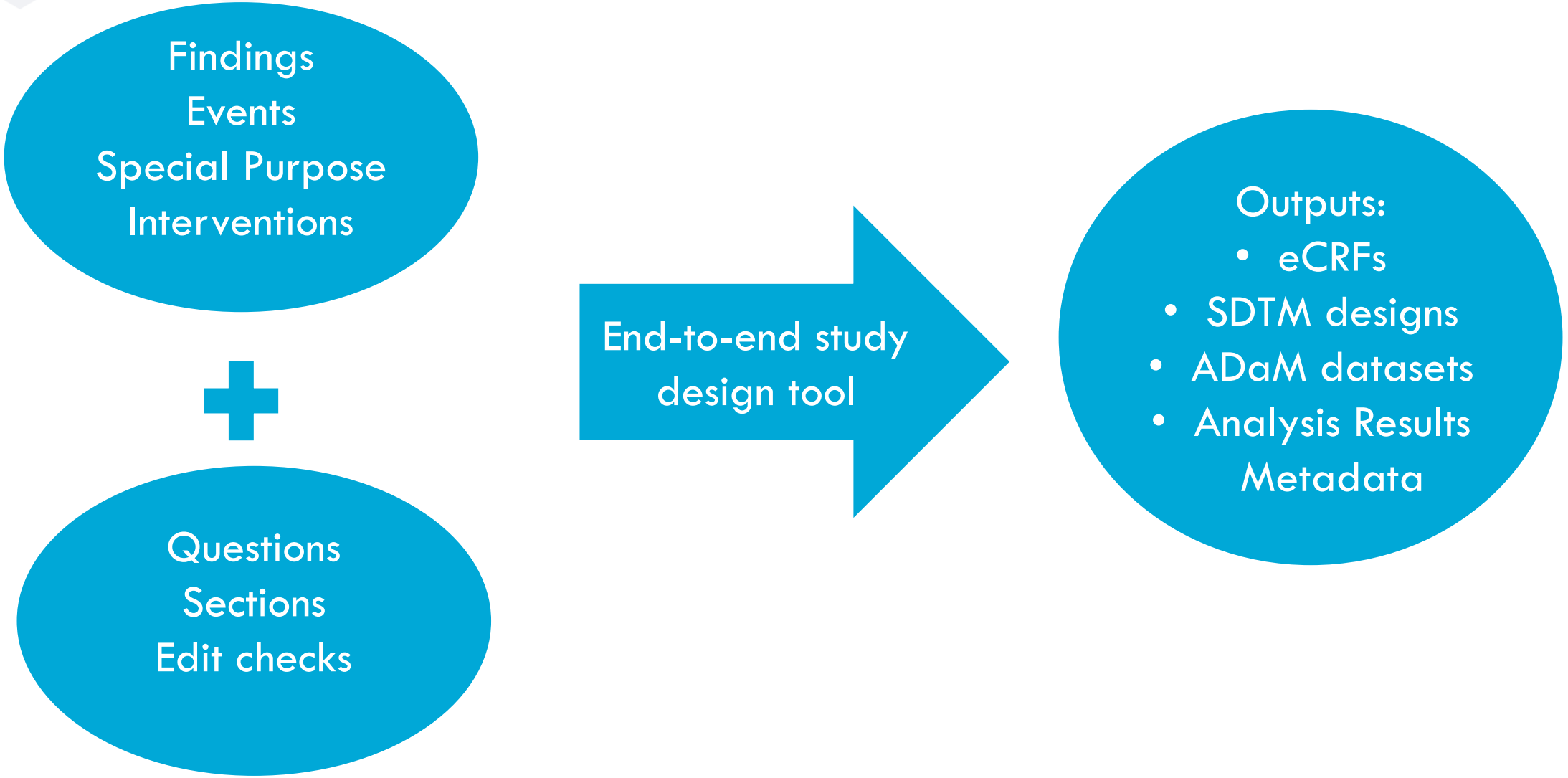
- Define & maintain organizational standards that can be used to build studies, increase data quality and reduce design time.
- Standardize specific therapeutic areas to make a more efficient study design process.
- Define rules for how standards are used in studies.
- View the compliance of studies compared to standards.

Effort level – standardization VS no standardization



N = No Standardization
S = Standardization

Using CDISC to design an end-to-end trial



Benefits of upfront compliance

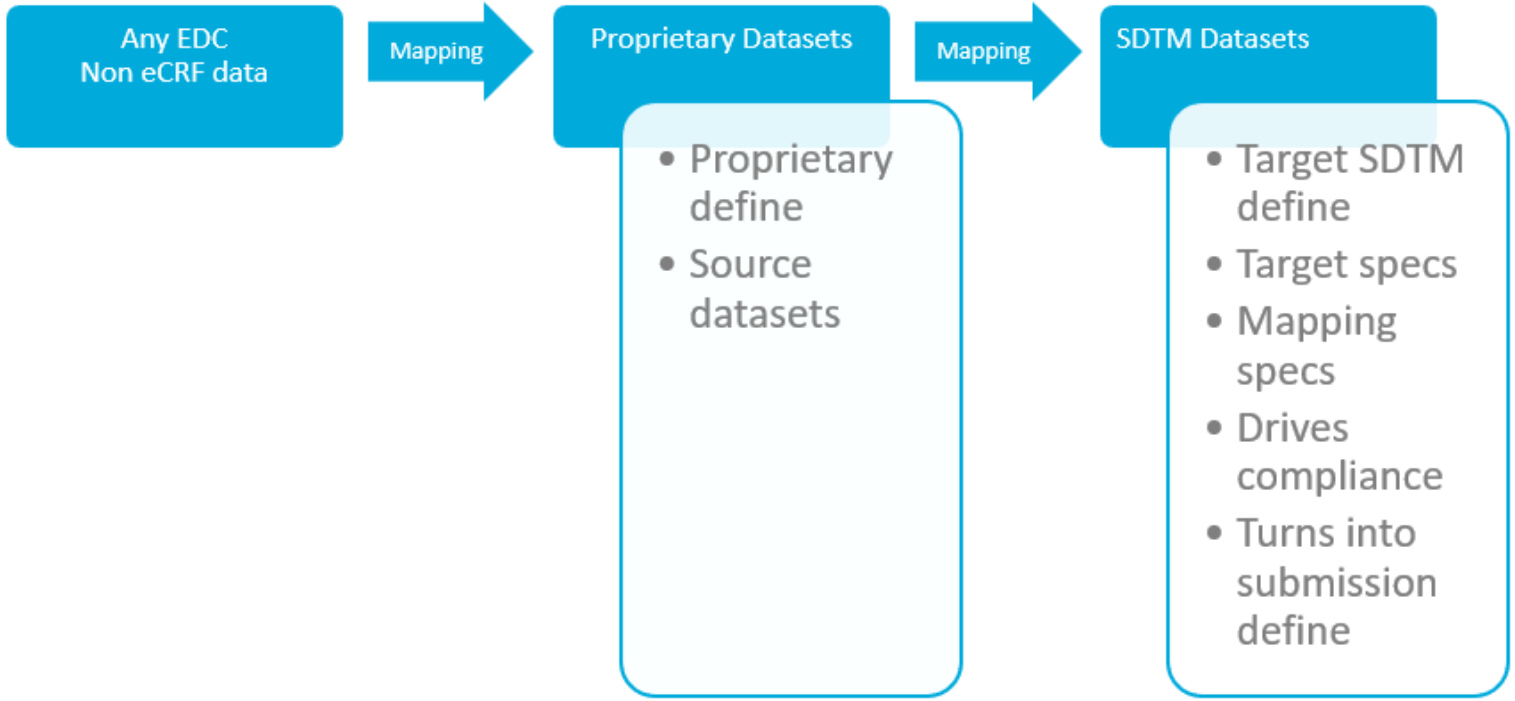
- Fewer errors.
- Better quality metadata.
- Increased consistency across trials.
- Avoid submission delays.

Automation

- Design studies end-to-end.
- Updated designs are visible to all stakeholders at any point in the end-to-end process.
- Link studies to the EDC system.
- Generate SDTM datasets from EDC and other source data.

Automated SDTM generation for COVID-19 trials

- A recent use case using enhanced SDTM metadata automation was for COVID-19 trials.
- Streamlined automation allowed SDTM generation to keep up with rapid changes in data and new findings.



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Thank you - any questions?

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How Organizations are Leveraging Standardization in Clinical Trial Design & Build

6 October 2022