Towards Collaboration

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# Change History

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# Introduction

When I think about the current situation within our industry, I see barriers, barriers to collaboration, barriers to better data. We speak the same language (CDISC) but different dialects. The bar to deploying the CDISC standards is set high, and tools are not readily available, especially to the academic community. Where tools exist, integration is difficult. The ability to pool data without a significant effort is elusive and we struggle to make use of such data for a variety of secondary uses and share it with others.

I was out walking while thinking about this article and I made some notes on my phone, sketched out some ideas. Later I airdropped the notes to my iPad and added some more info while watching some bad TV. I then dropped them onto my laptop. Why cannot I not do the same with my clinical study metadata and data? Why is it not possible to for sponsor A to “airdrop” a definition to CDISC, to sponsor B? The direction of information sharing is one way, standards come out from CDISC, but we cannot share a new definition electronically easily in the other direction, collaboration is not a two-way street.

Why can I not quickly deploy tools that assist me in collecting data that is of sufficiently high-quality that it pools with data collected by someone I have yet to think about collaborating with?

In the summer of 2020, I wrote a paper [1] about the need to define better APIs to assist vendors in building better tools and the need to align such APIs with an Industry Knowledge Graph. This needs to be made real such that the potential can be demonstrated to a variety of stakeholders.

This paper proposes developing that idea via the use of an industry knowledge graph implemented via a series of open-source micro-services. Iterations can then be used to expand functionality and demonstrate how industry could use such an approach to increase collaboration and remove silos.

This is not about prototyping; it is about a considered development executed iteratively designed to a) prove that data can have more utility other than the primary use case of submission; b) provide tools to the community at large; and c) provide a foundation for the community to build capability on top.

# Approach

The suggested approach is to:

1. Use recent experience to develop an industry Knowledge Graph (KG)
2. Use the KG to develop a set of open-source micro-services to that, as a set, provide an implementation to industry
3. Provide some simple User Interfaces (UIs) to demonstrate key facets of the implementation and key capabilities
4. Iterate and build capability implementing increasing coverage of the KG
5. Provide deployment capabilities so as to make it easy for those wishing to deploy the services

We should be guided by FAIR principles, see the section at the end of the document

# Knowledge Graph

The key to ensuring that we remove silos from our world is to have a single representation of our world that reflects that world but provides a practical implementation of it. BRIDG does this but is not easy to deploy and experience has shown that a knowledge graph can provide a solid base for implementation.

There is a need to provide a sound base for that KG and there is a case for a metamodel to be in place to ensure consistency across the KG. The ISO 11179 metadata standard can provide useful pieces but I feel it constrains the benefits provided by a KG so we need to mix with caution. There are many good semantic standards such as SKOS that can be leveraged.

The KG can provide an Industry knowledge graph that all can share and improve with well-defined sections with good interfaces that lend themselves to a microservices architecture.

The KG should incorporate knowledge from both BRIDG and Transcelerate’s DDF project. The KG should be dedicated to the task of being able to build and execute studies, automate the production involved in such and facilitate the rapid pooling of data from such studies.

One very important aspect of this suggestion is the knowledge graph. It provides for the single source of truth and everything we do is but a view of this graph. The service approach allows us to build useable components focused on one aspect and to build a solution by having the services cooperate.

# Services

## Overview

Once the KG has been developed to a sufficient level the graph can be implemented as a set of micro-services. The services should

* focus on one section of the graph
* implement the necessary business logic
* present a consistent interface via an API to consumers that could be an UI or another service
* be self-aware and allow for collaboration
* be able to load content from sources and thus front-end existing content
* users should be able to deploy one or more services easily

## Focus

Each service should be focus on one job and one job only. It should be self-contained with its own database and only collaborate via APIs

## Business Logic

The service should implement a common set of services and enough business logic that supports the ecosystem. This logic can be expanded over time through an iterative approach

## API

The API presented should conform to good design rules. The API will need not only to support the busines functionality required but also common functions to support such things as deployment, status monitoring as well as common functions such as CRUD operations

## Self-aware

A service should be self-aware, i.e. it should be able to communicate with another instance of itself. A sponsor terminology micro-service should be able to send a code list to another sponsor’s terminology micro service.

## Load

A service should be able to load content from sources of data and allow for new loaders to be incorporated. This will allow services to “front-end” existing content. For example, a sponsor may have an MDR that contains its terminology. The terminology micro-service should be able to incorporate a new loader such that the content can be loaded into the micro-service. This will then allow that content to be shared within the ecosystem.

## Deployment

Micro-services should be easy to deploy without technical knowledge. See the section below.

## Technology Neutral

Services should be technology neutral, they could be implemented in Java, Python, Ruby etc. In theory databases for services could be relational or graph but I think it would be wise, because of FAIR, to use a semantic approach and allocate URIs to items that persist through time. The KG drives us in this direction.

Services should be designed to make use of common libraries for the common functionality expected to be implemented within services. This will allow services to be implemented quickly.

# APIs

Every service type needs to provide a public API that is published to allow tool builders to build against or use that API within their own tools. The API should provide:

* Common API services – functions that are common to all services and that all services should provide
* Role Specific API – functions specific to the service

It would make sense to build upon the existing CDISC Library APIs and build them in a common style etc. But there may need to be some updates to allow the support of FAIR principles etc.

Services should also support import and export in specific formats such as ODM, Define.xml etc.

# User Interface

User Interfaces can make or break an implementation and are very important, but they are also expensive to build. It is suggested, initially, to build any UIs using R Shiny and make open source. As a principle it might be nice to have a simple open and free UIs such that any organization can quickly get up to speed.

With that in mind, experience has shown that people still love MS Excel. It is flexible and everyone seem to have it on their desktop “for free”. It would be interesting to see if we can we drive a service from Excel. I have had some initial thoughts on the challenges, and it might be possible in most cases. This may be of interest to individual users and smaller organizations.

User Interfaces, like the services, should be offered as open-source software with a single service focus. A set of UIs with a common look and feel will allow users to use the functionality immediately without cost. However, this does not prevent complex, expansive, and complete applications being built by vendors with vendors free to charge for those UIs.

# Deployment

As services become stable it would be beneficial to the community to be able to deploy them quickly and select associated user interfaces. It would be ideal if there was a portal whereby a user could select a set of services could be quickly selected, configured, and deployed on servers. This process should be made as simple as possible and would be of interest to smaller sponsors and academia.

# Services Envisaged

Below is a list of envisaged services. The list is not definitive, depends on design issues etc, but worth noting to give a flavour of what might be possible.

* Terminology (CDISC)
* Other Terminology
  + LOINC
  + MedDRA
  + Others
* Terminology Equivalence
  + CDISC <-> LOINC
  + Others
* BCs
  + Connect to BC mining. It would be possible to feed the BC service from the mining tool thus allowing a library of BCs to be quickly shared.
* Forms
* SDTM
  + CDISC core and Sponsor implementations of domains
* Collections
  + Base for TAs (a combination of domains, BCs and forms)
* Study
  + Study definitions such as endpoints.
  + Study Build resulting in a complete design.
  + Study Data attached to the appropriate design. This is the important service in that it is the one that allows the ecosystem to share data.
  + EHR / FHIR Interface. Take a study design and fulfil the study contract with data from an EHR, see [3].
  + Automate SDTM from Study Data, see [3].
  + Conformity. Does everything pass the appropriate checks?

# Scenarios

## General

The few “scenarios” described below have been included to give a flavour of what is possible and what could be achieved. They are not definitive and do not cover everything that could be done, they are purely for illustrative purposes.

## “Air Drop” Terminology

Imagine we have a single service. It knows about the structure of CDISC terminology, has a CDISC library API loader such that content is up to date and has a simple browsing and search user interface. We could spin up a service that sits in front of the CDISC library and allow people to look at the CDISC CT. Not really a step forward.

Diagram

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## Now, if that service implemented a few more features, say allowed better relationships between code lists such as RACE and RACE AS COLLECTED then it offers an improvement, albeit small. But it allows CDISC to provide richer content without disruption to the main library development.

Now a sponsor writes a loader that can take its terminology that is used in conjunction with the CDISC CT and populates an instance of the service. The same UI allows a user to browse and search its own CT.

A picture containing text

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However, if the services are self-aware then any search or browsing could include the content from the other service if that content has been made visible. Obviously the CDISC content would be, but the sponsors would probably not be.

Items (code lists) in the sponsor service could be made public and thus show up. CDISC could then, if it so chose, request a copy of an item (code list) as a draft for new CDISC official content.

Sponsors will be able to see draft content a lot easier if such content was placed into the service allowing for review etc.

Now a second sponsor runs up a service. The sponsors could, if they so choose, share some selected content by making the item(s) public. CDISC then has the option to pull that interesting content for the basis of new CDISC content after appropriate review.

Diagram

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We now have “air drop” capability and we have a terminology ecosystem.

More and more users can deploy a terminology service, federated searches are possible; “does anyone have content for X”, the conversation is two-way, the community is collaborating, and the cost of entry is lowered.

Note that a sponsor may not have an existing system and thus can just deploy the micro-service and a UI to drive it but join the collaborative world with little investment.

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## Study Build

This scenario is just here to illustrate a more complicated example of multiple services being deployed. Let us assume that CDISC has services for terminology, BCs, Forms and SDTM. A sponsor has the same set, but these are providing additional sponsor BCs, forms and sponsor configured SDTM domains. If we add a Study Build service, we have everything needed to build a study. Here we have two ecosystems as illustrated, the one sharing definitions between CDISC and the sponsor as above and then another for the sponsor and its studies. Of course, a second sponsor can have its own study design service and linked to the first sponsor’s if they wish to collaborate but CDISC isn’t concerned with study builds, just the tools and definitions to get there.

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# Ecosystems

As can be seen from the scenarios described above, as services are added, and those services grow in capability, you start to build an ecosystem. Such ecosystems might be of interest to those users in the academic community who need simple and quick access to the use of the CDISC standards. The ecosystem may also be useful to demonstrate capabilities and potential for such use cases as the Transcelerate DDF project.

In addition, by providing the services you open the door to the development of third-party user interfaces that go beyond the basic open-source ones provided.

# Iterate

Not everything can be built from day one. It is suggested that the initial focus be to demonstrate BCs and Study artefacts first. It would then be wise to expand and provide a constant flow of releases, add new services, and expand those contributing to the work.

# Issues

During the development the following issues will need to be resolved. They are noted here such that they are not forgotten:

* Resolvable URIs and FAIR usage
* Authentication, use industry standard mechanisms
* User Roles
* Service Location and Discovery
* Organizations and management thereof (ISO11179 related)
* Status of items using ISO11179, keep it simple. Align with CDISC Library.

# References

[1] Models, API and FHIT, A New World, Iberson-Hurst, July 2020

[2] FAIR Principles.  
See <https://www.go-fair.org/fair-principles/>

[3] Into the fire, Linking CDISC and FHIR, 2018.   
See <https://www.lexjansen.com/phuse/2018/si/SI12.pdf>

# FAIR

The following is reproduced from [2]. Inserted here for completeness.

## Findable

The first step in (re)using data is to find them. Metadata and data should be easy to find for both humans and computers. Machine-readable metadata are essential for automatic discovery of datasets and services, so this is an essential component of the FAIRification process.

* F1. (Meta)data are assigned a globally unique and persistent identifier
* F2. Data are described with rich metadata (defined by R1 below)
* F3. Metadata clearly and explicitly include the identifier of the data they describe
* F4. (Meta)data are registered or indexed in a searchable resource

## Accessible

Once the user finds the required data, she/he/they need to know how can they be accessed, possibly including authentication and authorisation.

* A1. (Meta)data are retrievable by their identifier using a standardised communications protocol
  + A1.1 The protocol is open, free, and universally implementable
  + A1.2 The protocol allows for an authentication and authorisation procedure, where necessary
* A2. Metadata are accessible, even when the data are no longer available

## Interoperable

The data usually need to be integrated with other data. In addition, the data need to interoperate with applications or workflows for analysis, storage, and processing.

* I1. (Meta)data use a formal, accessible, shared, and broadly applicable language for knowledge representation.
* I2. (Meta)data use vocabularies that follow FAIR principles
* I3. (Meta)data include qualified references to other (meta)data

## Reusable

The ultimate goal of FAIR is to optimise the reuse of data. To achieve this, metadata and data should be well-described so that they can be replicated and/or combined in different settings.

* R1. (Meta)data are richly described with a plurality of accurate and relevant attributes
  + R1.1. (Meta)data are released with a clear and accessible data usage license
  + R1.2. (Meta)data are associated with detailed provenance
  + R1.3. (Meta)data meet domain-relevant community standards