Clinical Analysis and Reporting Environment (C.A.R.E.)

The Industrialization of Clinical Trial Analysis and Reporting.

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Executive Summary

With an increase in the number of Clinical trials, new trial designs, the challenges presented by big data and globally distributed teams to name just a few of the challenges our industry faces. The approaches to the task of providing accurate, timely and compliant Clinical Submissions necessitates a rethink of our approach to how we formulate and deliver the statistical analysis product . The CDISC standards acceptance and maturation offers us a unique opportunity upon which to begin to build a scalable and modular framework. This poster takes a high level view of the C.A.R.E. framework and its surrounds. The purpose of C.A.R.E. is the automatic creation of a significant percentage of each Reporting Activity's deliverables for submission.

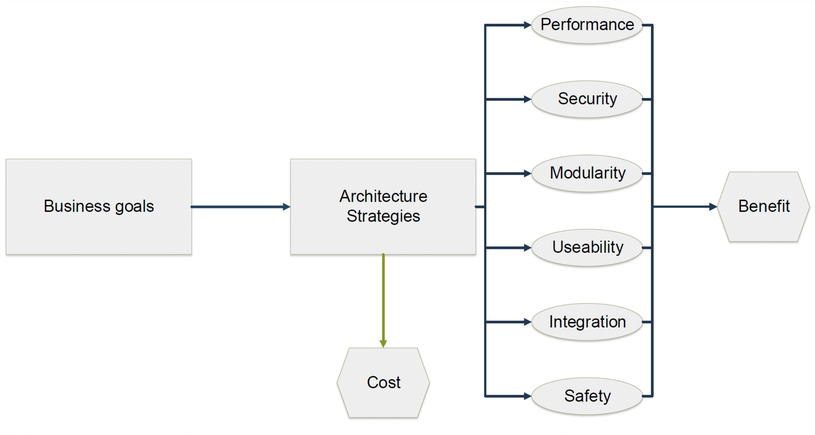
Abstract

The continuing maturation and acceptance of the CDISC family of standards has reached a point where it has become a realistic mission to implement a comprehensive framework for Clinical Analysis and Reporting Environment (CARE). The analysis and reporting of Clinical Trials is a field where this advance is essential. This poster provides an overview of the business drivers in play and the challenges to be faced in the pursuit of this industrialization goal. It further presents a view of the proposed system, its components and their relationships. A central component of the CARE framework is the clinical business rule engine because it allows for a scalable system that will tightly couple the Output Governance processes to those of Data Governance, Metadata Management and the business of efficient Trial analysis, package creation and submission.

Vision

To employ an agile system development approach to the provision of the C.A.R.E. solution framework that delivers a highly interoperating set of modular components, with the end goal of providing a way to automate the delivery of high quality Clinical Trial Analysis Packages. C.A.R.E would rely on a modern Object Oriented set of system development tools and methodologies for its implementation. SAS and R artifacts are to be considered deliverables from C.A.R.E..

Premises



When you consider the amount of money required to research develop trial and get a drug to market, the Clinical Trial Analysis and Reporting component is a relatively small slice of the overall pie. The cost benefit analysis question for CARE is an essential one to answer. A premise for the development of CARE is there is an economic case.

The firming up of CDISC standards and their growing use in the industry lead to, and make this an optimal time for such a framework to be built. The management of increasingly sophisticated statistical analysis, clinical data warehousing/study pooling also provide a convincing premise for the development of the CARE framework.

Where´s the Polymorphism?

It's one central concept you need to understand if you want to build any computer system of a non trivial size and scope.

```
class Shape {
  protected:
    int width, height;
  public:
    Shape( int a=0, int b=0)
    {
      width = a;
      height = b;
    }
    int area()
    {
      cout << "Parent class area :" <<endl;
      return 0;
    }
};
```

```
class Rectangle: public Shape{
  public:
    Rectangle( int a=0, int b=0)
    {
      Shape(a, b);
    }
    int area ()
    {
      cout << "Rectangle class area :" <<endl;
      return (width * height);
    }
};
```

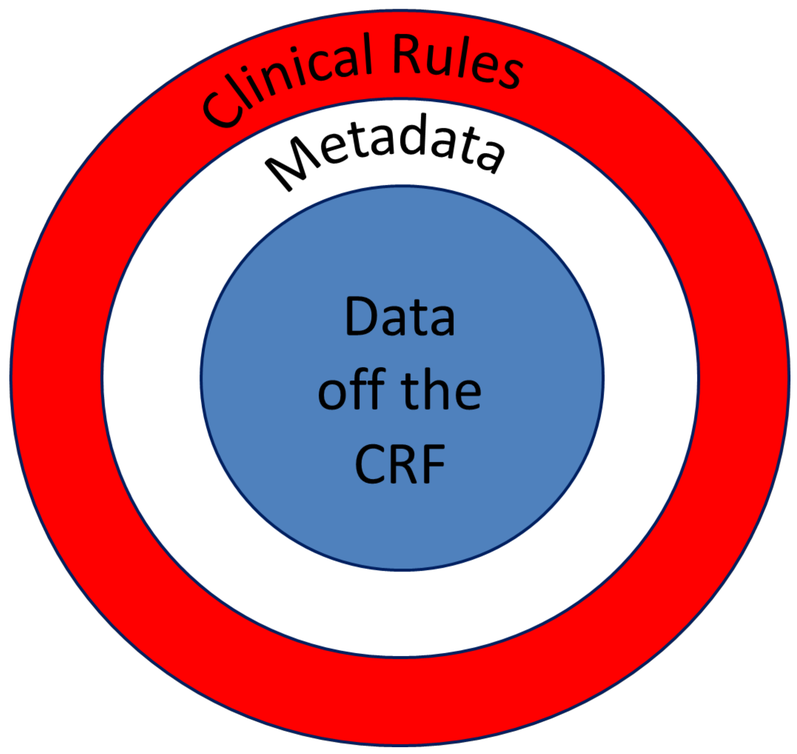
```
class Triangle: public Shape{
  public:
    Triangle( int a=0, int b=0)
    {
      Shape(a, b);
    }
    int area ()
    {
      cout << "Rectangle class area :" <<endl;
      return (width * height / 2);
    }
};
```

Vasa Syndrome

Most current industry solutions have at their core a library of validated SAS macro libraries.

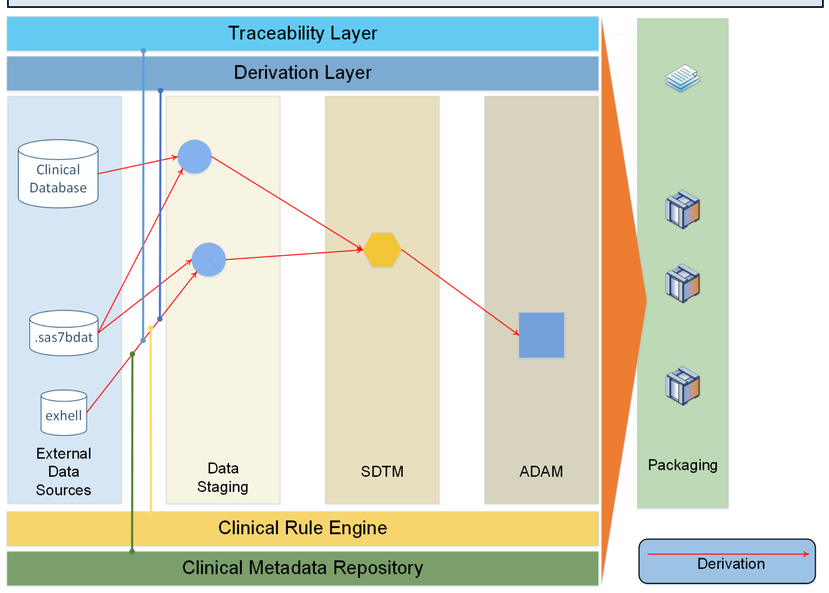
Observed Behaviour	Rational
Building or relying upon large libraries of SAS macro code.	C.A.R.E. treats SAS as an output. SAS or R are wonderful tools for data analysis. They fail to provide the developer sufficient facility to manage complexity and scalability.
Managing CDISC standards and Clinical Trial Metadata with excel spreadsheets.	There are too many dimensions and dependencies to manage solely with excel. C.A.R.E.'s broad definition of METADATA sees the combining of the CDISC, Protocol, Trial Metadata and Clinical Report Definition Language.
The cataloguing of output specifications in word or .png format	C.A.R.E. consumes output specifications into its MDR. With the Clinical Report Definition Language.
Implementing solutions based on Eclipse or netbeans.	The security and speed requirements, exclude these java based solutions. Internal dependency bloat.
Poor overall strategic positioning of systems.	Embrace the Agile Manifesto! Trying to cover too much ground without laying a solid foundation of metadata and clinical business intelligence.

Metadata



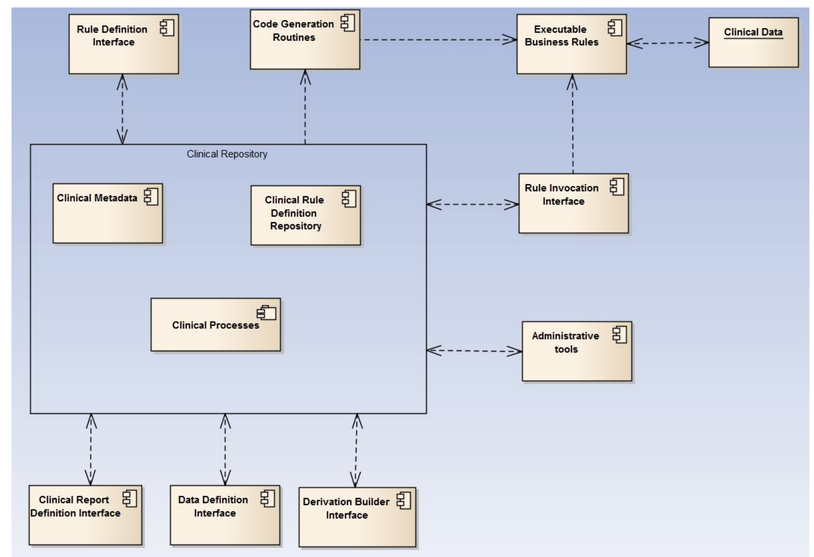
The word Metadata is often defined as 'data about data'. Clinical Metadata is any data not collected off the CRF. The C.A.R.E. framework is based upon a tight coupling of the Clinical Rule Engine Component and the Clinical Metadata Repository.

C.A.R.E. Operation



This diagram presents the major components of the framework. The stages that data passes through from External Data Staging, SDTM and finally ADaM. The traceability layer manages the capturing of all activities within the framework. The Derivation layer controls the creation and execution of sequenced atomic data operations within the framework. The Clinical Rule Engine layer exercise the business logic using the Clinical Metadata Repository.

C.A.R.E. Framework



C.A.R.E. System Components

Component Name	Description
Clinical Rule Engine	Central to the C.A.R.E. Framework Interface allows the creation of actionable rules.
Clinical Metadata Manager	Allows for the CRUD in the MDR.
Protocol Builder	Creates and Manages Protocol Definition as per the CDISC Standard.
Trial Design	Creates and Manages Trial Definition as per the CDISC Standard.
Clinical Reference Library	A library of clinical reference data and definitions used throughout C.A.R.E.
Audit Control	Set of functionality to manage the compliance aspects of C.A.R.E.
Derivation Builder	Manages the creation of derivation definitions and their sequences.
Output Definition Builder	Tool used by the output governance team to define and capture the deliverable catalogue.
Data Sources Management	Manages processes around data Staging
Deliverable Management	Clinical trial deliverables submission management

The Tool Set

Product	Why
C++	Secure, object oriented flexible and fast.
Sparx Systems EA Ultimate	System Analysis and Design software, which allows for the modeling of business rules.
Oracle Database	Well understood and reliable relational database, which scales.
SAS	Essential for Clinical trial analysis and reporting.

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