iCARE Programme

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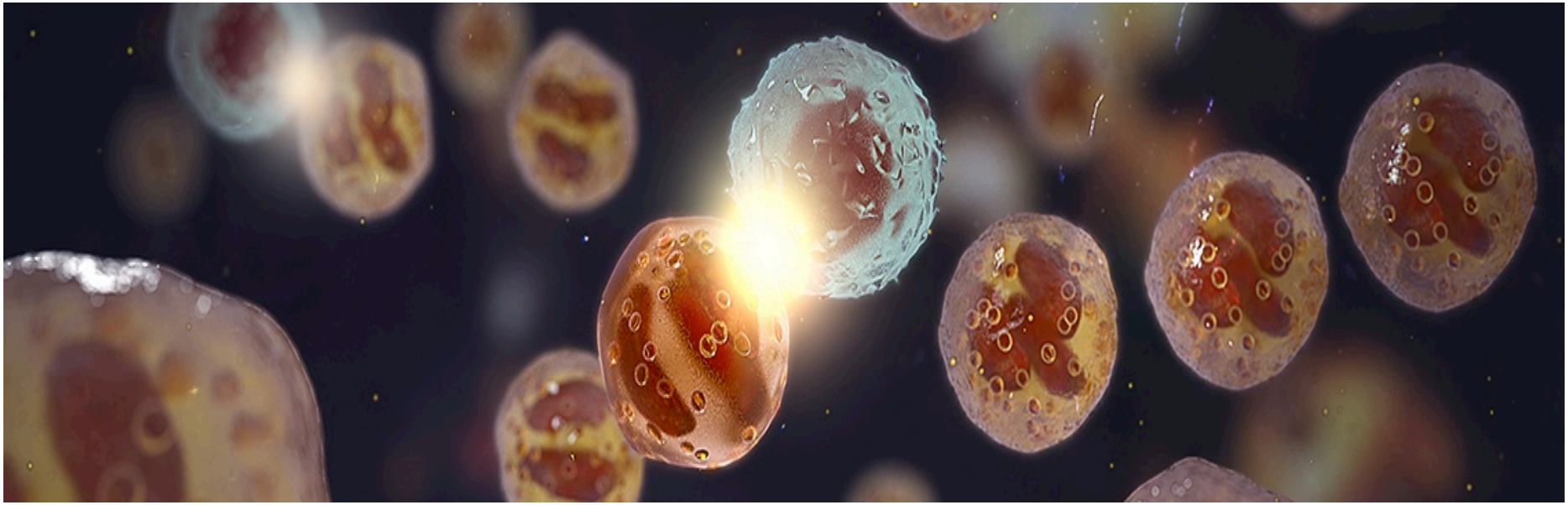
iCARE - Metadata-driven, Standards-based Clinical Analysis and Reporting Environment

May 23, 2016



iCARE Programme – PhUSE UK Presentation 2016
AGENDA

- What is iCARE
- Background / History
- Programme Organisation
- Solution Decision - entimiCE
- Programme Implementation Plan
- Phased Implementation Approach
  - Release 1
  - Future Releases

iCARE Programme – What is iCARE

iCARE- Programme objective
Integrated Clinical Analysis and Reporting Environment

iCARE delivers the technology and ways of working that enables collecting clinical data, verify quality against metadata, analyzing clinical data and produce input to submission files.

The major areas of benefit by delivering iCARE are divided into four areas:

1. **Simplification** of IS & application landscape, enabling consolidation of clinical data, one repository and integrated system for all science units
2. **Efficiency** by integrated systems and common and integrated business processes
3. **Flexibility and futureproof**, enabling the business need for flexible way of working and externalisation
4. **Streamlines end-to-end processes** from capture through to decision making

The new system "entimICE-AZ" will improve effiency and support increased regulatory submission activities, enabling us to get more innovative medicines to patients faster.

iCARE – Background / History

Problem Statement - Why is a change to the current situation needed?

1. **Analysis and Reporting**
   - Challenges with the current A&R systems :
     - Outdated Infrastructure and dependence on IT Commodity Services impact performance and stability which negatively impacts drug project delivery & submissions
     - Limitations for externalization and in-licensing
   - Does not facilitate Phase II to Phase III transition work

2. **Information landscape**
   - Clinical Data is copied and processed through many systems before becoming completely useful for final analysis.
   - Information exploitation and predictive science are not directly supported
   - Insufficient performance, stability and capacity

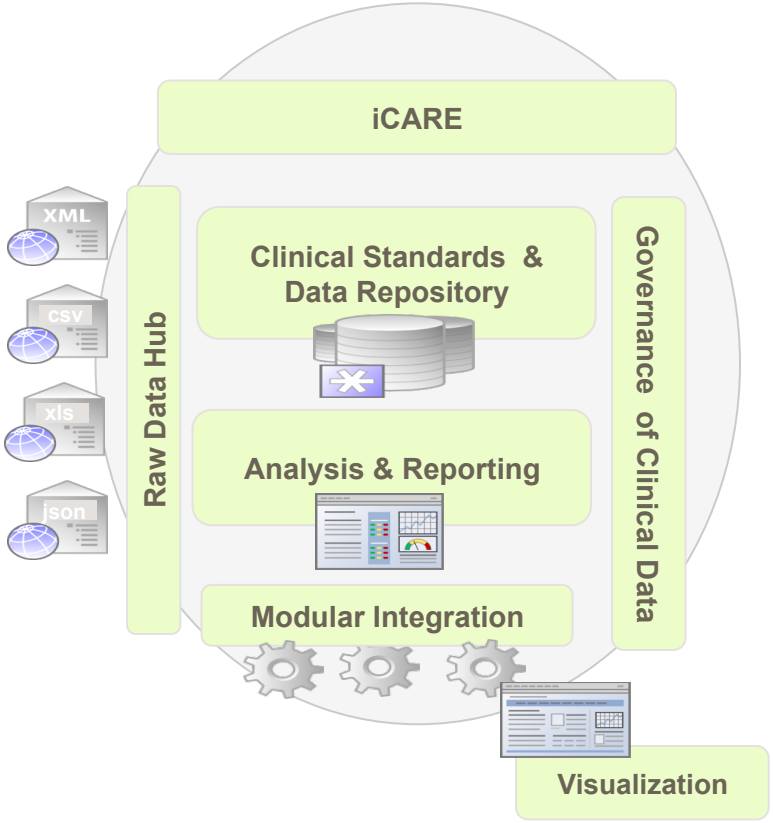
3. **Clinical Data Standards**
   - The current distributed and disconnected standards technology environment does not support searchability, traceability and scalability of AZ data standards
     - Vendors have a hard time delivering to expectations
     - Regulatory submissions are more complex/subject to error

iCARE – Background / History (cont.)

Cross Science Unit Delivery – Early Phase Research to Late Phase Drug Development

OVERVIEW:

- One Repository for Clinical Data
- Standards Metadata Repository (SMDR) supporting standards governance and workflow
- Supports capability for externalization and in-licensing of data
- Streamlines end-to-end processes from capture through submission
- More efficient information exploitation and decision making



OBJECTIVES:

- ✓iCARE will mitigate business risks and drive enhanced capabilities and usage of clinical data
- ✓Improved Operational Efficiency
- ✓Enable "Data for All" concept
- ✓ Reduced Risk of Delayed Regulatory Responses
- ✓ Reduced Risk of Delayed Submissions and other Cost of Poor Quality
- ✓ Support for In-Licensed Products
- ✓ Improved management of clinical data standards
- ✓ Reduced Technology and IS landscape Complexity

iCARE Programme – Background / History (cont.)

Approach

2013

- Combined 3 initiatives/projects into one programme => iCARE
- Gathering requirements for a cross functional holistic solution
- Completed a market analysis of commercial off the shelf tools

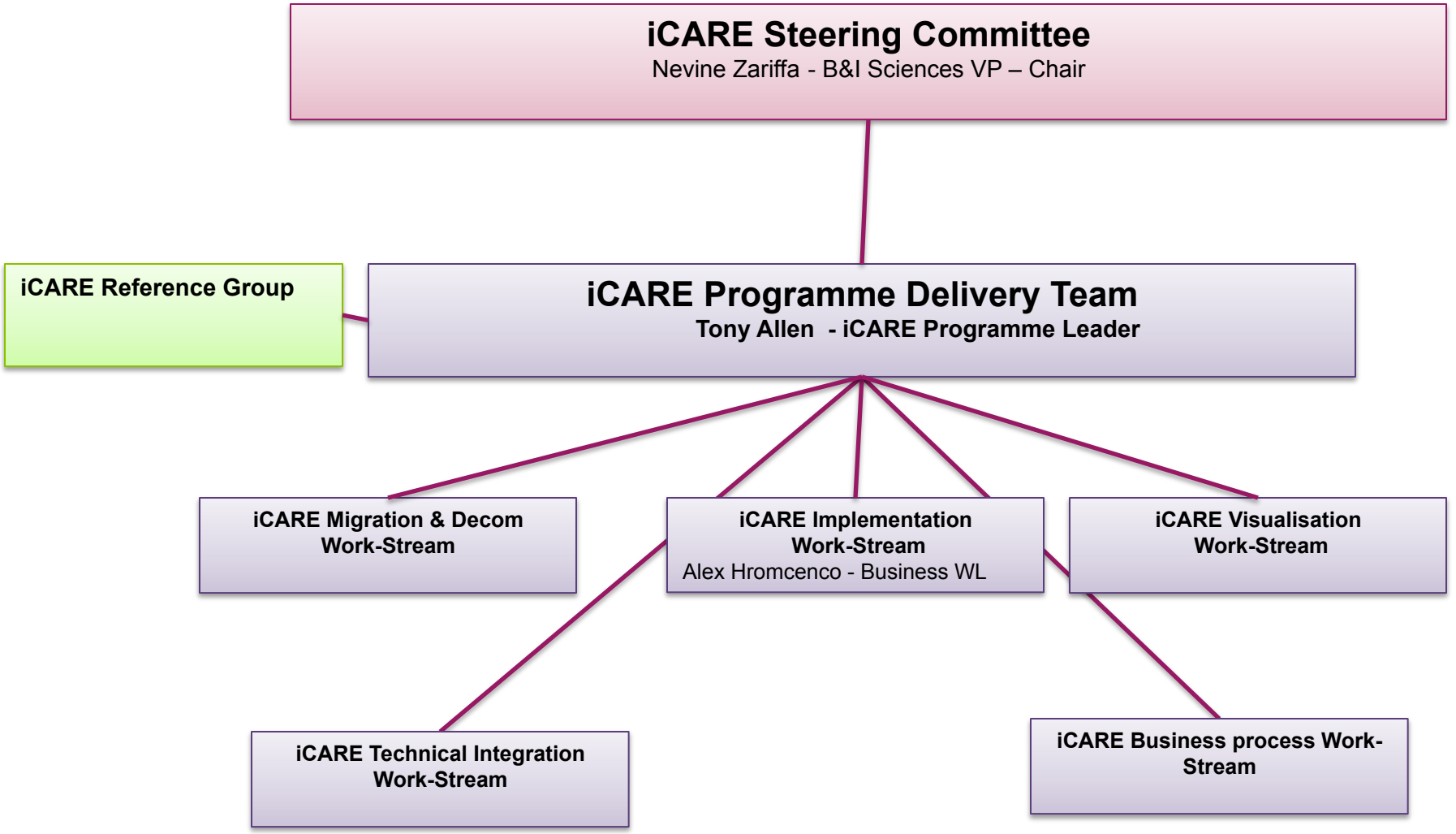
2014

- Executed 2 proof of concepts (on 2 different products) to ensure quality in decision
- Evaluated hosting options
- Decision of product = entimICE, delivered by entimo
- Executing a RFP for implementation, hosting and support services
- Decision of implementation vendor / hosting and support vendor = NNIT
- Audits of both NNIT and entimo
- Negotiations resulting in four contracts with the two vendors
- Capital Business Case Submission / Full approval

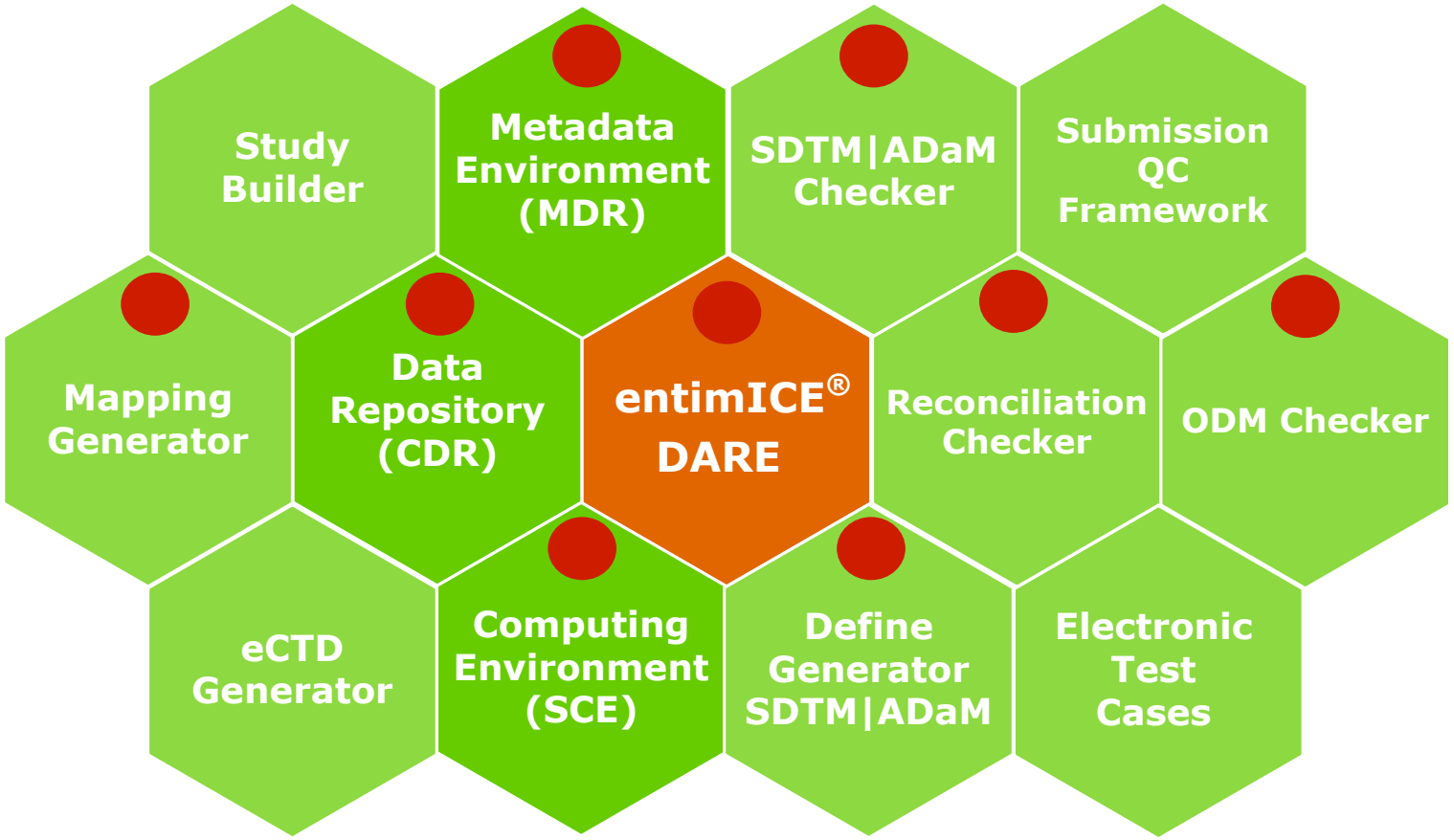
2015

- **Programme Execution Begins**

iCARE – Programme Governance & Organisation



entimICE
Integrated Clinical Environment



Included in AZ iCARE scope

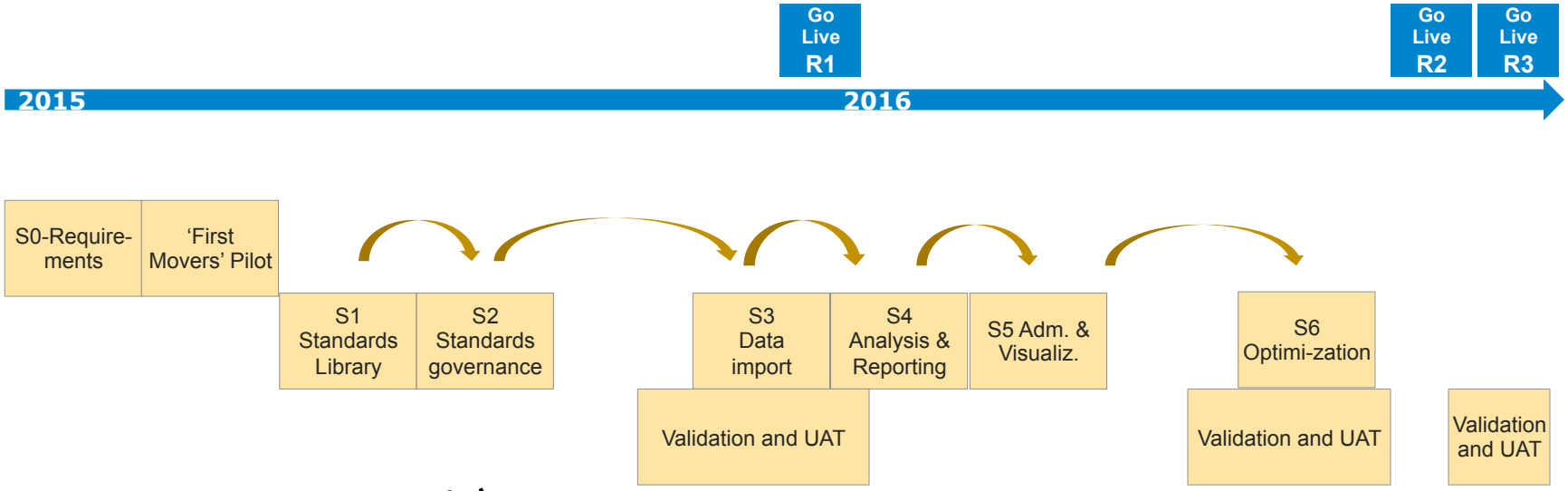
iCARE Programme
Solution Decision

The Entimo entimICE system met our functional requirements and was recommended as the CDR/SMDR/A&R/mapping environment for iCARE.

Highlights of the Functional Benefits include:

- Having the **SMDR, A&R and CDR** in the same system is a great advantage for data flow and process efficiencies regardless of Clinical Submission delivery method (e.g. In-Source vs. Outsource).
- **Traceability and Version handling** on all items (SMDR, A&R and CDR).
- Possibility to use data (and metadata) as well as store data **in a format other than just SAS (i.e. R)** provides great flexibility**.**
- **The system is very configurable**, and able to adapt to a new deliver method.
- **User friendliness** and intuitiveness of the system was very well received and highest amongst options.
- Out of the box integration with Spotfire Visualisation Tool

iCARE Programme – High level Implementation Programme Plan

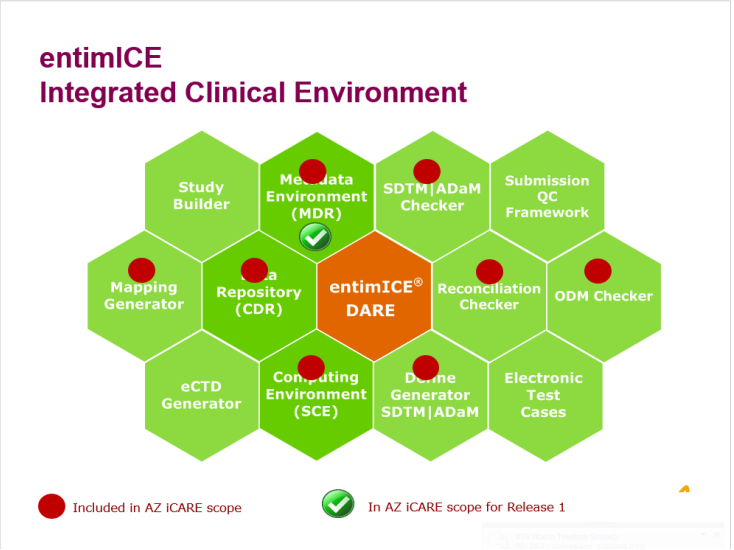


Each SPRINT is time boxed 35 days…

Target Training	Prepare Workshop	Execute Workshop	Document Workshop	Design and Build	CRP	Design Review	Plan next sprint
1 day	1 days	2 days	1 day	25 days	3 days	1 day	1 day
C CT	C BL	C CT	C	C AS	C BL	C CT	C BL
Training focused on the functionality and process in scope	Review of process, Use Case and Requirements Identification key decision points	Core Team review of process and proposed design and decisions	Document workshop decision points, design points	Use Case update Test case draft Configuration Specification	Test Case check and process execution	Agree on design Agree on decisions Review Issues Determine Sprint success	Evaluate outcome of UAT and determine scope of next

iCARE Programme – Phased implementation approach

The EntimICE configuration and set up will be delivered through a phased implementation with three releases adding on more and more functionality as described below:



- Release 1 – SMDR functionality: *DARE/MDR*
  - S0 – Requirements
  - S1 – Standard Library
  - S2 - Standards Governance

- Release 2 – Clinical functionality: *DARE/CDR and DARE/SCE and Mapper, Checker, Definer*
  - S3 – Data acquisition
  - S4 – Analysis and Reporting
  - S5 – Visualization and Administration

- Release 3 – Additional functionality
  - S6 - Optimization and catch up from previous sprints

5 W Model for Release 1

Who	Individuals involved in…. • Standards Development& Maintenance • entimICE Tool Training • entimICE Tool Support
What	▪ **Migrate and Implement Standards in the iCARE SMDR** • Create and modify standards versions • Review hierarchies • Create metadata sets from elements • Manage standards configurations, reference standards, programs, utilities, codelists and dictionaries ▪ **Administrative and User Access Functionalities** • Addition and maintenance of users • Management of access to standards and operational area ▪ **Implement Standards Governance Processes in iCARE** • Process for changes to Standards • Impact Analysis • Use of Change Request Form • Change Request Form Metadata • Distribution Lists for Standards Teams

5 W Model for Release 1

Why	▪ Implement and test SMDR content for the final iCARE release ▪ Build and Increase System knowledge among users of Standards ▪ Identify and document gaps in required SMDR functionalities (covered in Release 1)
When	The period in between Release 1 and Release 2
Where	Release 1 Production Environment

iCARE Programme – EntimICE-AZ toolset

SDTM/ADaM Checker

- This solution is used to verify compliance of clinical data with CDISC models. The tool inspects structure, content, terminology and value level metadata, run officially published and additional checks and provide detailed reports including result statistics

Reconciliation Checker

- This tool allows comparison of data and metadata based on configurable business rules, and creates a comprehensive report containing all used rules and detected issues. The tool can be used for such checks as key matches, conditional comparisons of datasets and metadata variables, baseline comparisons or checks of value ranges

ODM Checker

- This tool is used for content and structure validation of ODM files including define.xml.

Mapping Generator

- This solution is used for creating mapping specifications and programs based on metadata. The tool offers a metadata driven user interface to define mapping algorithms from source to target data structures.

Define Generator – SDTM/ ADaM

- This tool delivers Define.xml for SDTM, ADaM and other datasets.

iCARE Programme – Ongoing activities and Future Releases

- Functionality for managing Clinical study data
- Clinical Data Provisioning / Integrations with other AZ systems
- Relevant Business Processes and end user training
- Migration of Clinical data
- Decommissioning of current A&R systems

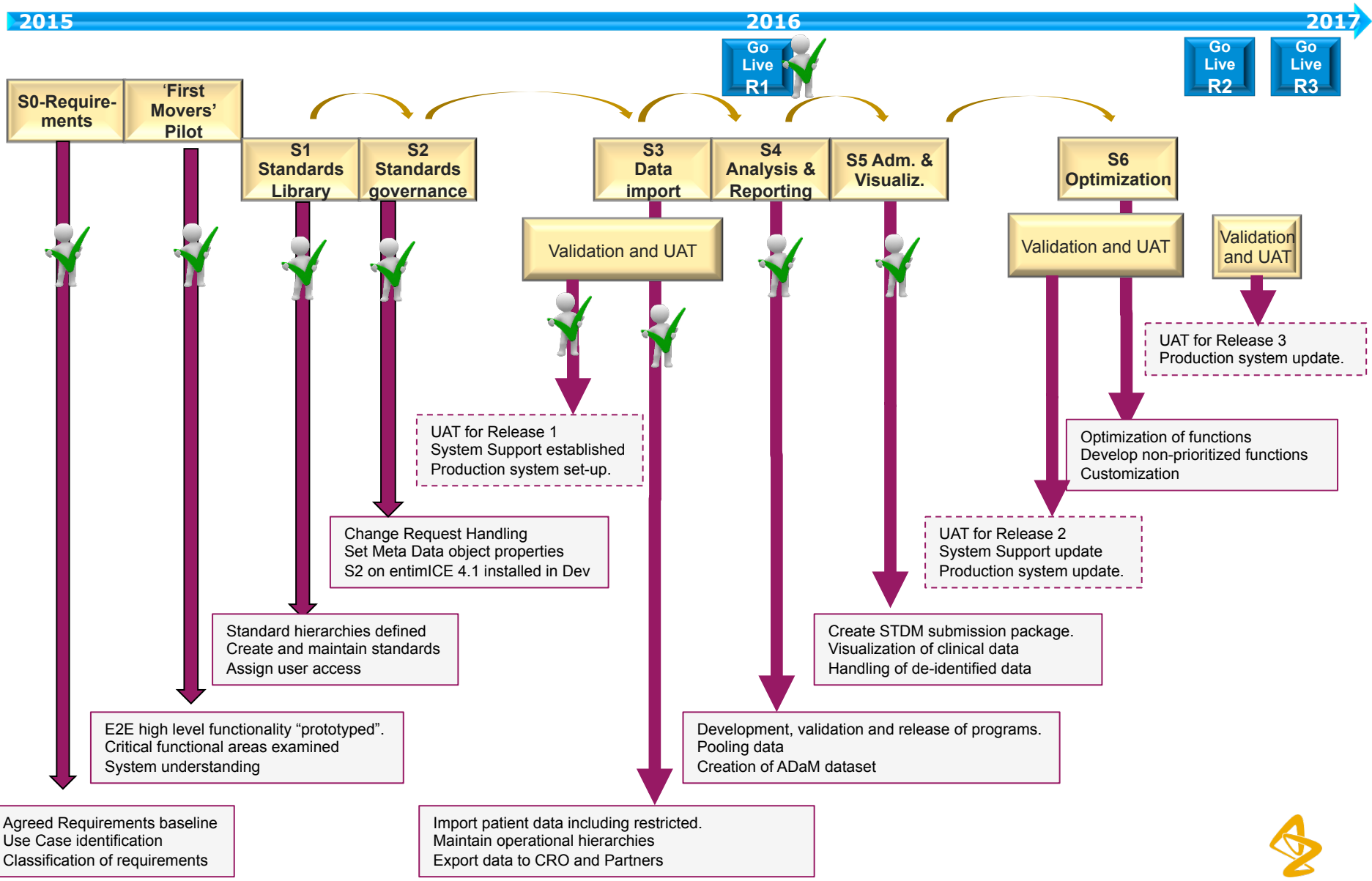

Study Builder
Metadata Environment (MDR)
SDTM|ADaM Checker
Submission QC Framework
Mapping Generator
iCARE
integrated Clinical Analysis & Reporting Environment
Reconciliation
ODM Checker
eCTD Generator
Computing Environment (SCE)
Define Generator SDTM|ADaM
Electronic Test Cases

THANK YOU!

BACKUP SLIDES

iCARE Programme – Release 1 Presentation 2016

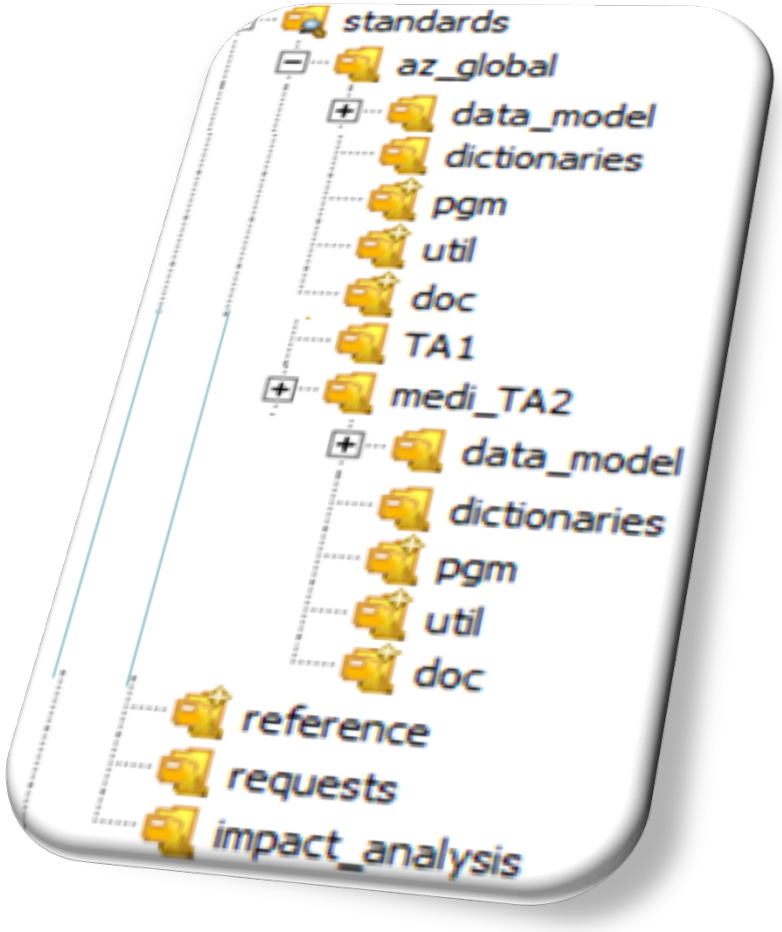
iCARE – Implementation Workstream Plan



EntimICE-AZ - System Details

- Standards Hierarchies
- Object Life Cycles
- Change Request Form
- Dictionaries
- Governance Process
- Metadata Driven A&R

Standards Hierarchy



Standards Hierarchy

A. Standards folder contains
   - Standards organizations
     - Any number of organizations: internal as well as external
       - reference (e.g. CDISC)
     - Folders added and named manually
   - Requests (Change Request)
     - One folder for organizing Change Requests
     - Fixed name
   - Impact Analysis
     - One folder for organizing Impact Analysis definitions and results
     - Fixed name

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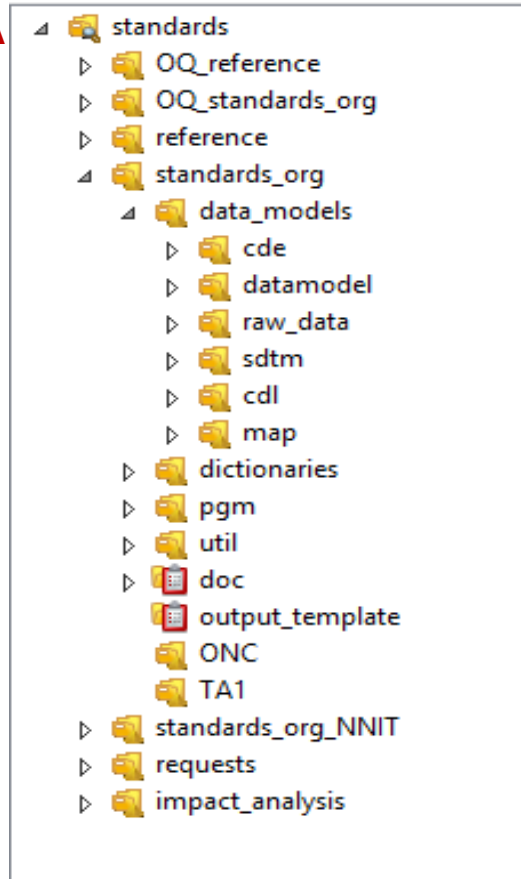

Standards Hierarchy
Data Models details

A. data_models folder
   - 4 different folder types can be chosen
     - cde (domain metadata and domain codelist elements)
     - data_model (SAS Metadatasets e.g. raw, sdtm)
     - codelist (SAS Datasets & SAS Catalogs)
     - mappings (Mapping templates)
   - All folders added manually
   - Multiple folders for data_model's, codelists and mappings
   - Naming of data_model's, codelists and mapping folders are user defined

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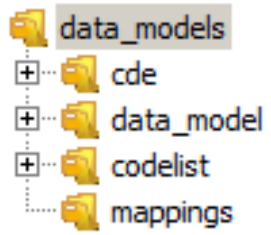
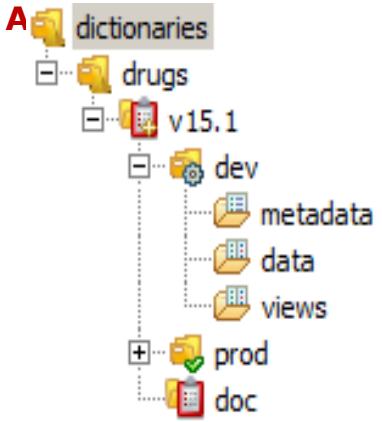


Standards Hierarchy
Dictionaries

A. Dictionary folder contains
   - One folder per dictionary
     - Name is user defined, but must start with a letter
   - Each dictionary contains one folder per version
     - Automatic creation of mandatory sub-folders: dev, prod, and doc
   - Dev and prod folders contain
     - metadata (SAS Metadatasets)
     - Data (SAS Datasets & SAS Catalogs)
     - Views
     - Folders names are fixed



Dictionaries - Approach

External Dictionaries

- MedDRA
- Upload as SAS datasets
- Available for reporting
- Multiple versions

Internal Dictionaries

- AZ Drug Dictionary (AZDD) and AZ Labcodes
- Maintained in SAS datasets within EntimICE
- Available for reporting
- Multiple versions

The maintenance programs and processes are currently being developed. It is planned that this will replace our current maintenance application, McRef. It is also planned that scripts will be developed to replace the current comparison and validation reports.

Standards Hierarchy

Standard program library

A. pgm and util folders
   - Areas for developing and storing standard programs and utilities
     - One sub-folder per program/utility type
     - Naming of program and utility folders are user defined
     - A business version contains life-cycle folders (dev and prod)
       - Dev and prod folders names are fixed
     - One doc folder with one or more sub-doc folders

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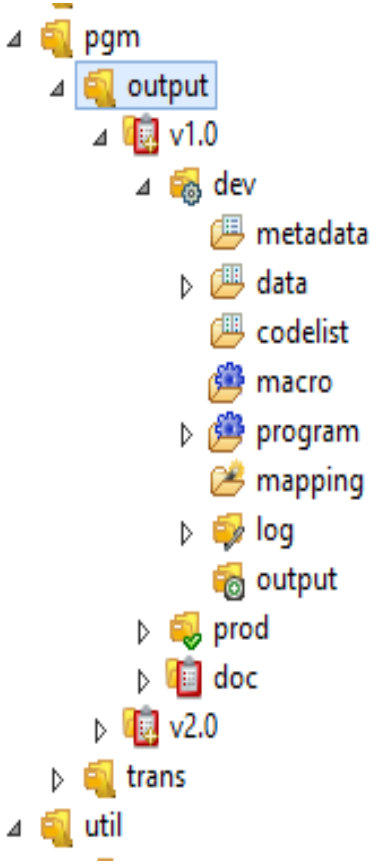
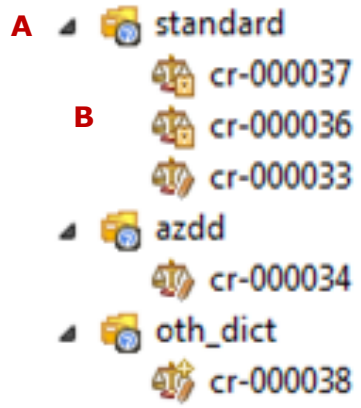


Standards Hierarchy

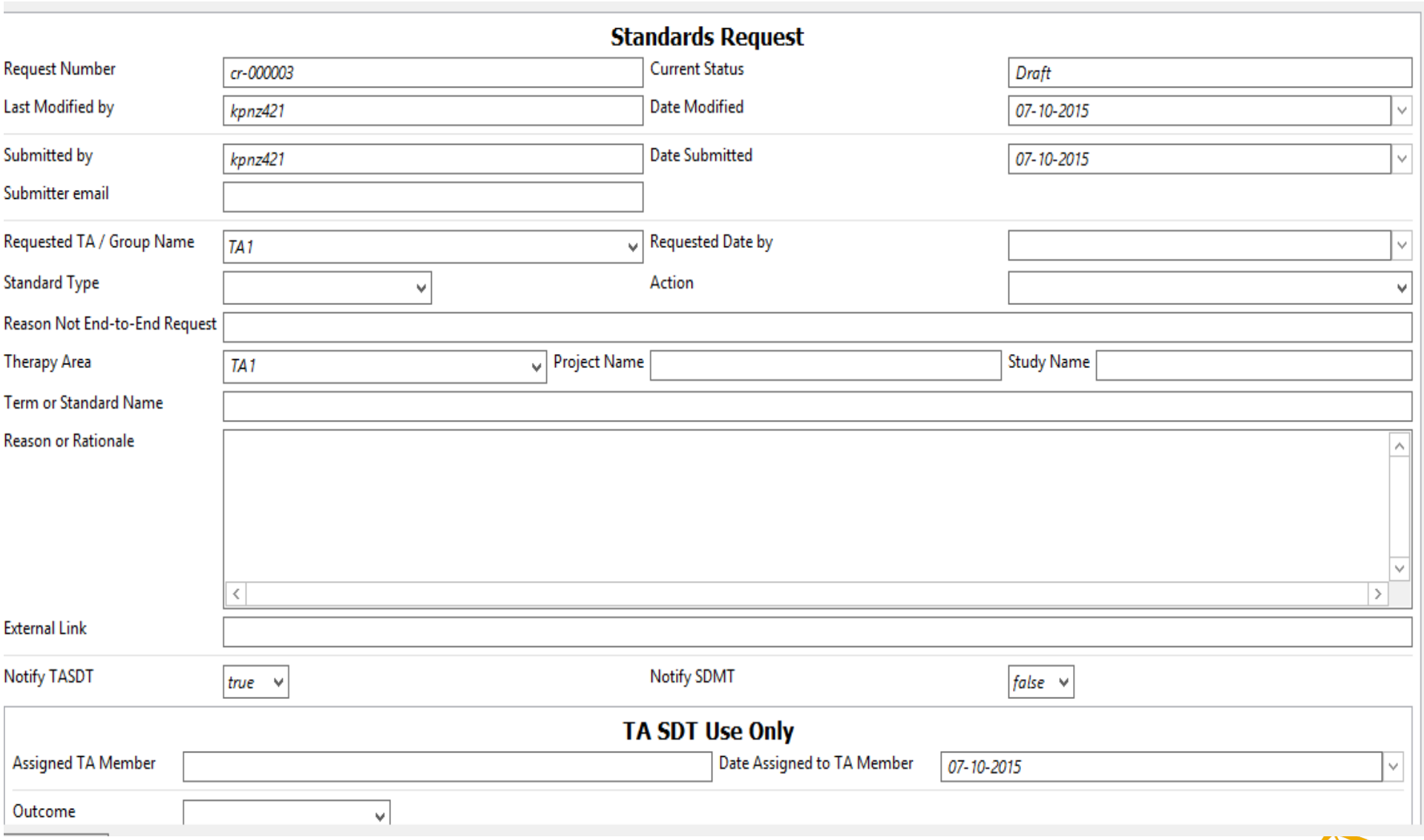
Request Forms

A. Request year-folder contains
   - 3 folders for organizing types of Change Requests
   - Fixed names
     - ❑ standard
     - ❑ azdd
     - ❑ oth_dict

B. Change Request forms
   - Unlimited number of CR-forms
   - Fixed names
     - System generated cr-xxxxxx
     - Running number across the type-folders



Standards Governance



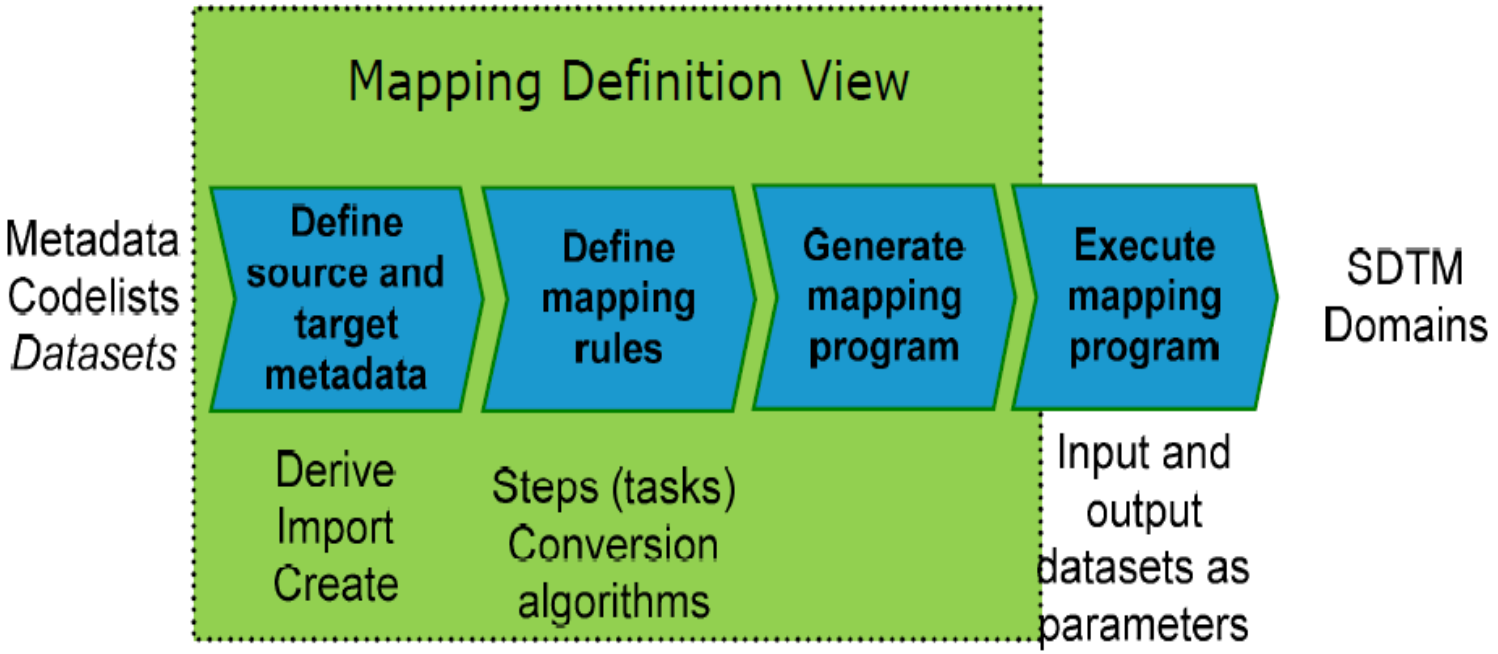
Standards Request

Request Number	cr-000003	Current Status	Draft
Last Modified by	kpnz421	Date Modified	07-10-2015
Submitted by	kpnz421	Date Submitted	07-10-2015
Submitter email			
Requested TA / Group Name	TA1	Requested Date by	
Standard Type		Action	
Reason Not End-to-End Request			
Therapy Area	TA1	Project Name	
Study Name			
Term or Standard Name			
Reason or Rationale			
External Link			
Notify TASDT	true	Notify SDMT	false

TA SDT Use Only

Assigned TA Member		Date Assigned to TA Member	07-10-2015
Outcome			

Mapping Process Overview



Mapping Definition View