

## The development of standards management using EntimICE-AZ

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### INTRODUCTION

Historically, using excel has been the main system for organizing and storing metadata, within AstraZeneca and the wider industry. Excel is particularly challenging when it comes to managing versions, reuse of the standards and sharing with vendors. In addition, within AstraZeneca there have been multiple science units with their own solutions to manage clinical standards.

In this paper, we would like to share how AstraZeneca is planning to change the standards governance using the implementations of EntimICE-AZ system developed by entimo.

For a small science unit like Early Clinical Development (ECD) within AstraZeneca, which specialises Phase I and II trials it is important to have easy access to the latest controlled standards to swiftly implement those in the dynamic study execution phase.

### SHAREPOINT CHALLENGE AND SHIFTING TO ENTIMICE-AZ SYSTEM



## entimICE-AZ Integrated Clinical Environment

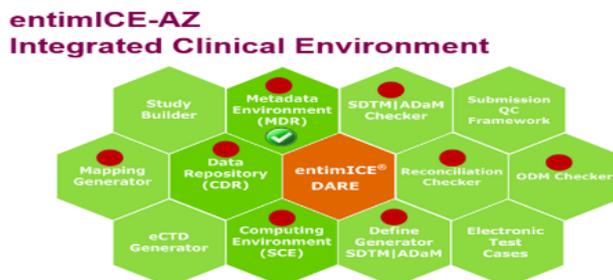
So far, all the legacy and current AstraZeneca standards are in excel spreadsheets by domain stored on SharePoint. Any updates to the standards must be sent to the Clinical Information Standards (CIS) team for approval (either corporate level or TA/project/study level). This is quite challenging and difficult, in particular, when it comes to version control, reusing the standards and sharing with vendor.

The ECD study phase often needs to collect new types of data for managing, monitoring and evaluating drug development and to test assumptions. In addition study designs are to a larger degree adaptive hence dependent of data captured and new modules could be added. There is a need to be flexible in how standards are applied and used in the data capture process as well as downstream for Analysis and Reporting activities, hence utilise standards to a higher degree! Most importantly, everything should be in one place for internal stake holders within AstraZeneca science units.

AstraZeneca has launched the Integrated Clinical Analysis & Reporting Environment (iCARE) program, which is an improvement project within AstraZeneca for Analysis & Reporting tools as well as the management of standards. The iCARE environment has three components called EntimICE-AZ, Clinical Trial Data Storage (CTDS) and Master List of Clinical Studies (MLCS).

EntimICE-AZ is the system within iCARE developed for standards, governance and Analysis & Reporting activities, which is the primary focus of this poster.

ENTIMICE-AZ



The name entimICE is the abbreviation for the “Entimo Integrated Clinical Environment”.

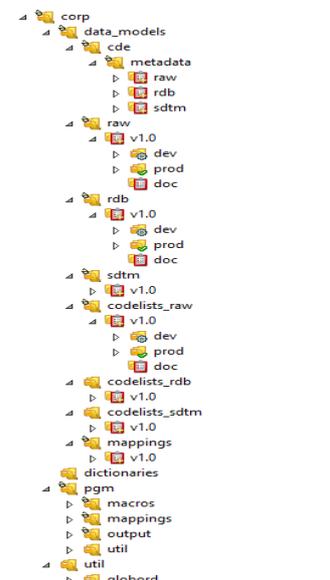
It is a system developed by Entimo, containing standards metadata repository (SDMR) or Operational repository, Standards governance, and Analysis & reporting tools.

The EntimICE-AZ will be organised into:

- Standard Meta data Repository
- Clinical data Repository
- Computing environment (Development and Production)
- Standards Request System
- Dictionary management
- Define Generator SDTM & ADaM
- Share internal within AstraZeneca for all science units

**STANDARD METADATA REPOSITORY (SDMR)**

All AstraZeneca science units will use the EntimICE-AZ standards hierarchy, the standards metadata repository (SDMR). Access will be granted to the standards hierarchy based on named users. All user who have access to system will also have read-only rights to all standards production directories. A separate hierarchy following the same folder structure will be created for the TA and drug project specifications.



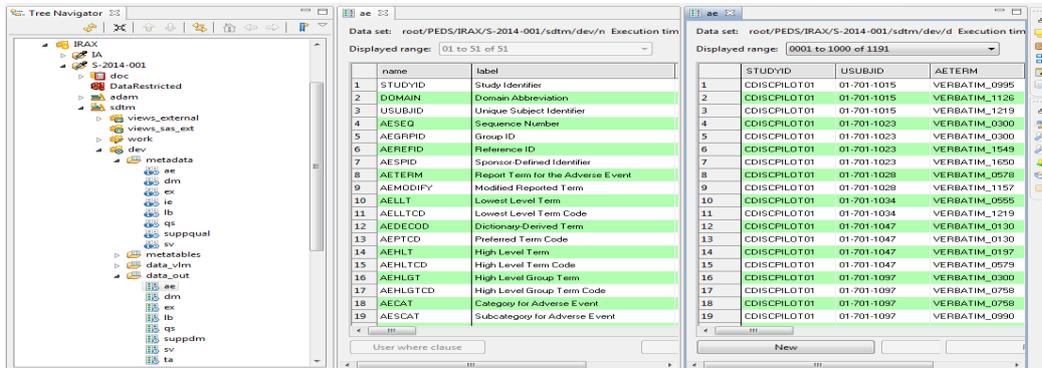
The standards hierarchy (SMDR) will be created as shown. TA standards will be stored in a hierarchy with identical structure to the corporate standards. However, the TA standards will be stored as indented one-level from the corporate standards to represent their relative position in the hierarchy.

The tool has been configured to allow for flexibility in the creation of data models (components) of standards, but a common naming convention still needs to be implemented. This naming convention should be used consistently across corporate and TA standards components.

TA directories, which are located as sub-directories of the “corp” level, will be created for the following TAs: oncology, inflammation, respiratory, CVMD etc.

When upgrading **Standards and Standards Metadata** in the hierarchy, the version naming convention will begin with the v1.0 for each type of standard, and will be incremented sequentially through time.

**CLINICAL DATA REPOSITORY**

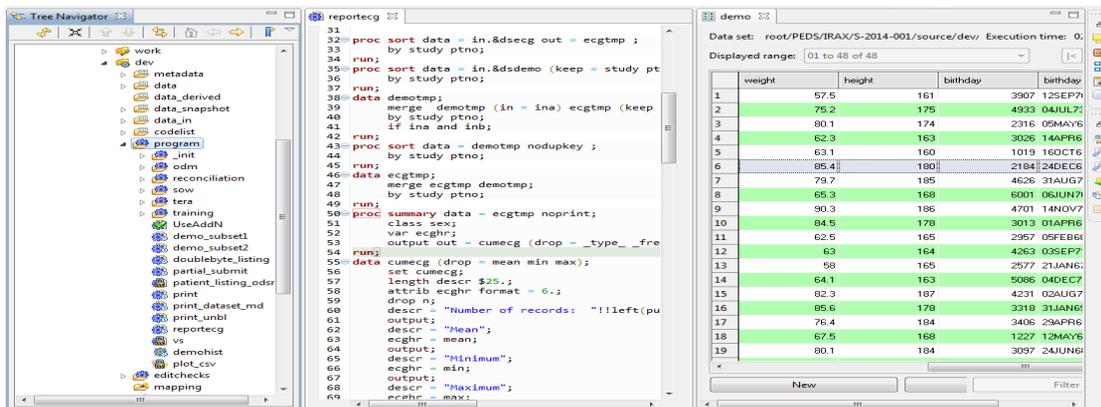


As a high-performing data repository, EntimICE-AZ offers a completely new analytical experience for statisticians and data scientists. With Teradata or Hive backend, EntimICE-AZ is able to integrate even Real World Evidence data as well as other data sources like safety data into clinical analysis. The solution allows the user to query, transform and pool data, develop and run ad hoc and standard programs, produce regulatory and management reports as well as submission packages in a fully controlled and traceable manner.

The highlights of Clinical Data Repository are:

- Fast load performance
- Data privacy and data restrictions
- Configurable and robust governance
- Metadata and standards re-usability
- Flexibility through dual storage concept

**COMPUTING ENVIRONMENT (PROD AND DEV)**



EntimICE-AZ is a metadata driven statistical computing environment with a tightly integrated data and metadata repository. The ultimate goal of the solution is to provide a unified programming interface for SAS, R with access to integrated flows of data from heterogeneous sources and value-adding tools. Numerous robust tools help you manage your programs, documentation, metadata, codelists, and provide for audit trails, versioning and lifecycles along the entire process.

The highlights of computing environment are:

- Development and Production environment features
- Unified and efficient programming
- Easy interfacing to source and tools
- Central library of reusable standards
- Transparent governance process

## STANDARDS REQUEST SYSTEM

The EntimICE-AZ request tool contains three different types of request: common standard related to data structures or output TLF. In addition dictionary requests are also allowed in the system. The request tool organises the requests via an internal incremental request number as shown in the left treeview.

Within EntimICE-AZ, any ECD requests for a study or AstraZeneca or TA standard should be submitted in the request tool. The TA or Corporate change request will contain a description of the proposed change, and rationale for why it should be applied to the TA or Corporate standard.

The Standards group will discuss the suggestion and if they decide it should be implemented they will update the relevant Raw/SDTM/ADaM or TFL standard, with support from the ECD representatives if applicable. Project specific ECD requests can be implemented before formal approval within the EntimICE-AZ system.

## DICTIONARY MANAGEMENT

EntimICE-AZ is not a terminology management system. However, the capability exists to manage dictionary data in SAS datasets. All critical functionality of the existing McRef system will be replicated via SAS programming.

External dictionaries such as MedDRA will be imported and managed within EntimICE-AZ as SAS datasets. These SAS datasets can be utilized in the same way that external dictionaries are largely used today.

Internal dictionaries, such as AstraZeneca Drug Dictionary (AZDD) and AstraZeneca Microorganisms Dictionary (AZMO), will be migrated to EntimICE-AZ and managed as SAS datasets. Programs will be written to upload new records from spreadsheets and run comparison reports to prior versions.

## Define Generator SDTM & ADaM

In EntimICE-AZ, a dedicated generator allows Define.xml for SDTM, ADaM and other datasets to be created from metadata domain definitions with just a few clicks. Define.xml generator is based, like other Entimo's tools, on a metadata driven architecture. Define.xml and Define.pdf files are created from metadata and can be used as communication tools in the data mapping process even before data is available. Terminology, value level metadata, and other data elements are included with consistent links. If any data elements have changed, you just need to press the button again for an up-to-date Define.

Define.xml Generator Highlights are:

- Re-usable Templates for Data Elements
- Value level metadata
- Transport files
- Controlled terminology
- Documentation and style sheets
- Define .xml generation

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## ECD BENEFITS

- Central organisation cross science units developing the corporate core standard
- Sharing/searching standards cross science units for swift access to standard references during standards enhancement
- One source of generic core standard for all AZ studies regardless of phase or science unit
- Simple request system within the system for quick standards augmentation
- Dedicated ECD area for specific early phase standards
- Support submission process once a project is handed over for late phase development when standards is used cross science units
- Build sufficient data quality processes within the tool for existing vendor models
- Long term potentials opportunity to invite vendors into well-defined process and functions in the system

## CONCLUSION

EntimICE-AZ is a complex system with ample number of new components for AstraZeneca to embrace. It is envisaged that the knowledge, process and efficiencies needs to be built over a longer period of time. The implementation of the system will therefore be phased having overlapping solutions until the complete EntimICE-AZ Suite content has been developed and deployed into the organisation.

## CONTACT INFORMATION

Your comments and questions are valued and encouraged. Contact the author at:

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