Paper TT09

Migrating a large users base from multiple legacy systems to entimICE-AZ: issues and lessons learned

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ABSTRACT

This paper discusses some of the user-related issues encountered when AstraZeneca (AZ) migrated GCP-related analysis and reporting activities from a number of legacy systems to a modern Statistical Computing Environment (SCE). At the same time historical and closed studies were moved from several file storage locations to a read-only one (Clinical Trial Data Storage, CTDS), from where they could be imported into the new environment if and when additional analyses were needed. While data, programs, etc. for studies migrated to the new SCE were remapped, those moved to CTDS were copied 'as is', thus maintaining their original folder structures.

INTRODUCTION

As many other companies in recent years, AstraZeneca decided to migrate from a number of legacy 'SAS®-on-a-server' systems to a single, modern SCE.

Their choice fell on entimICE®, by the German company Entimo® AG, and the AZ-specific configuration of entimICE was dubbed entimICE-AZ.

The migration was part of the wider Integrated Clinical Analysis and Reporting Environment (iCARE) project, which included several other initiatives, like the CTDS mentioned earlier. For more details on iCARE [1], as well as the desired characteristics of a modern SCE [2], please look at the References section below.

PLANNING

Plans for iCARE started in late 2013, well before I joined AZ in January 2016. Consequently I do not have any first hand details of this phase, but a few internal presentations I attended mentioned that entimICE-AZ and CTDS replaced a combined total of 17 old systems/file shares. The operating system (OS) chosen for the first implementation was Windows.

IMPLEMENTATION

For the implementation phase it was decided to use the services of a third-party implementation partner. The application was hosted externally to AZ, IT support was provided by the external partner and all queries had to go through their ticketing system. This decision was based on cost considerations.

RELEASE 1.0

The first version, released in 2015, covered just the Standards Metadata Repository component, and consequently only members of the Clinical Data Standards team had access to it.

RELEASE 2.0

The second version was released in the second half of 2016, used by one project team for a few months before it was opened up to all teams.

Since I had just arrived from a similar experience in another company, even if based on SAS® Drug Development (SDD) [3], I volunteered my team to be the ice breakers.

Several security issues were identified early on and needed to be fixed, so the initial roll out was delayed by a couple of months to allow the system to be upgraded to the latest entimICE version available at the time, 4.2.

The implementation partner provided also a tool, integrated with entimICE-AZ, to collate outputs into bookmarked PDF files.

RELEASE 3.0

The third version was released in early 2021, and introduced several major changes, including but not limited to:

- entimICE was updated to version 4.4 and installed on AZ servers
- The underlying OS was changed from Windows to Linux
- IT support was moved in-house
- Product support was provided directly by Entimo
- A new tool to collate outputs into bookmarked PDF files was developed internally
- Training material and business process documentation were completely revised

MAIN ISSUES

This section of the paper discusses some of the issues linked to the migration of the user base, with special accent on training, system support, business processes and programming environment.

Other issues linked to the migration of study data from legacy platforms to Windows and later from Windows to Linux are excluded from this discussion.

TRAINING

After a series of train-the-trainer sessions held by the staff of the implementation partner, training was administered by internal staff, as much as possible in person, but many users were only able to join remotely. Training material provided by the implementation partner was extensive but also quite basic, and the internal trainers had no previous experience to know which aspects were more important and should thus be highlighted.

After several months it was decided to shorten the training duration and change the training material into Computer Based Training (CBT), thus removing any interaction between trainers and trainees. Training material was then completely revised with the release of entimICE-AZ 4.4.

Weekly Help Clinic calls were established, regularly attended by an Entimo representative after the migration to entimICE 4.4 and with an agenda including both a training section and one devoted to live discussion of user-reported issues. An MS Teams chat and dedicated web pages were also created for offline discussions and documentation storage and organisation. IT colleagues created a specific knowledge base, covering the more technical aspects like issues with remote access for non-AZ personnel and Citrix servers.

BUSINESS PROCESSES

It was soon clear that the new system lacked tailored business processes documents. The documentation initially provided with the new system, apart from the generic entimICE user manual, consisted of three SOPs and two guidelines, and proved quickly to be insufficient to keep process variability at bay.

In practice users were left to decide how to adapt their existing ways of working to the new environment, with no clear directions on which were the new capabilities and limitations and how to exploit or avoid them.

Over time more and more documentation was developed, mostly of the ‘how-to’ type, with priority given to topics which were indicated as major pain points by the user base. As mentioned earlier, a full rework of these documents was performed as part of the release of entimICE-AZ 4.4.

PROGRAMMING ENVIRONMENT

The new system had all the characteristics needed for a modern GCP-compliant environment, including an integrated audit trail and separate locations for development work and final runs.

In theory programs could be written in SAS, R and S-Plus, but only SAS was fully usable from the beginning. It took several months to provide the users with global tools to help programmers porting over legacy programs, starting with a set of SAS macros to initialize the programming environment in a consistent way.

A commercial tool designed to help with the production of outputs using SAS, already available in legacy systems, was also made available, together with a set of template programs to produce outputs heavily based on it, but the uptake was minimal.

Lately a lot of work has been done to create a validated R environment, which has already been released but is still missing a number of common packages, which will make it actually useful.

SYSTEM SUPPORT

The choice to use a third-party vendor as implementation partner, linked to the lack of internal knowledge and several teething problems, created huge communication issues, since AZ staff was allowed to talk with the software developers very rarely; rather a sort of Chinese whispers game ensued, where the original message was turned into something else along the way, resulting in long exchanges to fix even the simplest issue.

It was reported that long-standing support tickets had been closed without the issue being resolved and the users being informed. In several occasions the system remained unreachable for a number of days at a time, seeding distrust about its reliability among the user base. The situation became serious enough that senior managers requested the creation of a Business Continuity Plan (BCP) solution, which was released roughly at the same time as entimICE-AZ 4.4.

The situation changed radically when IT support was moved in-house, and an internal ticketing system was adopted instead of the external one used initially: follow up actions have become faster and more open, as recognized by the users’ feedback.

CURRENT SITUATION

Six years after global release, the user base has reached in excess of 1500 trained users, and almost all clinical projects have been migrated to entimICE-AZ (one legacy system is still active, but is planned to be decommissioned in early 2023).

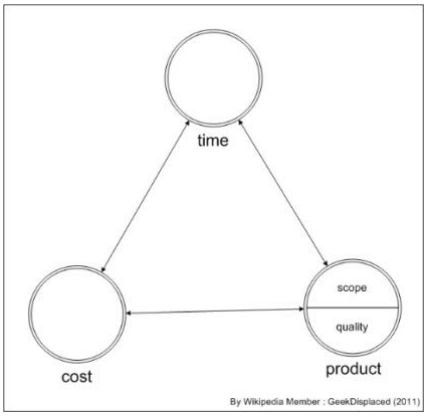
The introduction of entimICE-AZ 4.4 proved to be a game changer, since we have upgraded the system to the latest version, at the same time moving both business and IT support completely in-house. System reliability has increased enormously, and there was never the need to use the BCP solution due to entimICE-AZ being unavailable for a significant amount of time.

Having joined the trainers team early on allowed me to learn about the system philosophy and intricacies along the way, so that today I am one of the users with more knowledge of the AZ product implementation. So recently I was part of a team who supported the successful migration to entimICE-AZ of the staff (and study data) of a small company recently acquired by AZ; this happened soon after the release of entimICE-AZ 4.4, and due to the

availability of updated training and process documentation we observed fewer issues with effectively training the new users than with the existing ones.

CRITICAL ASPECTS

First and foremost, every plan must be drawn keeping in mind the iron triangle principle: "Good, fast, cheap. Choose two."



As I explained earlier I joined AZ when the system had already been designed and was in fact almost ready to be released globally, so I might point to choices which made sense at the time but proved to be less than optimal when implemented.

Having said that, and in light of my previous experience with SDD, some of the aspects I consider critical to be taken into account in similar occasions are listed in the following sections.

TRAINING

If no relevant experience is available within the company, proven external expertise should be brought in to help plan and support the migration.

While it is clearly important to cover the basic characteristics of a new system, e.g., GUI, folder structures, naming conventions, navigation, system roles, etc., in order to manage the issues inevitably following such a change it is equally critical to point out to both relevant similarities and differences, making sure the users understand the implications for their activities.

In the case of entimICE, most users were completely baffled by the role played by and the proper use of DataAccess/DataRead links. Other pain points identified early on were about the (now deprecated) use of SAS commands opening shells to the underlying OS, like X and SYSEXEC, and the consequences of SAS code being executed not ‘as is’ anymore, but sandwiched between `pre- and post-execution code, leading in some situations to some programs not running as expected.

A good example of the latter showed up for a series of reporting programs which, when run in entimICE-AZ, unexpectedly created empty RTF files. Upon further investigation the root cause was identified in a discrepancy between the ODS statement opening the files and the one meant to close them:

```
ods tags.rtf file='…';

proc report;
[…]
run;

ods rtf close;
```

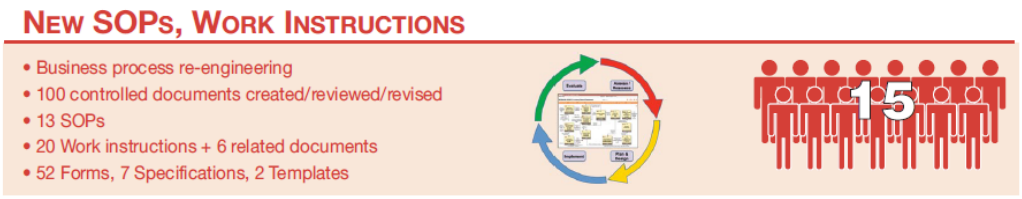
While this mistake did not create issues in a self-standing SAS session, the added complexity of the new system highlighted it, ultimately resulting in code of a higher quality.

BUSINESS PROCESSES

Business process documentation should be developed together with the system architecture, then refined and finalized during the pilot phase. Best practice detailing the recommended usage of the new system should be provided to the users from the very beginning, covering at least the basic day-to-day tasks. While SOPs are fine to describe high level processes, devil is in the details so how-to’s and user manuals are needed to direct the users on how to perform a variety of low-level activities.

Since these A&R environments deal mostly with Personal Data, identification and analysis of planned integrations with other systems, both upstream and downstream, should be performed during the design phase, and quality processes and related documentation developed to satisfactorily cover those aspects.

As an example of what to expect, these are the numbers from my previous experience with SDD:



SYSTEM SUPPORT

Being able to talk directly to the system vendor, while more expensive in some cases, allows a more effective and unfiltered interaction between the new users and those with the most thorough knowledge of the system itself. This reflects on the quality of the training, both in terms of trainers and material. Being involved in the discussions about the system setup will also allow the vendor to suggest which details should receive special attention, like a standardised folder structure specifically designed to implement automation more easily.

As always quality should be built into all processes from the beginning, including robust, thorough risk assessment and change management processes. Data integrity, as well as traceability, must be maintained.

If at all possible a pilot phase should be planned, to check the actual viability and effectiveness of the choices made, allow internal staff to start gaining hands-on experience and possibly be able to apply minor changes before the global release.

A clear distinctions should be drawn between active studies, which need to be fully migrated, and historical and completed ones, which can be archived 'as is'. Since migration involves in most cases a full remapping of all the study objects, reducing the scope of this task can help manage activities with less resources.

Proper levels of dedicated resources (Business, IT, etc.) need to be made available, not only for the design and implementation phases, but also for the long-term maintenance one.

Last but definitely not least, stakeholder expectations must be properly managed, especially in terms of budget and timelines.

PROGRAMMING ENVIRONMENT

Today users expect a modern A&R system to provide a number of programming languages, the most common ones being SAS, R and Python. Due to the overhead due to the regulatory compliance checks and balances which are built into such systems, the internal editors might prove not to be the best choice for intense code development: secure ways to interface with other development tools like SAS Studio or R Studio should then be investigated and provided at least to power users. On a personal note, being a long standing SAS programmer who started in late 1987 with SAS 6.04, I do not particularly like such tools, which in my opinion isolate too much programmers from actual coding.

The adoption, maintenance and enforcement of non-proprietary clinical data standards is paramount to fully exploit the automation capabilities provided. They should be paired to a set of validated, reusable programs and macros, capable of covering the creation of most SDTM domains, common ADaM ones and several standard outputs, common to all studies.

CONCLUSION

The migration from a system to another is a complex one, especially when the legacy systems lack many of the capabilities of modern environment, and when the number of source systems increases so does the complexity.

The task has many aspects, some less obvious than others. But for it to be reasonably successful, at least the most critical ones must be identified beforehand and properly addressed, to avoid fragmentation of the user base in terms of business processes or even failure.

So not that much has changed in 10 years, and the conclusions we drew then are still valid:

REFERENCES

[1] Perisetla S, Stahl PA. The development of standards management using EntimICE-AZ. PhUSE EU Connect 2016, Barcelona

[2] Pharma Statistical Programming Heads Council (SPHC). Statistical Computing Environment (SCE) White Paper, 2021

[3] Miller T, Nacci P, Schepers A, Woo W. The Clinical Data Repository Initiative at Novartis Vaccines and Diagnostics: a Revolution. FDA/PhUSE Computational Science Symposium (CSS) 2012, Silver Spring, MA

ACKNOWLEDGMENTS

I would like to thank the many people, both inside and outside AstraZeneca, keeping entimICE-AZ running with their daily work and passion.

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