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One size does not fit all: The need and art of customizing SCE and MDR for end users

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Abstract

In today's age of cloud computing and AI, it is hard to imagine the end-to-end drug development process done without the use of several different systems and tools employed at every stage. The last decade has seen a surge in the number of applications and solutions in the pharmaceutical industry improve the efficiency of the drug development process and shortening time to market. These applications and solutions cover the entire gamut ranging from data capture systems to reporting wizards to automated validators to SCEs and MDRs to AI-based SDTM mappers. Like any other application, the implementation of an SCE or MDR for an organization is a very critical process as it offers an opportunity for the organization to re-think the way they get things done. While having a fundamentally clear purpose, SCEs and MDRs also need to offer a large amount of flexibility to the organization that adopts them so that it can be adapted to the organizations processes and integrated with their existing systems.. The choice of which features of an application an organization should use decides the return on investment for the organization and this should also be supported by the product that has been chosen. To ensure a successful implementation, it is important that the business analysis team and the product design team work closely with the organization to provide a product that supports their core requirements and can be configured and extended to meet their needs.

Introduction

Over the past few decades, the drug development process has undergone remarkable advancements, propelled by stringent regulatory standards and improved controls. These changes have ushered in a new era of drug development characterized by greater compliance, enhanced efficiency, and reduced time to market. The pharmaceutical industry has witnessed a paradigm shift from traditional paper-based processes to modern electronic systems, such as electronic case report forms (eCRFs) and electronic trial master files (eTMFs). These electronic systems have revolutionized data collection, allowing for globally driven trials and streamlined regulatory submissions.

Furthermore, the integration of cloud infrastructure technologies and the adoption of Artificial Intelligence (AI) and Machine Learning (ML) have further accelerated the drug development process. These technologies offer innovative solutions for managing data, analyzing results, and optimizing processes, all while ensuring compliance with regulatory requirements.

In this context, it is essential to explore how modern tools like Metadata Repositories (MDR), Clinical Data Repositories (CDR), and Statistical Computing Environment (SCE) can contribute to further shortening drug development timelines. These tools play a crucial role in aligning submissions with regulatory standards and simplifying day-to-day operations for pharmaceutical companies.

Regulatory bodies, such as the Food and Drug Administration (FDA), the European Medicines Agency (EMA), and the Pharmaceuticals and Medical Devices Agency (PMDA), have recognized the importance of incorporating modern technology into their guidelines. They emphasize the need for robust data integrity, enhanced security measures, and increased privacy regulations to ensure full traceability, data lineage, and audit trails.

For clinical programming teams, the demands are multifaceted, requiring them to manage programming development, track deliverables, ensure compliance with Standard Operating Procedures (SOPs), and adhere to established workflows. Choosing the right tools and technologies is paramount to meeting these challenges effectively.

Commercial off-the-shelf (COTS) products like CDR, SCE, and MDR offer comprehensive solutions that can be tailored to the needs of clinical programming teams. These products provide robust functionalities that facilitate compliance with regulatory guidelines, streamline program management tasks, and enhance overall efficiency in drug development processes. By leveraging these modern tools, pharmaceutical companies can navigate the complexities of regulatory requirements while driving innovation and accelerating the pace of drug development.

Market Requirements

Meeting the demands of the market, a clinical programming team must possess a diverse set of skills and capabilities. Foremost among these is a deep domain knowledge, crucial for understanding the intricacies of report requirements and selecting the most appropriate statistical procedures. Moreover, the team needs to be adept at configuring role-based access and assignments to ensure smooth workflow management. Technical proficiency is equally essential, enabling the team to analyze data effectively and produce the required reports with accuracy and precision. This technical acumen also extends to providing regulatory bodies with the correct version of inputs, ensuring compliance with industry standards and regulations.

In addition to technical expertise, effective collaboration skills are indispensable for supporting clinical trials. The team must be able to seamlessly collaborate with various stakeholders, identify suitable resources, and coordinate validation activities to ensure the timely completion of tasks. Furthermore, a comprehensive understanding of regulatory GxP requirements is imperative. This encompasses ensuring data integrity and regulatory compliance by implementing mechanisms such as full traceability, auditability, and version control at every stage of the process. By possessing these skills and capabilities, a clinical programming team can effectively meet the rigorous demands of the industry and contribute to the success of clinical trials.

IDENTIFY THE RIGHT APPLICATION

In a market flooded with numerous applications, it's imperative to identify the one that aligns with your requirements and conforms to your policies and procedures. The chosen application should not only minimize human errors but also facilitate efficient program management complying with all the regulatory requirements. Let's delve deeper into the essential features of applications like MDR and SCE.

Auditability stands as a crucial GxP requirement, stipulating that any data transformation must be meticulously documented, and methods must undergo validation. Hence, a key focus of audits lies in scrutinizing program validation and the availability of procedures. For instance, any alterations made to programs in production or development areas should be accurately documented, including details such as the individual responsible for the changes, timestamps, and specific modifications, especially in versioned production programs. Similarly, all data movements into or out of the system should be meticulously recorded, capturing pertinent information like the origin, destination, and timestamps, ensuring comprehensive traceability.

Traceability denotes the ability to monitor an item as it progresses through its lifecycle, particularly in clinical trials where it pertains to data. This capability fosters transparency, accountability, and reproducibility. For instance, it enables tracking the version of inputs used to generate outputs in a program or tracing the path of a dataset moving between different folders within the environment.

Versioning and Version Control involve assigning unique identifiers to artifacts such as SAS programs or datasets every time they are created or modified. This practice facilitates tracking changes over time, distinguishing between different iterations of documents, and understanding their evolution. Versioning also streamlines collaboration by providing a common reference point for discussing updates and changes. Moreover, it enables users to revert to previous versions if necessary and compare versions when required.

Traditionally, these applications were developed in-house, tailored to meet specific requirements and customized during the development phase. However, managing such homegrown products proves to be costly over time. In recent times, Commercial Off-The-Shelf (COTS) products have emerged in the market, offering licensed solutions that can be customized to meet essential requirements and comply

with company policies and procedures. By customizing applications like CDR-SCE and MDR, organizations can effectively address their needs while ensuring regulatory compliance and efficient program management.

Customization of COTS product

When selecting COTS products, it's essential that they meet regulatory requirements straight out of the box, without requiring customization. However, any customization in non-functional requirements should focus on aspects like scalability, size, capacity, and integration capabilities with other applications. On the other hand, customization in functional requirements must align with customer policies and procedures. Additionally, customization may be needed for project management, facilitating day-to-day progress tracking and management.

Let's delve into the potential customizations required when implementing SCE or MDR and how they can help fulfill the company's requirements. We'll explore a sample implementation and examine the customizations based on industry best practices, as well as how modern tools in the market are being leveraged. Incorporating these best practices during customization ensures optimal utilization of the tools and alignment with industry standards.

Customizing of the application

Let's systematically customize this state-of-the-art modern-day application within a customer environment. The process will commence with the application onboarding, ensuring it meets GxP standards for authentication and verification. Typically, this involves implementing Single Sign-On with multi-factor authentication within the customer network and firewall. These configurations address both non-functional and functional requirements. The technical team will work on configuring the product to meet these specifications.

Next, the focus will be on defining Global Roles (GR) or Personas. These roles are identified, defined, and created based on requirements and company policies and procedures. Common GR/personas include Study Lead, Statistical Programmer, Statistician, Macro Programmer, Vendor Programmer, Read-Only, Data Managers, and Medical Writers. These roles are established at a global level to be utilized across the application with varying permissions and privileges. Once created globally, they can be applied for access differentiation across different studies. For instance, a user may have the role of a Statistical Programmer in Study 1, a Study Lead in Study 2, and read-only access in Study 3. The personas or roles are defined in alignment with current usage, application requirements, and nomenclature to ensure user familiarity and minimize confusion.

Choosing the hierarchy and folder structure is crucial. Gone are the days when waiting until the study was complete for submission was necessary. Now, submissions occur as the study progresses, with tailored packages for multiple analyses or milestones within each study. This includes activities like Integrated Summary of Safety (ISS) and Integrated Summary of Efficacy (ISE) submissions. The first step is deciding whether to catalog the studies under therapeutic area, compound, or project. Then, the standard folder structure for each type of submission activity needs identification. The company's culture, processes, and policies also play a role in determining these standard folder structures for different kinds of analyses.

Standard folder structures should be templatized. Using templates enhances efficiency, time management, and eliminates errors that may occur when creating them manually each time. It's beneficial to include global macros, standard programs, or predefined dictionaries that will be applied automatically whenever an analysis is generated from the template. Additionally, having standard user groups assigned is advantageous. It is always good to have multiple templates for different types of analysis.

A task assignment workflow should be established based on the customer's Standard Operating Procedures (SOPs) or policies. This workflow should facilitate collaboration, allowing for the incorporation of comments, feedback, and task closures.

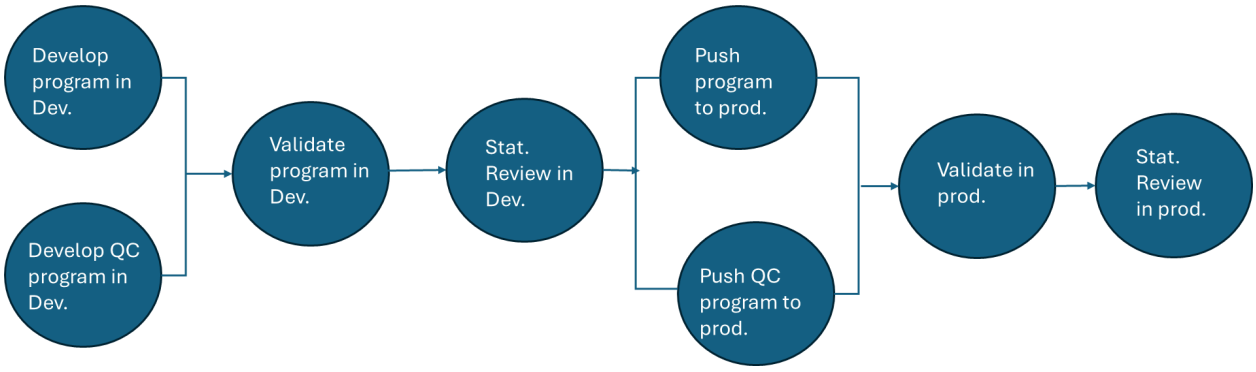

Figure 1. Diagrammatic representation of workflow

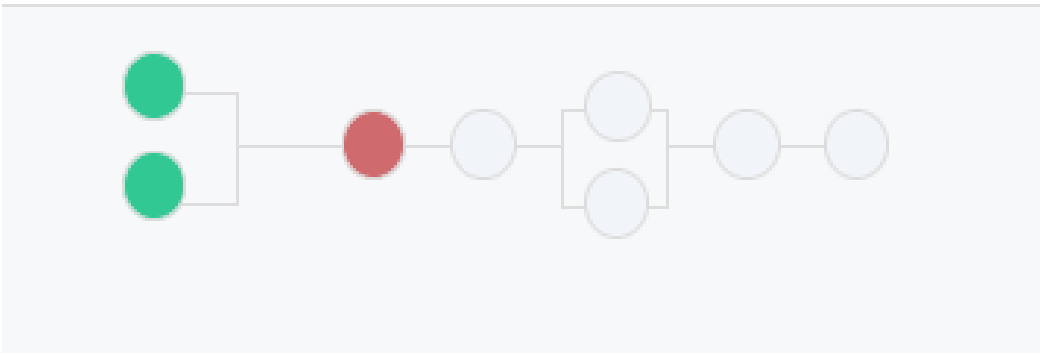

Figure 2. Diagrammatic representation of workflow progress

Integration

Integration is indispensable in clinical trial submissions, where both inbound and outbound integration play vital roles. Data originates from upstream sources and flows into the MDR and SCE. Once submission packages are generated, they are transmitted downstream to Medical Writers and other stakeholders for further processing. Hence, integration is crucial for maintaining traceability and auditability throughout the clinical trial submission process. It facilitates seamless communication and interoperability between different components of the submission system, ensuring efficiency and accuracy in compliance with regulatory requirements.

Scalability

The pharmaceutical industry is experiencing rapid growth, driven by advancements in cloud computing, artificial intelligence, and a plethora of programming languages over the past decade. This technological evolution is leading to greater acceptance of technology adoption within the industry. Furthermore, the continuous development of cutting-edge research technologies has resulted in a surge in clinical trials, generating vast amounts of data. Consequently, there is an expanded scope for data management and analysis, necessitating an increased presence of data managers and statistical programmers.

It is imperative that any modern tool, such as MDR or SCE, adopted by pharmaceutical companies, can adapt to the ever-changing technological landscape and accommodate the growing volume of data and users within the application.

Within SCE, configuration and integrations are necessary to meet organizational needs. This includes integration with various programming languages, third-party tools, performance enhancements, and storage solutions. For instance, organizations have the flexibility to utilize multiple programming

languages simultaneously, such as SAS, R, Python, or others. Additionally, integration with various third-party tools commonly used by companies, like P21, Beyond Compare, or Ultraedit, is feasible within SCE.

System ability to scale and increase storage as organizations grow are also critical and vital components for pharmaceutical companies. As the volume of data continues to increase due to advancements in research technologies and the rising number of clinical trials, it is essential to have systems in place that can dynamically adjust resources to handle fluctuations in workload. Scalability ensures that computing resources expand or contract based on demand, optimizing performance and cost-effectiveness.

Collaboration within the modern Application

In the pharmaceutical industry, collaboration is essential at every stage of drug development. Whether it involves developing SDTM datasets, ADaM datasets, Tables, Listings & Figures, performing QC for programs, or updating delivery statuses, constant communication among third-party teams is imperative. Various communication channels such as verbal discussions, phone calls, emails, texts, Instant Messages, chats, Excel spreadsheets, and SharePoints facilitate this process. However, without a defined communication protocol, misunderstandings can occur, leading to inefficiencies. Additionally, retroactively understanding the chronological sequence of events can be challenging, resulting in fragmented communication. Therefore, organizing and utilizing communication methods effectively is crucial for success in the industry.

In modern applications such as SCE and MDR, third-party programmers, study leads, and other users can leverage the built-in communication features to collaborate on daily tasks, monitor overall progress, raise issues during program validation, and approve outputs. All communications can be linked to specific tasks or deliverables being performed. Maintaining a record of these conversations is necessary to demonstrate the progression of events and decision-making processes. This streamlined communication process enhances efficiency by reducing the need for lengthy emails or phone calls and enabling quick exchanges of information. Furthermore, using the tool for all conversations ensures that a proper audit log is maintained, which can be referenced at any time if needed, and holds individuals accountable for their actions.

Product Roadmap

Many companies rely on custom-built, in-house products tailored to their specific needs. However, as these products are used over time, users often generate enhancement ideas and identify issues, necessitating product updates. Yet, updating an in-house product is a complex process involving various stages like code revision, quality testing, validation, and verification. This meticulous process can stretch anywhere from 6 months to a year. Thus, there's a significant time gap from when an issue is reported or an enhancement requested to when users witness the change in the application.

On the other hand, Commercial Off-The-Shelf (COTS) solutions dramatically reduce the turnaround time from product demo to user access, whether during initial deployment or subsequent updates. Companies benefit from bypassing additional rounds of validation, leveraging vendor validation reports for audit purposes. Consequently, the time it takes for a requested feature or fix to become available to business users is considerably shortened, promoting agility and responsiveness within the organization.

Conclusion

In conclusion, configurability with minimum customization is essential for the implementation of Statistical Computing Environments (SCE) and Metadata Repositories (MDRs), offering a vital solution to address the myriad needs and preferences of end users effectively. By embracing industry-centric design principles alongside module-based architecture and configurable/extensible features, we pave the way for customers to harness the full potential of data analytics tools. This not only amplifies productivity, efficiency, and user satisfaction but also fosters a dynamic environment where innovation thrives. Customization transcends mere technicality; it emerges as an art form, enabling organizations to unlock new realms of possibility and drive tangible value in the ever-evolving landscape of data analysis and management.

Contact Information

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