Paper SD02

Structured Protocol Authoring(SPA) – A catalyst for clinical protocol development

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ABSTRACT

Organizing, reusing, and availability metadata leading to the creation of a robust CDP and automating the creation of CRFs will expedite the clinical trial process in a user-friendly approach. SPA is a cloud-based SaaS application that achieves the objective of being a tool for collaboration space, allowing better and easier input from stakeholders and aiding in developing a robust protocol. It facilitates the capture of protocols in machine-readable form, eliminating duplicate protocol elements from standards and past studies, ensuring CDP structure and document templates are configured, improving quality, and preventing amendments. Also being in sync with familiar MS Office Online and visualizations tools using layout views for medical writing. SPA also synchronizes with a metadata repository (MDR) tool to kick-start study instances and converts SPA's Schedule of Activities into CRFs. The auditing capability ensures regulatory compliance making SPA, the most powerful SaaS footprint in our industry.

INTRODUCTION

Biopharmaceutical and medical device businesses are facing much more restricted economic resources in the present global operating conditions, while time-to-market pressures and clinical research activities are steadily increasing globally. Effective study planning for sponsors of the study is a challenging proposition. When businesses can optimize their study planning, they attain a greater return on research and development (R&D) capital and can compress cycle times for study planning, decrease timelines for implementation and decrease costs while preserving feasibility for the study.

In our domain, the Clinical Development Plan (CDP) provides an overview of the strategy for the entire development of a drug for all indications. It describes the plan for the clinical studies to be carried out. The CDP also acts as a trigger for initiating the planning of studies for the next phase of clinical development. A dynamic tool-based approach over conventional paper documentation will contribute to handling time-to-market pressure effectively.

CHALLENGES IN PREPARING A CDP

- Planning and forecasting techniques are neither sophisticated nor scientific.
- Frequently unable to tie project forecasts to historical data.
- No systems in place to archive and track past projects and activities.
- Intensive process resources and tough data comparisons.
- The lack of a centralized repository - leads to confusion in operations and project management, which leads to inaccurate budget planning.
- Time-consuming - It can take weeks or even months to create a clinical study plan and budget.
- Lack of security and audit trail of data changes.

INTRODUCING SPA

The Structured Protocol Authoring application (SPA) is a collaborative Clinical Trial Protocol Authoring and Structured Study Design environment that provides standard templates, libraries, and powerful search tools along with familiar editing using Microsoft Word. Using the SPA, it is possible to generate Clinical Development Plan and author Clinical Trial Protocol documents on demand using customer specific or industry standard templates such as TransCelerate's Common Protocol Template (CPT) and the NIH-FDA Clinical Trial Protocol Template.

The SPA keeps track of constraints and connections between Study Design Elements such as Objectives, Endpoints/Variables, Inclusion/Exclusion Criteria, Activities, and Trial Parameters. Users can view, edit and review all elements in the application in a familiar Microsoft Word-Online interface, export the study design in machine readable CDISC standard format, or export the Clinical Development Plans and Clinical Trial Protocol documents in Microsoft Word or PDF format. With the native integration with the Metadata Repository (MDR), organizations can incorporate the company and industry-approved clinical trial standards early on in the study design process.

FEATURES OF SPA

- **CAPTURING PROTOCOLS AND STUDY DESIGN IN MACHINE-READABLE FORM**

Historically, medical writers, working with clinical teams, have created study protocols with word processors and spreadsheets. Standardized re-use becomes a case of cut and paste with the inherent issue of out-of-date or just wrong versions, subsequent re-review, and re-work.

Once finalized, the protocol must be reviewed by clinical operations and data management to translate into a set of study implementation specifications, which in turn must be reviewed to ensure accurate interpretation. And then those specifications must be further 'transcribed' into the actual software systems employed to conduct the study. SPA provides 'structured' study designs where the aspects of a protocol most relevant to the implementation phase are already captured during protocol authoring in a form usable by downstream teams. This includes Objectives, Endpoints, Inclusion/Exclusion Criteria, Schedules of Activities, Trial Design, and Trial Summary Parameters.

The structured definition of the study data in SPA maintains interconnections, enforces proper constraints based on the connections, and promotes content reuse. SPA links with MDR to pull metadata standards including Code Lists and Medical Standards also known as Medical Concepts or Concepts so that the structured study design adheres to company and industry-approved standards. Structured study definition is exportable in forms suitable for both human and machine consumption, bypassing multiple transcription and re-review steps.
This study definition can be used by MDR studies to kick-start building the CRF metadata

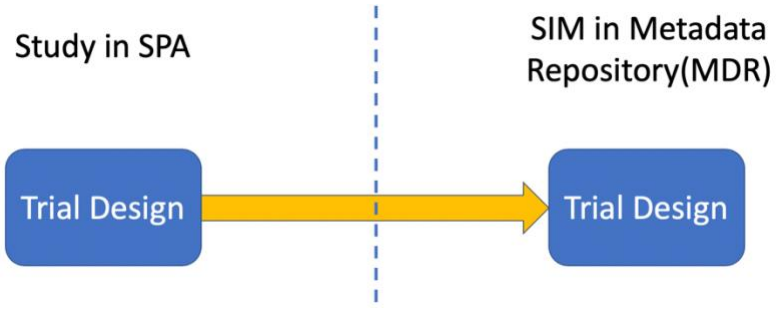

Figure 1: Flow of Trial Design from SPA to MDR

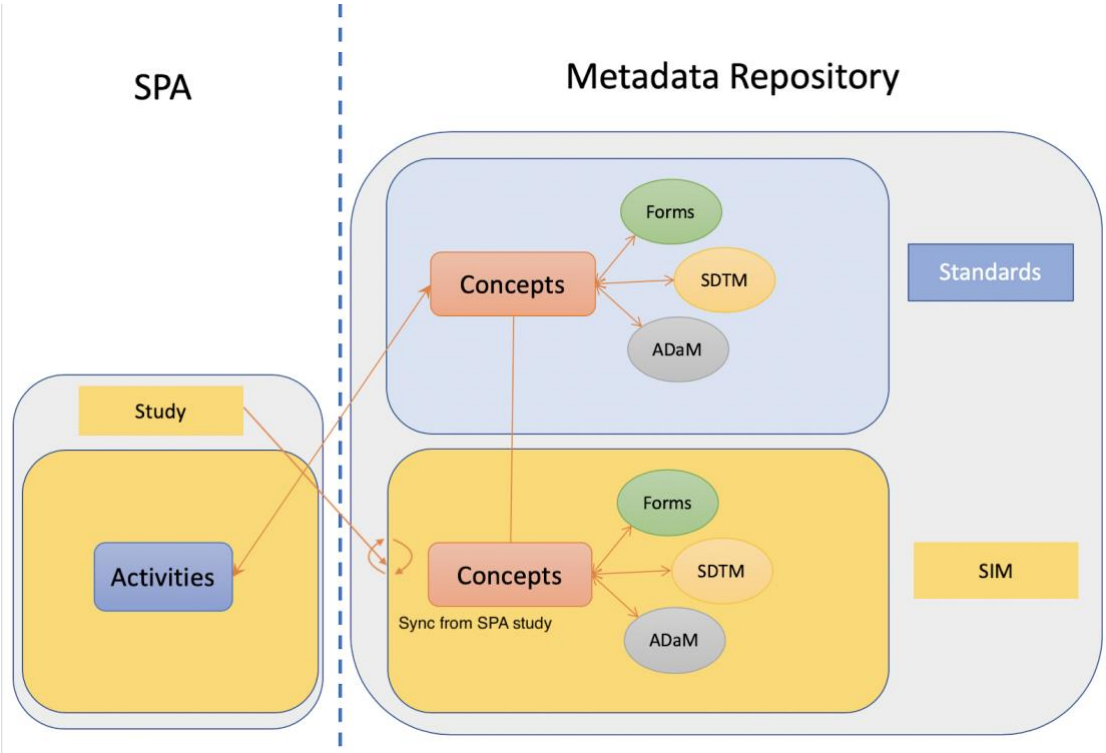

Figure 2: SPA pulls metadata standards from MDR

- **REUSE PROTOCOL ELEMENTS FROM APPROVED OR PAST STUDIES**

There is often repeated content across study protocols. These may be required sections that must be filled in for each unique instance. Or standardized content that reflects the planning and study practices of a given company or clinical area. This extends to terminology, study design implementation practices, and submission standards. Historically, much of this standardized and re-used content is managed inefficiently in multiple locations in multiple tools and formats.

Wherever possible, the SPA solution seeks to assist medical writers and other clinical team members involved in defining studies by making standardized material and prior exemplar material readily available for review and selection. A complete catalog of study design elements is available for re-use during the study definition process and the ease of re-use is facilitated by search and comparison functionalities. SPA application is also able to select content.

- **CONFIGURE CDP STRUCTURE AND DOCUMENT TEMPLATES**

SPA combines structured content with canned and free-form text blocks in templates to generate Clinical Development Plans and protocol documents in Microsoft Word and PDF formats. These deliverables are critical for management teams, regulatory bodies, study teams, safety review boards, site personnel, clinical development partners, and anybody else who may be involved in the planning, execution, and review of clinical programs and individual studies. SPA ensures that these documents are created consistently, using standardized material wherever possible, and then versions and stores those documents along with the structured content, providing a controlled, single-source-of-truth solution.

- **EXPORT CDP PROTOCOL DOCUMENTS**

It is possible to export the CDP and protocol documents, or structured study design out of SPA. The CDP and protocol documents can be exported in human-readable forms such as Word or PDF. The study design can be exported in Excel format, adhering to the CDISC SDTM Implementation Guide. The study design export in Excel is both machine and human-readable. The export functionality facilitates the delivery of key documents or files critical for management teams, regulatory bodies, study teams, safety review boards, site personnel, clinical development partners, and anybody else who may be involved in the planning, execution, and review of clinical programs and individual studies. By providing a CDISC-compliant export as well, SPA content can be delivered in machine-readable form for downstream systems requiring the same information.

- **SECURITY**

SPA contains sensitive and proprietary information for client companies. While not strictly under the governance of 21 CFR Part 11 and related regulations, access to the system must still be secured to only properly authenticated users. Specific content view/edit rights must be applied to users once in the system. And who has what rights and who has been in the system must be visible to and controlled by customer administrators.

LIFE CYCLE OF CDP DOCUMENT

Within SPA, users define the CDP and Study information in a structured manner. They add, update and delete the information within the tool. The end goal of the process is to produce documents e.g. a Clinical Development Plan (CDP), a Study Protocol, or a Study Synopsis. Hence, once the information attains a certain milestone, users generate CDP and Study documents using Templates available within the tool.

Medical Writers work on documents in Word Online. They add more details to provide textual explanations to the structured data exported from SPA. Reviewers look at the documents and provide feedback and enter comments. Medical Writers incorporate the feedback in the documents and if necessary, back in SPA.

As the CDP / Study progresses, users enter more information in SPA. The updated information is exported to the document by generating a new version of the document from an existing version since the existing version has additional textual information entered by Medical Writers. Alternatively, instead of generating a new version, one may create a new copy of the document using an existing document.

To facilitate offline documentation and review, certain users may provide feedback or content by downloading a copy from Word Online and working in MS Word locally. Also, in cases where document templates need an update with new or more expressions, one can modify the Word Document locally and upload the document with expressions.

Following the process above, the final versions of documents are prepared and distributed among stakeholders internally and outside the organization.

REGULATORY COMPLIANCE IN SPA

CDPs and studies defined in SPA will change over time until they take their final shape. SPA is intended to be the single-source-of truth for these designs and documents. Various change management features in the SPA help users keep track of the state of their studies and manage the changes to their CDPs, structured study definitions, and their documents.

An audit trail captures every change made to the structured study design with the old and the new value. This not only ensures regulatory compliance but also makes tracking and rolling back changes, if necessary, easy. Study workflow allows easy management and tracking of various study design milestones and keeps tabs on changes by locking finalized data. CDP and protocol documents can be versioned. Edits made in documents are automatically saved to avoid accidental loss of information.

CONCLUSION

Leading biopharmaceutical businesses and medical devices show that greater yields on the research and development assets are achieved through optimizing the study planning. The ability to perform what-if scenario planning quickly and accurately as well as higher visibility of the operational and financial plan for a study. Benefits have been gained dramatically from abbreviated planning cycle times, faster delivery rates, lower costs and yet maintaining study feasibility.

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