Paper SD02

SPA – A catalyst for clinical protocol development

Suhas Giriraj, Ephicacy Lifescience Analytics Pvt Ltd, Bangalore, India

ABSTRACT

In the clinical domain, Clinical Development Plan (CDP) provides an overview of the drug development strategy for all indications and describes the plan for the clinical studies to be carried out. A tool christened **Structured Protocol Authoring** (SPA) is a cloud-based SaaS application for collaboration space, allowing better and easier input from stakeholders aiding in developing a robust protocol. This tool is used to capture protocols in machine-readable form, saving time by promoting reuse of protocol elements from standards or past studies, configuring CDP structure and document templates, thus improve quality and preventing amendments through comparison against benchmarks and competitor studies; being in sync with medical writing with familiar Microsoft Office Online and visualizations in powerful layouts views(Gantt charts or tables). SPA's audit trail feature captures every change made in structured study design and CDPs. It ensures regulatory compliance making it the most powerful SaaS footprint in the biopharmaceutical 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 overview of the strategy of entire development of a drug for all indications and 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. Dynamic tool-based approach over conventional paper documentation will contribute in handling time-to-market pressure effectively. The clinical development plan is a complex document that entails entire clinical research strategy of a drug, describing the clinical studies that will be carried out for a would-be-drug/entity researched by a pharma company. The CDP is based on the information of the target product profile i.e., TPP, which gives an overview of the goals for the drug product, estimates the net value and also provides information for the go/no-go criteria.
The elements in CDP aids in knowing more:

1. Understanding the concepts to know what must be done successfully to complete the pre-clinical and clinical research project of a drug
2. Establishing the efficacy and safety of a drug for use in humans, in a dose range and schedule that provides an acceptable risk /benefit relationship
3. Budget estimation of the project
4. Attaining regulatory approvals
5. Bringing the product to the market

The main elements of CDP are:

- Background pharmacology, scientific summary and rationale of the drug
- Clinical studies planning
- Work breakdown structure, milestones
- Costs related to development
- Risks
- Regulatory requirements and strategy
- Market strategy

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.
- Lack of a centralized repository - leading confusion in operations and project management, this 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 changes to data.

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 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, with 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 in 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.

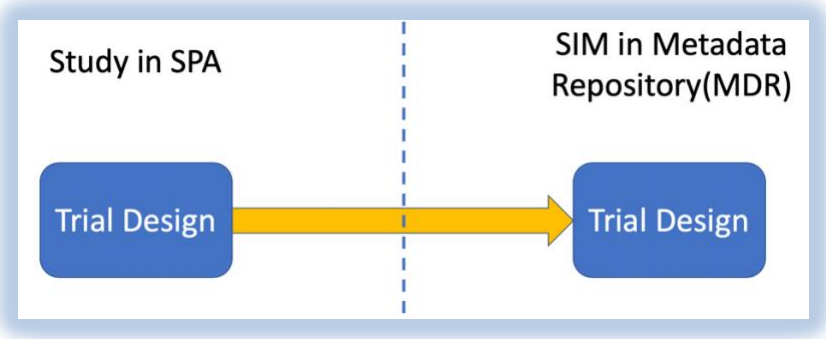

Figure 1: Flow of Trial Design from SPA to MDR

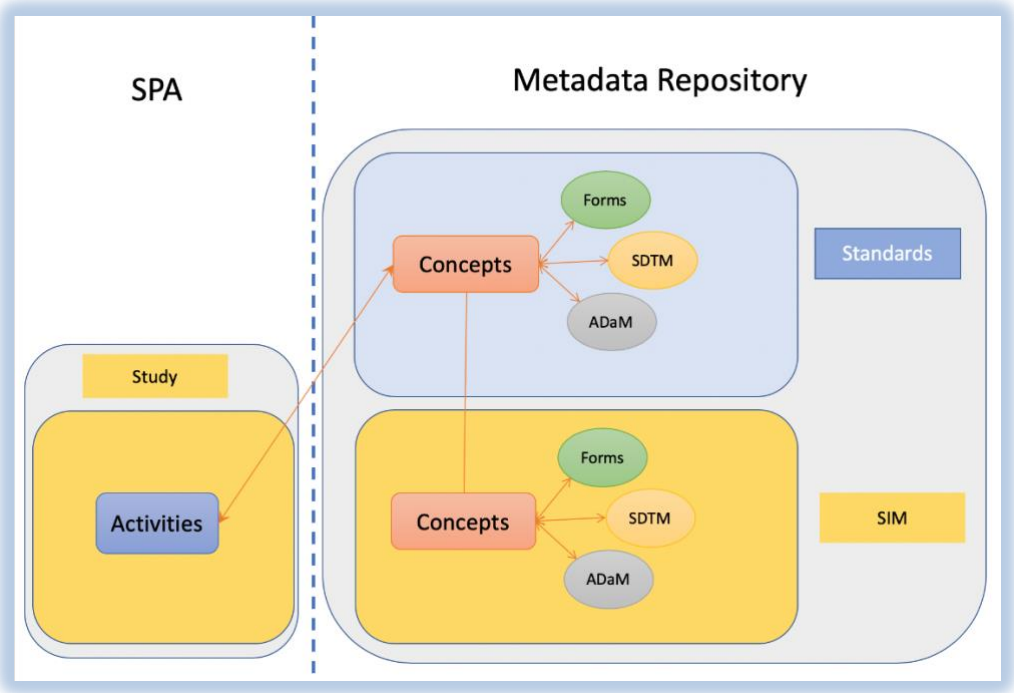

Figure 2: SPA pulls metadata standards from MDR

- **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, 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 the comparison functionalities. SPA application is also able to select content from.

- **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 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.

- **USABILITY**

The SPA is carefully designed and developed based on better usability and user experience in the way users can make their work more productive in terms of quality and time, thus resulting in better efficiency in delivering the protocols with accurate results. Customers being the real time users of SPA have participated more in sharing the real-world experience with the existing system and expectations in making their life better by replacing SPA into their business.

- **SECURITY**

SPA meets the needs of cyber security needs of pharmaceutical industry standards. Which contains sensitive and proprietary information of pharma companies. Under the governance of 21 CFR Part 11 and related regulations, access to the system is secured to only properly authenticated users. Specific content view/edit rights is applied to users once in the system. The admin rights rest with few at the customer level and the admin controls access provision. SPA being a SaaS product, every data in the cloud servers are securely transferred and received in Secured Socket Layers(SSL) using standard data encryption encoding algorithms.

LIFE CYCLE OF CDP DOCUMENT IN SPA

Within SPA, users define the CDP and Study information in a structured manner. They add, update and delete 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 the documents using word formats. They add more details to provide textual explanations to the structured data exported from SPA. Reviewers review 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 progress, users enter more information in SPA. The updated information is exported to the document by generating new version of the document from an existing version, since 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 work in any local word software. 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.

UPGRADES & ENHANCEMENTS

As every product needs new features and customised requirements from different pharma companies, this tool will undergo changes and upgrades to enhance the value of the product in terms of usability, custom requirements, changing regulatory requirements and. Hence product owners, development teams and customers are actively participating in shaping the product with active developments and patches to the product.

CONCLUSION

Leading biopharmaceutical businesses and medical devices show that greater yields on the research and development assets are achieved through optimizing the study planning. CDP is the essential tool to bring a novel product to the market and SPA supports this vision completely. The ability to perform what-if scenario planning quickly and accurately as well as higher visibility to 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.

SPA is an effort to decrease the cycle time, lower costs and ensuring data security. This tool will be customizable for the needs of the customers and user-friendly too. Application support will be available ensuring the goal of customer satisfaction is met.

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Director - Strategic Initiatives & Quality
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Shanmugarajan Muruganandam
Sr. Project Manager - Product Development
Ephicacy Lifescience Analytics Pvt. Ltd

CONTACT INFORMATION

Contact the author at:
Author Name: Suhas Giriraj
Company: Ephicacy Lifescience Analytics Pvt Ltd.
Address: No.6, II Floor, II Main Road, Arekere, Off Bannerghatta Road
City / Postcode: Bangalore - 560076
Work Phone: +91-80-41463195
Email: suhas.giriraj@ephicacy.com
Web: www.ephicacy.com