How an FSP Team Implementing Standards Can Help Ensure On-Time Delivery of Trials

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Clinical data management (CDM) functions have seen transformational developments over the years, moving from data entry of 100% paper-based trials, to EDC (electronic data capture) becoming one data source among many, including eCOA (electronic clinical outcome assessment), central laboratory data, and others. More recently, the rapid adoption of decentralized clinical trials has led to the proliferation of data sources such as genomics, video, real-world data (RWD) and continuous data streams from sensors and wearables.

More complex clinical trial designs are also generating much higher volumes of data. For example, Phase III clinical trials collect an average of 3.6 million data points, three times the data collected by trials a decade earlier.[1]

Even as the volume and complexity of data collected in clinical trials grows exponentially, the pressure is on to deliver on increasingly aggressive timelines. The pressing question: What can be done to decrease the time between data generation and data consumption?

Reduce Time-Consuming Tasks with Standards Carried out by an FSP Team

Implementing data standards using a Global Library (GL), a centralized repository containing reusable metadata and coding standards, is an often-underutilized approach to drive more efficient clinical data management processing. The library functionality, for example, allows for the copying of pre-validated objects, such as variables, code lists and edit checks, from the GL into new projects without duplicative reprogramming or testing, thus eliminating time-consuming tasks.

However, organizing standards in a GL is only one piece of the puzzle. It is also critical to have a stable team in place to develop the standards, apply them consistently, gather user feedback, and make incremental improvements. A growing number of sponsors are turning to functional service provider (FSP) models to gain dedicated data management teams who are there for the long term to apply their client-specific expertise and knowledge. And because efficiencies multiply as the GL is used across multiple trials—allowing standards and incremental learnings to be applied at scale—an FSP team working across a portfolio of trials significantly reduces the time and effort required for clinical data management and downstream tasks.

Best Practices to Unlock the Potential of the GL

To maximize the benefits from data standards, users can build them directly into the GL, allowing the standards and their associated efficiencies to be carried throughout the trial from database design/build through submissions. With the library in place, the team can pull objects into the new study and not have to create them from scratch each time.

The GL has long been recognized as a valuable resource for optimizing efficiency in startup activities, especially the database build phase. However, many data management teams face challenges with disorganized or oversized GLs, challenging them to find and manage GL objects such as case report forms (CRFs).

Creating individual standards based on therapeutic areas is a simple yet effective approach that FSP teams can implement to allow users to easily pull relevant CRFs from the GL into their studies, eliminating the need to recreate forms from scratch.

Another recommended GL best practice is to ensure that CRFs are fully SDTM (Study Data Tabulation Model) and CDASH (Clinical Data Acquisition Standards Harmonization) compliant. The Clinical Data Interchange Standards Consortium (CDISC) is a nonprofit organization that develops data standards, including SDTM and

CDASH. SDTM facilitates the structured organization of trial data, ensuring consistency and compatibility across different studies. CDASH standardizes the collection of data elements, fostering clarity and analysis ease.

While governance and maintenance of CRFs per the latest CDISC implementation guideline can be cumbersome, embracing SDTM and CDASH compliance within the GL does offer numerous benefits. It facilitates seamless integration and exchange of data between different systems and stakeholders, eliminating interoperability challenges. Secondly, compliance improves consistency while reducing the burden of creating customized data structures for each study, resulting in time and cost efficiencies. Finally, regulatory agencies, including the FDA, encourage the use of standard, uniform study data to help them process, review, and archive submissions more efficiently and effectively.[2] Failure to comply could pose significant obstacles to submission approval.

Another aspect of clinical trial operations where the GL shines is edit check programming. Within the GL volumes, pre-validated data cleaning edit checks for each CRF are readily available, minimizing the need to create time-consuming validation processes. Users can simply copy these pre-validated checks along with the CRFs, layering in efficiencies in this crucial step.

Similarly, in unit and user acceptance testing, the GL's pre-validated metadata offers an evidence-based automated tool for exact match elements, bypassing the need for extensive testing. Study teams also can leverage the standard GL documentation, such as database review forms and test logs, to further streamline their testing processes.

Beyond aiding in database build and testing activities, the GL can also be leveraged for data review purposes. By using SAS macro automation programs, users can generate robust listing outputs quickly and efficiently, facilitating timely data reviews and analysis.

Finally, some words of caution: any changes to the GL design for those "nice-to-have" or "aesthetic design" requests can add complexity and potentially cause delays, which may require additional testing and would require impact analysis for downstream activities, potentially reversing the savings of having a well-defined GL. To ensure your standards program continues to deliver substantial efficiencies, updates to the GL must be managed within a well-defined governance structure.

Beyond Data Management

The GL also offers benefits for other stakeholders, including biostatistical programming teams. For example, by organizing EDC and eCOA collections modules by therapeutic standards, the GL makes it possible to create standard table, listing, and figure (TLF) expectations. These standardized TLFs can then be easily incorporated into the statistical analysis plans (SAP) table of contents (TOC) housed in a biostatistical programming therapeutic GL. By providing a standard inventory of therapeutic-focused TLFs and program templates that, optimally, can even prepopulate shells, annotations, and generate program shells based on the TOC selection with the SAP TOC, the GL allows the biostatistical programming teams to not only save time but ensure consistency in TLF generation across studies.

Analysis Data Model (ADaM) mapping is another critical area where the GL can be instrumental for biostatistical programming teams. With core elements already organized by therapeutic area and taking advantage of industry standards, a centralized biostatistical programming therapeutic GL allows for efficient specification and development of analysis datasets based on the standard SDTM structure. Standard ADaM specifications and programs housed within the GL enable researchers to leverage pre-existing elements and focus on the unique analysis requirements of each study.

Involving a range of other key stakeholders and seeking their input and review is also crucial in the development of a comprehensive GL. This collaboration may include a diverse range of stakeholders such as regulatory personnel, medical monitoring, clinical operations, and others. Incorporating cross-functional input from the start promotes ownership, buy-in, and active contribution to the GL's maintenance and updates. This ensures that downstream activities, such as database builds, data review, analysis, and submissions, are streamlined, consistent, aligned with regulatory requirements and reflect the perspectives and expertise of those involved in the trials. For example, a clinical research associate (CRA) can provide early feedback on the CRF design and overall flow to help reduce site burden.

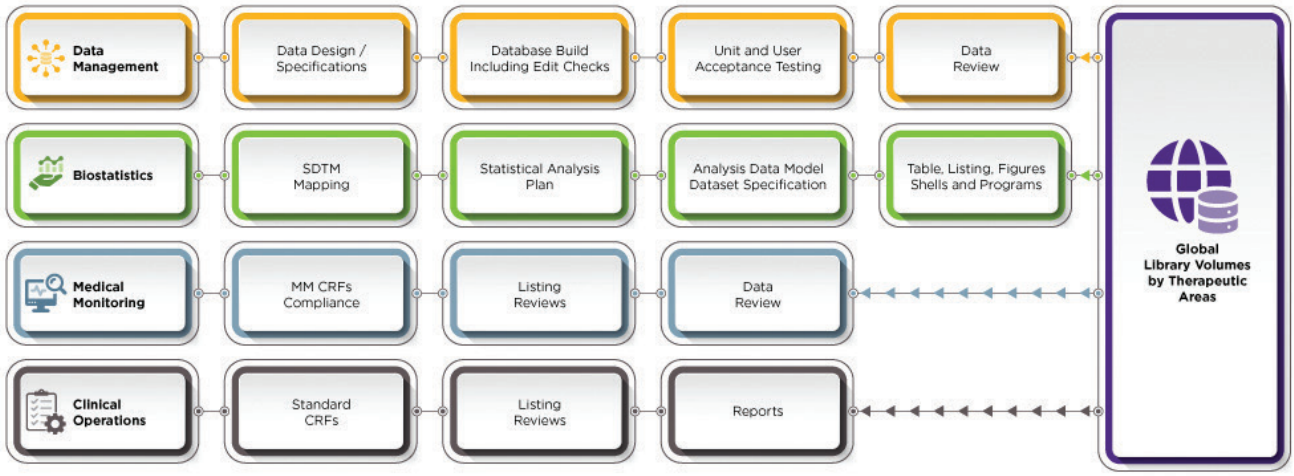
The FSP model also excels in promoting this cross-functional collaboration, as it provides ready access to functional operational, clinical, and regulatory experts who can offer insights, best practices, and industry-specific guidelines as needed. This rich collaboration, in turn, helps create a comprehensive GL that provides a variety of different stakeholders with different efficiencies, as illustrated in the following graphic.

Future Enhancement through Automation

Standardization plays a critical role to enable the introduction of advanced artificial intelligence (AI) and machine learning (ML) techniques in the future of clinical trials. For instance, employing natural language processing (NLP), protocol eCRF information can be extracted and compared with Global Library metadata, facilitating the creation of study eCRFs and implementing edit checks. Additionally, a role-based model can be used to establish an efficient review, approval, and finalization process, streamlining the study build.

Furthermore, centralizing all clinical trial data in one location enhances data quality and consistency, improving patient data handling. This centralized approach brings us closer to the vision of real-time availability of patient data, enabling informed clinical decision-making, risk mitigation, and optimal patient safety. Normalizing data and organizing it by category enables rapid and effortless query and report generation, while harmonization of data increases its value and utilization. This harmonization also allows for the transformation of fragmented and inaccurate data into actionable information, enabling the generation of new analyses, insights, and visualizations.

Figure 1. Examples of efficiencies gained by different stakeholders



Taking a future view, standardization, combined with advanced tools like AI and ML, which enable automated study build and data harmonization, can potentially save up to 80% of the time and effort traditionally invested in CDM activities. For example, a typical database build of 12-14 weeks can be achieved in less than two weeks.

About Outsourcing Options

When considering outsourcing a clinical trial, there are various options to choose from. Full-service models provide comprehensive clinical development services on a trial-by-trial basis, while FSP models involve the outsourcing of specific functions for one or more trials, potentially across a portfolio. Additionally, there are hybrid models that combine elements of both approaches.

Each model offers its own set of advantages and disadvantages. However, using a dedicated FSP team that consistently offers the breadth/depth of its members' reliable expertise and know-how will ensure the benefits of data standardization are maximized. Ideally, this FSP team would work across a portfolio of trials, allowing them to gather feedback on optimal approaches and standards and continuously improve the GL while driving more efficient processing. By creating a feedback loop, the FSP team deepens its sponsor-specific expertise and knowledge and applies data standards at scale over time across trials, significantly reducing the time and effort typically required for CDM and other downstream activities.

Sponsors are increasingly choosing FSP models to enable consistent implementation and governance processes of standards to help them meet challenging drug development timelines. More broadly, growth of the FSP model has been steadily increasing. In 2018, market use of full-service outsourcing (FSO) models was 72%, with FSP model use at 28%, but in just three years, FSP usage grew to 41%.[3] And in the face of increasingly competitive talent markets, a mix of FSP and hybrid FSP/FSO models has become even more common, now representing two-thirds of arrangements. Outsourcing individual functional services also has allowed organizations to complement their internal strengths with a partner's deep bench of clinical development experts and services, gaining greater flexibility as well as operational and financial efficiencies while delivering projects on time.

Conclusion

The ever-growing volume and complexity of data in clinical trials have placed immense pressure on CDM teams to improve efficiency to meet aggressive deadlines. By implementing data standards within a GL, carried out by an FSP team that has the experience and expertise to help create these standards and consistently apply those advances at scale across trials in a portfolio, CDM teams can significantly decrease the time between data generation and consumption, delivering on timelines and data quality and integrity expectations.

Finally, implementing a GL for consistent standards across a trial not only reduces manual burden and resource-intensive efforts, it also frees the clinical trial team to dedicate more of its time and effort ensuring consistently high data integrity, increased critical thinking and generating valuable insights from the data.

References

1. Tufts Center for the Study of Drug Development. Rising Protocol Design Complexity Is Driving Rapid Growth in Clinical Trial Data Volume. Published January 12, 2021. Accessed July 18, 2023. https://www.globenewswire.com/en/news-release/2021/01/12/2157143/0/en/Rising-Protocol-Design-Complexity-Is-Driving-Rapid-Growth-in-Clinical-Trial-Data-Volume-According-to-Tufts-Center-for-the-Study-of-Drug-Development.html.
2. FDA. Data Standards in the Drug Lifecycle. Published online February 9, 2019. Accessed July 20, 2023. https://www.fda.gov/drugs/electronic-regulatory-submission-and-review/data-standards-drug-lifecycle
3. PPD FSP strategic growth plan analysis using ISR and Avoca research. 2021. Data on file.