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Initial Investment in CDISC Data Standards in Clinical Organisations: Knitting fog, herding cats, and other challenging endeavours

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ABSTRACT

One of the main goals of CDISC standards is to make the collection, transfer, analysis, submission, and review of clinical trial data in clinical organizations more efficient. To best ensure this, the role of initial investment of discussion and decision-making before implementation cannot be overlooked.

From my experience on both sides of the pharmaceutical industry, pharmaceutical companies and contract research organizations, it is apparent that every hour of up-front thinking into the necessary components of an effective standards governance framework is invaluable. It is my objective to share that experience in this presentation.

An effective standards governance framework not only ensures compliance to standards, but also that the efficiencies inherent in standards usage are realized for the sponsor organization. It encompasses people, standards, processes, and technical solutions.

INTRODUCTION

At the heart of CDISC standards is the knowledge that standardization of data in clinical organizations makes the collection, transfer, analysis, submission, and review of clinical trial data more efficient. This is simple. The utilization of those and other standards within an entrenched clinical organization is not.

BACKGROUND

While the focus of this presentation is not to prove the value of standardization with CDISC standards, it is imperative to set the stage for the topic of standards governance by demonstrating real world examples and metrics of the benefits.

From a standpoint of success stories of standardization in the business world, one has to look no further than the use of standard metadata in the banking industry. This has allowed a global network to develop where the use of ATM (automated teller machine) cards to obtain cash in the local currency is widespread across the globe. On the negative side, a lack of standardization within the electrical utilities industry has created an environment where global travelers must carry multiple converter plugs to be able to use their electronic devices in foreign lands. [2]

Looking at clinical trials from a point of view concentrated on analysis and submission, there are notable issues that standardization not only facilitates, but actually enhances. While there are many more than the three listed below, these activities would appear near the top of industry lists:

- In the submission of data to regulatory authorities, integrated standards provide built-in harmonization from collection to analysis to submission. The prime benefit of this when a regulatory reviewer has questions about the source data when reviewing an analysis. The data transparency and traceability from final analysis results all the way back to collected data reaps enormous benefit in providing the reviewer with the necessary data confidence.
- It is incumbent upon clinical organizations running clinical trials for emerging therapies to responsibly search for safety signals to protect patients. Adherence to standards provides the foundation and common structure that allows for quick and effective data mining across studies for trends and signals in the interest of patient safety.
- Regulatory requirements are continuously progressing, and thus the timely incorporation of emerging regulatory standards by sponsor organizations leaves them well-positioned to take advantage of the benefits of these new standards in terms of decreased review time and increased data accuracy.

CDISC standards are platform-independent data standards that enable information interoperability between systems, developed with an eye towards balancing improved efficiency with support for the scientific nature of clinical research. These standards align with the ultimate goal of creating regulatory submissions that are easily understood by regulatory reviewers and minimize misinterpretation, and are the result of collaboration between volunteer subject matter experts from across the pharmaceutical industry and the contract research organizations that support them, in addition to input from FDA representatives.

The strength of CDISC standards is due to the relative simplicity of their structures and focus on meeting the needs of both the pharmaceutical industry and the FDA. They simplify end-to-end data handling processes via the integrated nature of the succession of models (CDASH-SDTM-ADaM). CDISC has also provided controlled terminology that is constantly expanding in scope, and included best practices in the various implementation guides to serve as a package for both structure and content.

With specific focus on CDISC Standards, metrics are emerging that demonstrate the value of CDISC Standards implementation. Table 1 displays the results of a business case impact analysis performed by PhRMA, Gartner, and CDISC in 2006 and updated in 2007. The metrics displayed therein are regarding the impact of CDISC standards implementation on both clinical study cycle time and cost. [1]

Table 1: Impact of CDISC Standards Implementation on Clinical Study Cycle Time and Cost[1]

Clinical Study Activities	Current Industry Average (months)	After CDISC Standards Implementation (months)	Time Savings (months)	Cost Savings (USD Million)
Study Start-up	5	1	4	4.4
Study Conduct	4	2.4	1.6	1.8
Analysis & Reporting	5	2.5	2.5	2.8
Cumulative	14	5.9	8.1	9

It would be negligent not to mention that there are obstacles to successful implementation of CDISC Standards (or any standards) that exist in many, if not all, clinical organizations. Some of these are rooted in established, long-term practices and preferences, while others emanate from the fear of change. It is not the purpose here to dissect or refute these obstacles, only to acknowledge the challenges that are present in attempting to implement CDISC Standards. This is not an exhaustive list, but merely a sampling of the most common ones:

- Fear that standardization will inhibit scientific innovation
- Perception that governance of standards is just another bureaucratic layer that will render clinical teams unable to meet their targets for deliverables
- The business need of completing today's business directly competes with the allocation of resources to work on standards for the future
- Unacceptable cost in time and resources to migrate, integrate and validate of standards implementation
- Fear that the standards themselves will not be stable

STANDARD GOVERNANCE FRAMEWORK

As standards of any kind are brought into a clinical organization, be they CDISC or any other, there exists a simultaneous need for standards governance that is all too often ignored. Standards without substantive means to govern them are akin to having no standards at all, because their use by clinical operations becomes irregular, non-compliant, and eventually non-existent. Looking across the industry, the most effective manner for effective standards governance is a framework that at a minimum encompasses and defines the roles and responsibilities of those people needed for standards governance, and whom must be the key drivers in the determination of a technical solution for standards governance.

There is no one-size-fits-all answer for all companies. Company size, available resources, and existing systems are among the variables that determine the best answer. So while the standards governance framework will vary in size and scope, it should have four major components necessary for successful standards implementation.

- **People**
- **Standards**

- **Processes**
- **Technical Solutions**

People form the foundation for this framework. Securing the services of the appropriate people within the data, statistical, and clinical sides to the business is an important first step. They will form the leadership, the content decision-makers, the developers, and the data stewards within the project teams. One often overlooked human component is the importance of a high-level, visible, management directive that lays the groundwork for buy-in across the entire organization.

The actual **standards** themselves are the engine that powers the standards governance framework. Whether they are tool-specific constructs for use at an operational level or the standard metadata that define databases and reporting programs, the standards are the reusable parts that allow for efficient and consistent execution of clinical trials. CDISC Standards will bring inherent challenges for implementation, considering their focus and structure are sometimes very different from existing industry practices. If time is not allowed for well-thought out decisions about these challenges prior to implementation, there is a real risk for wasteful re-work and delays.

It is crucial that **processes** be put in place before the CDISC standards are in use. These necessary processes are not limited to just the application of standards within operational tools (e.g.: eCRFs), but they also span processes that address approval of requests, define the scope of standards governance, and dictate standards maintenance and development. This enables consistent, reproducible application of standards, timely turnaround for new requests, and thus breeds a measure of trust by the clinical organization regarding the use of standards.

Technical solutions such as a metadata repository, document version control, and a request/issue tracking system enable the people and processes to work efficiently. Decisions on these solutions are often placed at the tail end of the whole CDISC implementation process, but they are as important to deriving maximum benefit from standards as anything else. A request tracking system, be it minimal or robust, enable the standards governance team to be quickly responsive to the requests of clinical teams, while a metadata repository allows the standards to be maintained at an elemental level and also to be exported to drive the clinical systems all along the clinical data lifecycle (e.g.: EDC database set-up).

It is crucial that as much of this standards governance framework be in place as possible before the implementation of CDISC and other data standards to best ensure the following: compliance, maintenance, integration, accountability, and consistent application of the standards. The framework needs to define and control all of the associated work processes necessary for successful implementation and maintenance.

PEOPLE

The foundation for this standards governance framework is people. Securing the services of the appropriate people within the data, statistical, and clinical sides to the business is an important first step. They will form the leadership, the content decision-makers, the developers, the administrators, and the data stewards within the project teams.

Standards governance roles can be loosely grouped into four categories:

- **Content Decision-makers** – subject matter experts for the medical and clinical nature of the data who can evaluate and deliberate on matters of the content of the data within the standards
- **Developers** – technical and operational experts with the ability to develop and finalize the implementation of the standards and make it available for practical use by the project teams
- **Administrators** – a role requiring proficiency in administrative tasks that can range from tracking requests to updating metadata to uploading the latest version of the standard into a system
- **Data Stewards** – a role that combines knowledge of data with knowledge of a specific functional or therapeutic area in order to both convey standardization decisions down into the area they represent and just as importantly raise standardization issues from their area upwards to the governance framework

Obtaining the right people to perform standards governance can be challenging in the current business environment of more work done by less people. The phrase “need dedicated resources” is one that triggers adverse reactions within the management ranks of most clinical organizations. The initiative to fulfill the people aspect of a standards governance framework must not be one of acquiring an “empire” of full-time resources, but one that seeks a blend of full-time and part-time resources that are dedicated to the effort necessary for effective standards governance.

Even though the part-time resources will likely far outnumber those who are full-time, it is the full-time resources that fill the key operational roles in standards governance. They become the team leader(s) and the decision-makers on

development. Their dedicated focus on standards day after day keeps the governance framework on target in its mission to be efficient, respected partners with the project teams in the ultimate goal of executing clinical trials on time.

The part-time resources are also vital to standards governance in that even though only a percentage of their time can be allotted for standards tasks, they bring the knowledge and expertise that has been amassed from throughout the clinical organization and incorporate it into the standards. Just because their level of involvement is not full-time, does not mean that their contributions are any less important to ensure that the standards are usable and reflect the needs of their clinical organization. Examples of the kind of expertise needed can range from all parts of the organization.

- An Oncology physician who provides medical input to the proper development of standards for RECIST tumor measurements according to the directives of their Oncology therapeutic area
- An experienced EDC screen developer who builds the new standard eCRF according to the approved standard metadata, but does so incorporating the considerations that the clinical monitoring require for effective site monitoring
- A statistical programmer who modifies and validates program code for standard reporting and analysis programs in order to use the new standard collection data structure that will yield efficiencies and align with the goals of integrating the standards across functional areas
- An IT business representative to the clinical function who serves as a liaison between the technical needs of the standards governance framework and the IT project managers, in order to address situations from access control to global library maintenance to necessary upgrades to existing systems

The idea of “data stewards” or “data champions” is not new to the pharmaceutical industry. In fact, it has taken hold in so many different companies that the meaning is now a varied one. For purposes of standards governance, the definition applied in this paper is listed above on page 3.

Whether the data stewards represent functional areas or therapeutic areas is a decision best left to each individual company after careful evaluation of the influence and the needs within the entire clinical organization, but they should never represent both. Such an arrangement would yield an amount of work that would prove far too excessive for a part-time resource. The nature of clinical trials will inevitably bring a multitude of issues for each single area.

This issue brings the conversation about governance to the idea of representation. What interests and stakeholders need to be spoken for regarding standards governance? In an ideal situation, every function and every therapeutic area would be represented, but since companies vary in size and composition, the depth of this will vary also. At a minimum, representation should include the functions that oversee data collection, data storage, statistical programming, biostatistics, clinical monitoring, and clinical physicians. Other functional areas that would be more peripherally involved include pharmacokinetics, regulatory, and drug safety.

A common oversight when determining representation is the omission of the IT function, as their placement within the overall organization is typically somewhat removed from clinical. Since standards will inevitably involve technical issues at some point in time, the IT function must have a voice at the governance table. This cannot be stressed enough.

One often overlooked human component is the importance of a high-level, visible, management directive that lays the groundwork for buy-in across the entire organization.

While many standardization efforts begin at the ground level of a clinical organization because that is where the knowledge base exists and that is where the benefits will be most realized, it is the high-level vision from the upper layers of management that usually transform standardization from a “nice-to-have” to a “must-have”. This vision should come from a level high enough to span all clinical and regulatory functional areas, from a singular voice that is well-respected and trusted, and delivered in such manner that it can be taken as an authorization by operational management to expend resources. The content of such a directive that addresses the need for standardization can include:

- Improved data quality
- Improved data transparency
- Accurate, consistent submissions
- Speed of study execution
- Maximization of study execution resources

- Cost savings
- Compliance with anticipated regulatory requirements
- Keeping up with competitors who are becoming more streamlined

Before the topic of people in governance is concluded, the issue of who will drive this standardization initiative must be addressed. Without key people to advocate for standards, champion the cause for governance, and provide support towards the goal of compliance, standardization initiatives eventually falter. The key positions that will serve as drivers for standards and their governance cannot be singularly identified across all clinical organizations. It will differ from company to company, but there are clear characteristics of an effective driver that can be spelled out and used as criteria to find those key people, whatever their role or department.

Effective drivers should:

- Hold a position at a high enough level in the organization to bridge gap between the strategic vision and operational know-how
- Demonstrate a working knowledge of standards & their use within the functional areas, but does not have to be a standards expert
- Have the ability to be a champion for standards in their functional area, which includes both spreading the standardization message down into their functional area and escalating standardization issues from the functional area upwards to management

STANDARDS

The engine that powers the standards governance framework are the actual standards themselves. They are the reusable pieces that are utilized to efficiently run clinical trials. As customization of these pieces increases each time a study is executed, the study execution time increases, the consumption of resources increases, and the consistency of the data from study to study is decreased. Examples of these reusable standard pieces include, but are not limited to:

- Data definition files
- eCRF screens
- Data extracts from an EDC system
- Utilities or programs that routinely check data for errors and inconsistencies
- Macros that execute repetitive code for a standard result
- Programs to generate analysis datasets or tabulations
- XML files that transfer data from one system to another

The goal of any standardization initiative should not be the ultra-strict, 100% compliance of a clinical organization to the standards. This breeds resentment and stifles creative thinking so necessary to clinical trials. Instead, a more appropriate target that inspires trust in standards governance would be the 80/20 rule:

- **80%**: Of the total content that a function delivers for a study, 80% should come from quick, efficient, reusable standards
- **20%**: The remaining 20% of content that a function delivers for a study should come from customized or newly developed standards

This 80/20 rule ensures that more time and resources can be spent on the operations that need creative and complex thinking, rather than on repetitive tasks that could easily be reduced by standardization. This is applicable regardless of whether the functional area is for collection, submission, clinical monitoring, or analysis and reporting.

Internal company standards exist in most clinical organizations, but it is the degree of standardization and the compliance in use of them that varies the most across the industry. It is not surprising that the most successful CDISC implementations usually occur in clinical organizations that have a relatively high level of standardization already in place and the necessary compliance.

Due to the complex nature of clinical trials, there will always be cases where divergence from the standard is necessary, if not vital. Distinct therapeutic areas (TA) have differing needs which may force the data to be slightly altered. A common example of that is in Oncology where disease related adverse events are considered disease progression and thus require additional data fields be collected. Another example is a vaccination trial where it is

imperative that the data for swelling or a rash around a vaccination site needs to be augmented with further data regarding location, size, and vaccination site number.

One method of managing these differing standards is to classify them into the following strata:

- **Global** – standards that apply across the entire clinical organization, typically for standard safety domains and standard questionnaires, with the expectation that all studies would use them
- **Therapeutic Area** – standards that address specific needs within a TA, perhaps for safety and/or efficacy, with the expectation that studies across a specific TA would use these consistently
- **Project** – standards that are developed more in response to an unmet need rather than a deviation from global or TA standards, typically for efficacy parameters of narrow focus, with the expectation that only studies within that specific project or brand would use them

In order for these three strata of standards to be an effective factor in meeting the 80/20 rule, the distribution of standards that are used for any clinical trial should be approximate 60% from the global standards level, 20% from the TA standards level, and 20% from the project-specific level. This ensures that close to 80% of the standards are used off-the-shelf, while only 20% require customization and development.

It is very common when going through the standardization process to allow the standards to be tool-specific, in that the names, structure, and function of the standards are driven by the tool they are used in. For instance, collection items that are named and structured for the needs of the specific EDC tool rather than aligned with CDASH standards. Not only will this obviously cause problems if a better EDC tool is later brought in-house, but this will make a CDISC implementation problematic while also limiting the use of these same collection items when exchanging data with external vendors.

For every single company, regardless of size, an implementation of CDISC standards will present some challenges. Sometimes these are challenges due to the existing systems and processes at that company, but sometimes implementation challenges are inherently due to the CDISC standards, considering their focus and structure are sometimes very different from existing industry practices.

This list below of implementation challenges are practical situations that are common throughout the industry, compiled through experiences gained from both the sponsor and external provider sides of the industry. It is advised that any time an organization spends discussing and deliberating on these issues during the early stages of CDISC implementation is time spent very wisely, for many of these will eventually appear later during the implementation process when goals, timelines, and demands are more urgent. They are not listed in any specific order, priority, or importance, as this will vary from company to company.

- For Findings class domains (VS, EG, etc.), is it better to implement these domains into collection as horizontal or vertical structures when doing a CDISC implementation?
- If SDTM mapping of collection data is necessary, are the standard CRFs in a stable state so as to avoid wasteful re-work of mappings at a later date?
- If SDTM mapping of collection data is necessary, where is the best location in the data lifecycle for it to occur (e.g.: part of EDC extraction, during ETL load into a clinical data warehouse, just prior to creation of analysis datasets, etc.)?
- Does SDTM experience exist in the EDC functional area? Are they able to contribute vital SDTM input into the mapping of collection data to SDTM?
- How are clinical comments currently collected? What are the needs of the clinical organization for comments in SDTM?
- Is it feasible for the clinical organization to follow industry best practices and implement a linear process for SDTM and ADaM (i.e.: collection to SDTM to ADaM)?
- Where does the data checking take place, and can it accommodate the new CDISC structures?
- When will it be possible to identify which small studies in the near future would be suitable for use as a pilot to demonstrate successful CDISC implementation?
- Where in the database(s) is the data needed to build Trial Design domains? Is our organization ready for Trial Design?
- What are the CDISC capabilities of current external vendors (e.g.: central labs, CROs, niche service providers, etc.)?
- Do any internal business guidelines exist that address the use of CDISC standards? Who has been responsible for this and who is most qualified to be for implementation?
- Will it be feasible to implement standards governance review early in the data development process?

- Does any standards governance group(s) currently exist in the organization? If so, will they be able to manage CDISC standards also?
- Are there physicians within the clinical organization who have some data expertise that could be utilized as part of the standards governance?
- Are there any current drug programs that by their very nature should remain outside of conversion to CDISC (e.g.: co-developed drugs with other companies, in-licensed drugs in late stage development, etc.)?
- Do current metrics exist on the execution of clinical trials by the organization as a whole? Do metrics exist for specific activities of the study (e.g.: EDC build, time span from database lock to analysis, etc.)?
- What will the template be for defining metadata? What attributes does the organization need the metadata to contain?
- How can SDTM and ADaM metadata be used to drive processes and systems that are both upstream and downstream in the clinical data lifecycle?
- How will the define.xml file be constructed? What function will be responsible for this?
- Do the organization's existing systems make use of XML technology in order to enhance system interoperability?
- What will the plan be for CDISC training for the organization, both at a high-level and model-level? How will the roles be identified that need practical training on specific CDISC models?

PROCESSES

Processes for standards governance are important to ensure consistent application of standards and quick turnaround for new standards requests, but this can be most fully realized only if they are put in place before the CDISC standards are in use. This is vital to creating that measure of trust by the organization regarding the use of standards, rather than being seen as a bureaucratic bottleneck that will make daily tasks more difficult.

The first construct that needs to be put in place for standards governance is a governance charter. This is a high-level document that defines the structure and organization of the governance framework, clarifies the role of governance to the clinical organization, spells out how governance will take place, and sets the scope of what will fall under the standards governance umbrella. To ensure that standards governance will be at a level that is appropriate for each clinical organization, input into this document must be solicited from upper management, functional leadership, and any pre-existing governance groups.

As with nearly every process in clinical trials, the Standard Operating Procedures (SOPs) is the foundation. They clearly lay out the procedures that will be followed, and provides a set of instructions s the level of expectations that the clinical organization can count on from standards governance. When good SOPs are written, good clinical practices are the result. Below are a few examples of topics for SOPs that could be a part of standards governance:

- Development of standards
- Maintenance of standards
- Request process for new or revised standards
- Waiver process
- Role of the data steward in governance
- Access control for standards storage

One additional piece of documentation that will be important in providing the consistent application of CDISC standards is a set of Business Guidelines, which are essentially a collection of the decisions and practices for use of CDISC standards. In a perfect world, this document would be finalized simultaneously with the start-up of standards governance, but in reality this knowledge and expertise only becomes fully realized in an organization as the standards are being implemented. This demands that a small but dynamic and proactive set of resources be dedicated early to this endeavor to incorporate all the decisions and practices as they are being defined as the implementation unfolds. For example, decisions on how to map TA-specific medical history data to SDTM consistently can be inserted into Business Guidelines early so that subsequent TAs can follow the same directive.

Scope of standards governance can be tricky and even slippery to determine. While the intent is often there to bring the entire clinical data lifecycle under standards governance from the beginning, it is often wise to institute scope in a pre-determined, chronological fashion. For example, CDISC expertise might only exist in a single functional area, and thus might be a good starting point for governance to address in the first year. This can be expanded to include upstream and downstream functional areas in the second year once they have been trained and their CDISC proficiency has taken root.

Functional areas are the most obvious application of scope, but other considerations of scope exist as well, such as documentation, standards storage, standards maintenance, metadata maintenance, and issue escalation. How far will the scope extend when it comes to processes such as who will perform hands-on standards development, who will communicate decisions on requests for standards, or who will determine access to the standards storage area?

There a few companies that have inserted a waiver process into their standards governance. A waiver process can be described for these purposes as a path that study teams or even therapeutic areas can follow in order to seek approval from standards governance for them not to be required to follow the standards. For those organizations that took a very lenient approach to the use of waivers for their study teams, it is no surprise that compliance to standards, and thus the benefits of standards, has suffered because of it. Alternatively, there are cases where a strict, yet thoughtful approach to the waiver process ensured compliance to the standards while simultaneously bringing a measure of respect and trust from the clinical study teams.

Before leaving the topic of standards governance processes, it is important to note that when questions of timing arise during development of processes, the smart process will be the one that forces the organization to think through issues earlier rather than later, thus avoiding time-consuming re-work later to correct errors from inaccurate or unstable input. For example, a governance SOP that defines the process for requesting new standards might dictate that requests for new standards can only be submitted by study teams with a finalized protocol. Not only does this ensure a stable source (protocol) for the EDC study build, but also forces the study team to think about and deliberate on which new data they need to collect and report on, rather than procrastinating that evaluation until the middle of the EDC study build or the onset of the analysis and reporting activities. Time-consuming re-work is the unnecessary result.

TECHNICAL SOLUTIONS

In many clinical organizations, the CDISC implementation process often focuses primarily on getting the standards into everyday use as quickly as possible, without any thought as to the technical aspects of executing that. The decisions on technical solutions are just as important to determining maximum benefit of standards as anything else. Having said that, it is important to keep in mind that technology should not drive the use of standards.

These technical applications can only be considered solutions for standards governance if they enable the people and processes to work efficiently and effectively. Systems that prevent or restrict those in standards governance from doing their jobs in a timely manner are not solutions, but merely obstacles.

While there are literally dozens and dozens of conceivable technological solutions to standards governance, there are three that experience has demonstrated that best maximize the benefits of standards. It is not the intent here to advocate for any specific application or vendor, only to provide solutions at a conceptual design level:

- Standards request system
- Clinical data repository (CDR)
- Metadata repository (MDR)

A **standards request system** serves as the face of the standards governance framework for many users in the clinical organization. It is the first point of contact in the interaction between study teams and governance regarding standards, usually involving a request for a new or revised standard. While this system need not be an expensive application with many bells and whistles, it must however provide quick, efficient functionality that promotes a comfort level among users that their requests are being addressed in a timely effective manner. The real benefits of this system though are not in the front-end, but in the back-end inner workings that allow the governance resources to efficiently log, track, and resolve the requests from the clinical organization quickly. Examples of functional requirements can include:

- Allow study teams to quickly submit requests for new or revised standards
- Provide associated entry points for user files that support standards requests
- Provide access to standards documentation and SOPs related to standards
- Assign unique identification number to each singular request
- Track requests on the basis of date, resolution, user, priority, CDISC model, etc.
- Enable governance resources to enter discussions, questions, and decisions about the request
- Connect the original request with subsequent governance discussions, questions, and decisions
- Provide users with access to the status of their request
- Provide reporting capabilities as to status of requests, grouping of requests, and governance metrics

A **clinical data repository** serves as a central hub for the proper data flow in a clinical organization. It can be implemented with any standard data model as its basis for extraction, transfer, and load (ETL), but if the normalized Janus model used by the FDA is chosen as the basic data structure, it aligns with the structure that will be required for submission data by the FDA. Early decisions on conceptual design need to address the question of what activities will take place in the CDR, both for data management and analysis and reporting. This will sharpen the focus of what functional requirements are needed. Examples of functional requirements for a CDR that supports standards governance can include:

- Repose all clinical data in a single standard centralized location
- Import, storage, and export of data in SDTM
- Export of SDTM with minimal select number of appropriate ADaM derivations
- Validated inbound ETL process
- Promote standardized, validated data import and export
- Ensure controlled read and write access to clinical data
- Support availability of clinical data across the organization
- Support the production of analysis datasets and clinical study reports
- Support data integration of integrated summaries (ISS/ISE)
- Maintain proper version control, data traceability & audit trails
- Promote business intelligence reporting
- Interoperability with clinical systems across the clinical data architecture
- Enterprise-class framework

A full-featured **metadata repository** provides the ability to house the standard metadata from the entire clinical data lifecycle, to deliver that metadata to systems across the clinical data lifecycle, and to provide standards governance workflows that support the governance process that develops and uses the standards. This technical support is needed to ensure that the new standard developed is usable across many studies without study-specific exemptions that slow down data flow, and that the standard is actually used by the study teams without customization. While a full-featured MDR would incorporate many if not all of the following examples of functional requirements, even a scaled-down MDR can be effective with some thoughtful discretion on which functional requirements are most important for the specific clinical organization's needs:

- Repose all the standards metadata in a single standard centralized location
- Repose study definition metadata
- Support study definition process per the standards
- Ensure controlled areas for standards at all levels (global, TA, project)
- Export standards metadata to metadata-driven systems and processes across the clinical data lifecycle
- Interoperability with clinical systems across the clinical data architecture
- Support standards development (Gov)
- Support standards maintenance (Gov)
- Generate and track of governance process workflows
- Maintain proper version control, data traceability & audit trails
- Enterprise-class framework

CONCLUSION

It is becoming a common view in the pharmaceutical industry that standards are a necessary aspect in the race to become more efficient in the execution of clinical trials, with the ultimate goals being cost savings, maximization of resources, and quality of regulatory submissions. However, there is a limited recognition of the important need for and substantial effort required for effective, thorough governance of standards by a definitive standards governance framework in order to reach those goals. Successful application of CDISC standards in clinical organizations can be a reality, provided that the proper up-front investment is made in regards to **people**, **standards**, **processes**, and **technical solutions**.

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