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Today's Standards Governance: Getting a Boost from Leveraging an MDR

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ABSTRACT

As sponsors meet the requirements regarding clinical data submissions in CDISC format as per the regulatory directives in Japan and the US, they still find it difficult to efficiently and effectively manage these standards internally. They struggle to avoid emerging as a bureaucratic bottleneck that makes daily tasks more difficult and pressure-filled across the organization. The standards metadata, both CDISC and sponsor-specific, that they labor so hard to manage become stagnant, resented artifacts that can't be leveraged properly to benefit their clinical teams. How can MDR technology help to address this?

Having spent time in standards governance on both sides of the pharmaceutical industry - sponsor companies and contract research organizations - I intend to explore weaving sound governance processes and fit-for-purpose technology together that facilitates fast, efficient change requests, ensures consistent application of the standards, and opens up the standards metadata for use across the clinical data lifecycle.

PUTTING GOVERNANCE PROCESS UNDER THE MICROSCOPE

For anyone who has tried to manage standards requests without a well-defined set of clinical processes, it is clear how quickly this oversight can become burdensome, frustrating, and ultimately impossible. Processes that focus on minimizing the number of required steps to approve and implement a standard can result in timely turnaround for new requests and quick, reproducible application of standards in trial execution. This intelligent framework of processes and activities inevitably will breed trust for the clinical teams that actually have to use standards and are tasked with setting up their studies in a standard way under tight timelines.

Across the industry, standards governance groups serve an important and integral part of a sponsor's adherence to the regulatory standards that it is committed to. At a high-level, these teams are charged with:

- Oversight for the development and maintenance of clinical data standards
- Ensuring that a standard is developed efficiently, consistently, and properly used across the clinical trials organization
- Insurance that maximum clinical process efficiency from a standards-based clinical data lifecycle is achievable

While sponsor organizations vary in the extent of tasks that they ask of their standards governance group, for the purposes of this paper we will focus on the 3 basic governance steps at the heart of every standards group's process:

1. **Request** – Submission of a request to the Standards Group explaining the need for a new standard or revision to an existing one. This could consist of multiple potential activities such as:
    - **Submittal** – Provision of a request in which customary information is relayed to the standards team that sufficiently explains the need for the new/revised standard.
    - **Triage** – Initial, perfunctory assessment of the request by a standards resource knowledgeable in multiple functional areas of the clinical data lifecycle in order to expedite the request to the appropriate person or team for action.
    - **Impact Analysis** – Electronic appraisal of the revision upon existing standards, often reaching across the clinical data lifecycle and/or to the study level.
    - **Evaluation** – More extensive investigation into the request as appropriate, often by a group of standards experts, data stewards, or therapeutic area specialists.
    - **Escalation** – In rare circumstances, a request can have such a broad impact or be too controversial for the standards team to reach a sensible decision, and thus require the decision-making to occur at a level of higher management.
    - **Waiver** – Again in rare circumstances, the standards team may grant a waiver for a clinical team to use non-standard structures and representations in the face of immediate, major safety or financial considerations.
2. **Develop** – Leveraging the decisions and information from the Request stage to tangibly create or modify the metadata that describes the standard. This could consist of:
    - **Metadata Definition** – Development of the metadata that defines the standard by standards resources experienced in metadata curation, sometimes including expertise in specific areas of the standards or therapeutic areas.
    - **Review** – Peer review of the newly created or modified standards metadata to ensure that it conforms to the intent and decision of the request and is compliant to any regulatory restrictions that governs it.
    - **Operational Representation** – Creation of the representation of the standards metadata that will be used operationally within functional areas, such as standard eCRFs, standard dataset structures, and standard macros.
3. **Approve** – The completion of the governance process in readying the decision of the request for general consumption by the larger clinical organization. Potential activities could include:
    - **Promotion** – Final approval and movement of the standards metadata from a standards development area into a locked down production area for viewing and usage of the standards.
    - **Classification** – Identification and documentation of any distinct strata or division of the standards based on therapeutic area, compound, project, etc., along with the necessary access considerations.
    - **Export** – Delivery of the standards metadata from the centralized MDR to clinical systems across the clinical data lifecycle for usage in performing their activities upon the clinical data in a standardized, conformant manner.

The standards resources, the actual operatives within these governance processes, need well-defined roles (and appropriate training) to ensure the successful application of standards within an organization is achieved. The constructive structure and relationships of these standards governance roles can make or break the governance process. Below is an example of a such a set of roles.

Requestor

- Well-informed messenger of the business need from the study team to the standards group
- Physically submits the request into the system, supplying all necessary information
- Reviews the standards team output of the request if needed

Request Triage

- Performs initial assessment on the request to expedite processing
- Ensures completeness of request and communicates with Requestor
- Routes the request to a Developer if appropriate
- Escalates the request if necessary

Standards Committee

- Thoroughly evaluates the request in context of regulatory guidance and existing standards
- Provides cross-functional consideration and input into the request
- Determines outcome and approval for the request

Metadata Developer

- Develops the metadata that defines the standard according to
- Provides subject matter expertise into development

Peer Reviewer

- Reviews the developed standards metadata
- Determines readiness of developed standard for implementation

While clinical processes are necessary to approve requests, maintain standards, and utilize standards, they can also be considered burdensome and frustrating for the clinical resources that work within them. Paying attention to this frustration when developing and implementing these standards governance processes can help mitigate potential obstacles down the road. In particular, focusing on timely turnaround for new requests and quick, reproducible application of standards in trial execution will breed a significant measure of trust by the clinical organization regarding the use of standards.

The standards governance teams that strive for positive outcomes with standards at their respective sponsor companies can sometimes experience challenges in their efforts. Some of these are inherent in the dynamics of the unending "standards vs innovation" debate within their clinical organizations, while others can be due to the differing priorities and unhealthy choices made within the clinical processes surrounding the clinical data flow. Regardless of the source of the "pain point", sensible governance process design can help alleviate the pain of situations such as:

- Low reusability of standards because there is frequent clinical team insistence upon using "one-off" structures due to specific exceptions for their study
- The implementation of standards for a study was singularly tied to the First Patient In date without regard for the length of time needed to develop the new or modified standards
- When determining s study's need for new or modified standards, a clinical team uses an unstable draft protocol as the origin, thus facilitating much re-work in the development of the standards and the testing of their representations such as eCRFs
- Partially developed standards were released for use before approval and thus considered "at risk"
- New standards development processes were not correctly sequenced among existing clinical execution processes, such as the deadline for submission of standards requests scheduled to occur after the UAT for the eCRF build

A clinical trial can simply be boiled down to the practice of taking a clinical hypothesis from theory to result. However, it is a complex undertaking that requires a mixture of standardization and innovation to effectively and efficiently produce those results. The standardization yields efficiency (and thus cost reduction), while the innovation yields effective and precise results (and thus regulatory approvals). Balancing these 2 components in a sponsor's clinical processes is critical if they are to deliver successful submissions that are regulatory-compliant and also obtain faster time-to-market for their products.

WHAT CAN THE TECHNOLOGY DO FOR YOU?

Sponsor organizations have recognized that CDISC standards and the CDISC SHARE metadata repository have opened the door to opportunities for implementing standards-based, metadata-driven processing. But how? What are the challenges that need to be tackled to have your standards metadata support, drive, and ultimately quicken your clinical data flow? In the end, everyone desires more efficient methods to produce their critical regulatory compliant deliverables. However, the often-disregarded factor in reaching this goal is the dependency on a technology solution that serves as both the central source of truth for their standards metadata and the integrated dispersal mechanism that distributes the standards for use across the lifecycle: the metadata repository (MDR).

Across the industry there exists a broad range of practices on how sponsor organizations are managing their metadata. It is still common for metadata to be stored and managed in what has been labeled as a "first-generation metadata repository": Excel spreadsheets. While this tool does provide a favorable comfort level to clinical staff, it is limited with regards to the operational maintenance, elemental-level versioning, and effective utilization. Sponsors on the leading edge in the industry are implementing technology solutions that allow their standards governance organizations to consolidate their metadata in a central location, to efficiently manage it according to company guidelines, and finally to deliver it for use by their clinical systems and processes to consistently produce regulatory-compliant data.

At a high level, several business requirements stand out as critical factors for a successful MDR implementation. These logically fall into 4 buckets as described below:

Oversight

- Centralized single source of truth for the standards that is depended upon by the clinical organization to meet the needs of regulatory requirements
- Logging and subsequent tracking of standards requests that demonstrate transparency to the clinical organization at large and breeds collaborative trust with the clinical teams
- Administrative ability to manage access to the standards metadata based on need, role, job, or group

Control

- Rigorous control of the standards metadata that the clinical teams can depend on
- Electronic relationships that tie standards requests to the actual standards metadata that define the content asked for in the request
- Provide an impact analysis that reveals the impact that a change would have upon existing standards
- Well-defined, yet adaptable versioning of standards metadata that enables clinical teams to choose from multiple versions accepted by regulatory authorities
- Logical electronic relationships between separate metadata that defines the structure of the standard, such as a variable related to a codelist which is also related to the values within it
- Auditable metadata that can demonstrate the who/where/when of changes and the traceability of results back to sources

Workflow

- Electronic governance activities prescribed and adhered to within the MDR tool, effectively moving a request from submittal to approval without relying on the standards team to manage the workflow manually
- Generation of meaningful metrics that demonstrate the performance of the standards governance process but also adherence to standards across the clinical organization

Action

- Central repository of standards for the clinical teams to search, explore, and utilize the standards most appropriate for their trials
- Export of standards metadata to clinical systems across the clinical data lifecycle that enables efficient, standardized metadata-driven processes of the clinical data flow

With the rise of CDISC standards and the CDISC SHARE metadata repository, the opportunities for implementing standards-based, metadata-driven processing are increasing too. Standards metadata, be it from SDTM, ADaM, or sponsor-specific sources, can serve as the consistent consumable for processes that are part of the clinical data lifecycle, with the goal being more efficient mechanisms to produce regulatory compliant deliverables. The often-overlooked factor in leveraging metadata in this fashion is that the benefits are highly dependent on this metadata being centrally and effectively managed before distribution across the lifecycle.

A “Next Generation MDR” that centrally manages and governs the metadata within an interactive tool and a stable metadata model delivers metadata that can be reliably consumed by clinical processes and systems. The centralized governance facilitated by this level of MDR yields adherence to standards across the organization, and thus consistent data meaning and easier integration of data for analysis and submission purposes. The MDR that also incorporates governance workflows within the tool itself, can also bring about shorter, more transparent standards development timeframes that beget increasing trust in the standards governance effort across the clinical groups.

Once a sponsor’s metadata is centrally located and managed within an MDR, several things suddenly become possible:

- Consistent usage of the same metadata for multiple uses by multiple users
- Relationships between metadata can be identified and utilized via the inherited electronic linkages within the MDR, regardless of taxonomy or structure
- Efficient standards governance and maintenance of metadata according to SOP-compliant workflows and approvals
- Faster, better informed standards decisions can be made based on thorough impact analysis results
- Grouping and binding together relevant data elements through the application of medical concepts to metadata under a single medical meaning, ensuring clarity of data meaning across the clinical data lifecycle

- Clinical systems upstream and downstream use the same related standards metadata and deliver consistent, compliant data meaning as a result of the export of centrally-managed standards metadata across the clinical data lifecycle

BLENDING THE PROCESS AND TECHNOLOGY TOGETHER

So, the governance processes are agreed upon and a metadata repository has been put in place. What now? How can these 2 separate pieces be brought together to remove the barriers to efficient study set-up and execution? Where are the appropriate connection points that breed compliance without also causing strife with the clinical teams? Without becoming tool-driven, what are the challenges in determining which governance processes need to be represented in the tool, and which might need redesign to better function in a more effective and timely manner?

It cannot be stated clear enough that getting the process right before MDR implementation is a key building block towards effective standards governance within the tool. A simple yet purposeful, tool-agnostic design of the governance process enables the standards team to quickly incorporate the tool into their everyday practices without feeling bogged down with additional bureaucracy. Simple process design leads to efficient workflows. In my experience, too many standards governance groups attempt to complicate and overstretch their process in order to fully utilize the full functionality of the tool. “If it can do it, then let’s do it.” However, this invariably leads to convoluted workflows that unnecessarily burden the standards team members while confusing and frustrating the clinical teams that view them as bureaucratic formalities and the “Standards Police.”

Not every single little governance task or activity needs to be incorporated as an electronic workflow within the MDR. In some cases, trying fit the proverbial square peg in to the round hole causes more problems than it is worth. For example, trying to wedge an approval or review from a clinical operations resource into an electronic task within the MDR can be burdensome and inefficient if that resource has no other reason from being in the MDR. A needless bottleneck could very easily form, eroding the efficiencies that the tool could bring. A more reasoned approach might exclude this clinical operations approval from the electronic workflow and instead prescribe a standards team member to directly interact with the clinical operations resource to obtain the approval and then enter the approval verbiage into the tool themselves to serve as the documented, auditable response.

The exercise of implementing governance processes into electronic workflows provides the opportunity for process improvement. For instance, perhaps the standards team is overwhelmed with requests for the highly specific details for the eCRF builds because the Governance SOP states that it falls within the scope of responsibility of the standards team. This has heaped enormous amounts of work on the team without the level of resourcing needed to address it properly. In this resource-constrained environment (not uncommon among today’s sponsors), perhaps it would be more efficient to have the standards team only manage the most important features of the eCRF as standards, and allow the study build developers to make the remainder of the decisions on the details of the eCRF builds.

An MDR with electronic workflows provides the opportunity to connect the standards decision-makers with the standards developers, a very difficult proposition for standards teams not supported by technology. In the past, the standards team members had to maintain logs in spreadsheets to track and notify developers of their work in developing the standards metadata. Not to mention, there was absolutely no connection between this tracking and the actual metadata in development. An MDR provides this, basically through the electronic linkage between the standards request, the associated decisions, the assignment of the developer, and actual standards metadata that defines the content in the request. All contained in one centralized tool that is entirely auditable and transparent.

Standards governance processes need to be designed, implemented, and executed with an eye towards their “customer”, the clinical teams. The MDR can seem like a monolithic obstacle to clinical team members who are just trying to do their jobs and are not the most data-savvy. Care must be taken by the standards team to engage the clinical teams with cooperative processes and interfaces that make the use of standards a positive activity where the standards team and the clinical teams are collaborating, not clashing. For example, the clinical process of extracting from the protocol the standards (existing and new) that are needed for a study sometimes turns antagonistic when the back and forth exchanges with the standards team seem harsh and punitive from afar. A more supportive tactic might be to have the standards team member present in the clinical team meeting to dynamically helps them perform their assessment of the protocol with the MDR open in front of the meeting. This would not only save time, but also guide the clinical team on the necessary information to fill out he request while serving as an opportunity for the standards team member to spread the “standards message” in a positive and easily embraceable manner.

While the standards themselves are the vital, reusable components that promise to yield benefits to the sponsor (decreased run-times, consistent data meaning, shorter regulatory review times), unchecked customization of these

standards will do the opposite (increase study execution time, increase consumption of resources, erode data consistency within a submission). Astute standards governance processes and the associated messaging around reasonable compliance targets inspires trust in standards governance, especially when a sponsor's standards governance is early on the learning curve with an MDR. It can produce a favorable mindset of "pulling down" the standards rather than having the standards be "pushed down" onto study teams from above.

CONCLUSION

There exists no fairy-tale path of standards governance that every sponsor should follow. Far too much variability between organizations persists to ever enable a single governance solution to be a one-size-fits-all method. Amidst that irregularity is the opportunity for sponsors to invest the time and effort to cleverly weave the process and technology together to yield a solution that helps standards governance groups and clinical teams meet tight timelines as partners. The remarkable benefit is the harmony that results between standards governance and the clinical teams, based on a collaborative rather than antagonistic relationship.

REFERENCES

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