Spurring Efficient Drug Development Through a Processes Management Framework

Currently in the clinical development ecosystem, industry guidance for quality is fragmented across multiple documents from multiple sources. Although quality systems exist in other industries, there was not yet an industry-wide framework for Clinical Quality Management that aims to improve performance in complex clinical development specific environments. As a result, organizations have historically struggled to deliver promising treatments to patients without delay.

This challenge led TransCelerate's Quality Management System (QMS) Initiative to develop a vision and outline for a clinical QMS (cQMS) conceptual framework, which provides support to allow companies to develop an integrated and flexible system through which organizations can systematically define quality objectives linked to their broader strategic goals. Three years later, at the start of in 2019, TransCelerate took an important step to help clinical organizations implement a primary element of an effective cQMS: clearly defined, documented and managed processes.

In this article, we sat down with Lora Lee Zoller-Neuner, Senior Quality Document Manager, Clinical Quality Systems at Sanofi, to discuss why a Process Management Framework is fundamental to ensure the efficient delivery of clinical development programs, enhance quality and productivity, and deliver needed treatments to patients faster.

Development and distribution of medicines on a global scale has served to significantly benefit many, but has also added certain complexities. The need for clear and consistent processes, associated documentation, and training to help staff execute these processes is becoming increasingly important for the effective delivery of medicines worldwide, while safeguarding patient safety.

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To help address this, TransCelerate’s QMS Initiative published a new Therapeutic Innovation and Regulatory Science (TIRS) manuscript in January 2019, titled, “Process Management Framework: Guidance to Successful Implementation of Processes in Clinical Development.” The intent of the manuscript, notes Zoller-Neuner, “was to create a model framework for process mapping, risk-based process documentation, and training to assist clinical development organizations in understanding the basic components of process management.” It describes how companies can begin managing their cQMS to certify that processes are identified, defined and implemented in a clear and uniform way.

This is a fundamental shift from the traditional (function-driven) approach to an end-to-end process (customer-driven approach). In a traditional approach, organizations are often siloed since they are structured and measured by individual department goals and objectives. The executive leaders operate as a team, but are dedicated to sometimes singular functions. Comparatively, in a customer-driven approach, organizations concentrate on cross-functional process capabilities and serving the needs of their customers. “These organizations realize that products and services for customers aren’t produced by departments or functions, but by processes that span across functions. This is important to our industry, since our central focus is on the patient,” says Zoller-Neuner.

To further aid clinical organizations in the implementation of the process framework, TransCelerate also developed the “Toolkit for Implementing Processes.” The interactive toolkit provides specific tools to support clinical organizations with the application of the concepts described in the Process Management Framework manuscript. It takes the user through six main steps, as seen in Figure 1.

Overall, the toolkit helps sponsors identify clear and consistent end-to-end (E2E) processes, ensure well-defined documentation with the appropriate level of detail and controls to mitigate risk, and implement an optimal learning approach to drive business deliverables and performance.

“This is a ‘must have’ in today’s landscape,” adds Zoller-Neuner. “It allows the Sponsor, Service Providers, Regulatory Authorities and Investigators to better understand the key activities needed to get drugs approved in a compliant and efficient manner, which ultimately benefits our most important customer—the patient.”

These resources have also created tangible value for stakeholders. In fact, according to a recent TransCelerate Member Company case study, “key elements from the QMS Process Management manuscript and Toolkit for Implementing Processes were used to simplify and harmonize multiple documents into one global process. This helped to reduce the number of quality documents by 83%.”

While impressive and helpful progress has been made in process management, implementation for many companies is still ongoing and may take many years to complete. Moreover, as the clinical trial ecosystem continues to evolve, and additional process complexities inevitably arise, there will be a need to provide further support for members and the industry at large.

“That’s why,” Zoller-Neuner highlights, “enabling adoption, sharing key learnings and finding new and innovative ways to add value to all stakeholders in this space will be a key focus for the QMS Initiative, and TransCelerate, as we look ahead.”

Figure 1

1. **Identify High Level Process**
   Identify all steps of an end to end (E2E) process by mapping core processes, sub-processes, and enabling processes.

2. **Map & Model Process**
   Capture the SIPOC metadata (key process roles, inputs, outputs, interdependencies, and related documentation).

3. **Determine Process Risk**

4. **Documentation Strategy**
   Determine which processes require controlled documentation vs. managed information based on the process risk score.

5. **Optimal Learning Approach**
   Assess the Critical to Quality (CTQ) process and documentation to develop the Learning Plan for controlled documentation vs. managed information.

6. **Management Review**
   Evaluate process health performance as part of Management Review by defining line of sight goals, metrics, roles, frequency and forum.

For additional supportive resources, check out this list of Process Scenarios that offer practical examples for how organizations can apply the Process Management Framework. You can also visit TransCelerate’s Quality Management System Initiative website to learn more.
It goes without saying that it’s critical and patient advocates? track: here are three questions they can ask design and execution of clinical trials, integrate the patient’s voice into the sponsors continue to try and better collaborative efforts with patients. As sponsors can kick-start their own learned a few takeaways on how stakeholders in the drug development regulators and all other major side by side with patients, sponsors, care and even guidances for patients on how they can become partnership ready. We cite several of the most helpful resources in our Patient Protocol Engagement Toolkit User Guide.

Furthermore, we took some time to connect with regulators, which included face-to-face meetings with the FDA. Current regulation, such as the 21st Century Cures Act, which was designed to expediate innovation and advances to patients who need them, demonstrate that patients are also at the forefront of regulators’ minds. Regulators have also started to realize a need for guidance documents on how to include patient voices in trials, and as sponsors establish their own engagement plans, it’s advantageous to be sure their goals align with regulations such as the Cures Act or the European Union’s General Data Protection Regulation (GDPR).

3. Have I prioritized building long-term trust?

To truly produce meaningful tools for patients, a level of shared alignment, clarity and joint respect between all invested groups is imperative. Sponsors must assert each stakeholder is linked by the common goal: bettering the patient experience. Only once that link is established can sponsors then take the necessary steps to improve transparency by assigning specific roles and responsibilities among stakeholders. Internal processes can be aligned, and points of contact established. It’s our hope that during this process, a greater level of trust is developed leading to increased mutual respect. This can then lead to longstanding continuity of relationships and elevated levels of responsiveness across stakeholders.

It is true that sponsors stand to gain from better patient engagement. Improved engagement has the potential to increase patient participation, decrease attrition rates and ultimately advance the delivery of medicines to market. Ultimately, however, we are obligated to keep the end goal in sight: to decrease patient burdens, integrate their perspective into drug development, and boost patient satisfaction. Only with this clear objective in mind, will we be able to continue making strides in incorporating the patient voice into the design and implementation of clinical trials.
Within the biopharmaceutical industry, the topic of Protocol Deviations (PD) is met with a wince. Currently, clinical research sponsors struggle to interpret certain elements of ICH E3 and other associated guidelines related to PD which has led to both over and under interpretation of deviations. These challenges are echoed by sites who report receiving conflicting instructions for the same scenarios. This ambiguity has led to an opportunity to share ideas and experiences about how to make improvements in this area.

In this Spotlight, we sat down with Catherine Stewart and Laura Galuchie, co-leads of TransCelerate’s PD Initiative to discuss the value TransCelerate's PD Initiative delivers to the biopharmaceutical industry.

With feedback from the FDA, the Protocol Deviations team has proposed a revised definition of important protocol deviations and developed a toolkit.

Q: Catherine, could you share with our readers a little background on TransCelerate’s Protocol Deviations Initiative and why an initiative like PD is necessary?

A: In response to a survey of member companies, we learned that there was variability, sometimes across trial teams, when interpreting the multiple guidance documents on this topic. This was creating challenges in the identification, collection and reporting of deviations. Both overreporting and under reporting can influence the reliability of the study results and patient safety signals. These discrepancies have created roadblocks to the effective delivery of new medicines.

So, we took this to TransCelerate and said, “We have an opportunity with PD to come up with an output that will identify and potentially drive best practices within Member Companies and with key stakeholders. More importantly, we can better enable sites to support clinical trial participants by reducing ambiguities and inefficiencies where possible.”

Q: Laura, what benefits does the Protocol Deviations Initiative provide to sites and sponsors?

A: The confusion regarding the regulatory discrepancy makes things more difficult for both sites and sponsors to be proactive in their approach to reduce protocol deviations in the first place.

A main benefit for sites is reduced burden in protocol deviation definitions and associated site processes for management, reducing confusion and increasing speed of identifying important violations. This may allow for an increase in time with study participants.

Sponsors may also feel a reduced burden through increased consistency in protocol deviation planning, processing, analysis and reporting mechanisms. Applying ICH E3 R2 concepts of risk-based approaches to protocol deviation management processes may support more rapid identification of situations which could directly impact patient safety, reliability of study data, human subject’s protections and/or data quality.

The PD Initiative has been dedicated to creating a sustainable framework that helps sites and sponsors in developing their own methods for consistently interpreting “important” deviations across all levels of their organization, leading to reduced burden for sites and sponsors, better reporting of issues that matter and methods to apply a risk-based approach to the management of PD.

Q: Catherine, where can regulatory authorities expect to see greatest value?

A: We want to focus on what impacts the safety of the subjects in our studies, what influences the integrity of the data we collect, and what is important to regulators when they look at our studies and try to evaluate the data. Our mission is to evoke the following questions: does this study do what it intends, is the data to be trusted, and are the results meaningful?

At the same time, we want to satisfy regulator requests for documentation and a process for risk reduction that will result in fewer issues.

Regulators will experience decreased protocol deviations reporting “noise” and deviation reporting with an increased focus on what really matters, i.e., deviations associated with patient safety, reliability of study data, protections for human subjects and data quality.

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There’s a lot of opportunity to improve consistency and transparency with what we say and share with sites and IRBs. Adoption of the PD toolkit could really help sites, and other research stakeholders, focus on clarifying their messaging and emphasizing what is critically important.

Q: Laura, can you tell us what is included within the PD Management Toolkit?

A: The Management Toolkit consists of a Protocol Deviations Process Guide which is a proposed framework describing flexible Protocol Deviations management approaches, elements for consideration based upon proposed interpretation of the ICH E3 definition for important protocol deviations and other associated PD Guidance with links to the PD Process. We also developed a Protocol Deviations Map of the proposed PD management process for both important and non-important deviations and feedback loops. Lastly, the toolkit also includes a Protocol Deviations Assessment Plan which serves as a template to assist in the identification and documentation of protocol specific important deviations.

Download the toolkit here: https://transceleratebiopharmainc.com/protocol-deviations-initiative-assets/

Mark Your Calendars

TransCelerate leaders and Member Companies are invited to participate and present at many biopharmaceutical research industry conferences and meetings across the globe to provide a perspective on industry challenges and clinical trial issues. Take a peek at a few places we will be presenting this year. For detailed information on speaker presentations, visit the events page on the TransCelerate website.

- Patients as Partners
  January 27-28, 2020
  London, United Kingdom

- SCRS EU
  March 9-10, 2020
  Lisbon, Portugal

- DIA Europe
  March 17-19, 2020
  Brussels, Belgium

- Eyeforpharma Barcelona
  March 31-April 2
  Barcelona, Spain

- Eyeforpharma Philadelphia
  April 15-16
  Philadelphia, United States
Your Perspectives

Your curiosity is important to us. In this section, we’ll address questions from Academia, Sites, Technology Companies and CROs.

Q: I am having problems with the complexity and variability of my study protocols, is this something TransCelerate is working on?

A: Yes! In 2015, the first version of the Common Protocol Template (CPT) was released and it has been evolving ever since. The CPT is a harmonized and streamlined approach to the format and content of clinical trial protocols.

The CPT includes a common structure, proposed model text, and regulator-accepted endpoint definitions for use across protocols with little to no editing at the discretion of the user. This year, we created publicly available eTemplates for the Common Statistical Analysis Plan (SAP) which provides a common layout and model content for SAP documentation and the Common Clinical Study Report (CSR) which aims to provide a lean, common, and streamlined structure to report data (no benefit/risk interpretation).

At present the templates are designed to be human-readable but are intended to prepare for a future state with machine driven protocols and metadata driven processes.

These assets are now part of our Clinical Content & Reuse Initiative. We are also soliciting feedback on the protocols.

Q. What is TransCelerate doing to speed up the time between protocol completion and study start-up?

A: Currently, there exists an average lag time of four months between protocol completion and study start. Furthermore, third-party conversion of data to SDTM lengthens cycle time and presents limits for traceability and re-use. Finally, working in a document-based environment results in significant manual duplication of effort.

One of our initiatives, Digital Data Flow (DDF), aims to drug development process from a current state of manual, study start-up asset creation (i.e. Case Report Forms, Procedure Manuals, Statistical Analysis Plans and Schedule of Activities) to a future state of fully-automated, dynamic, study start-up readiness via an open-sourced, vendor-agnostic technical solution that will reduce cycle times and improve data quality for sponsors, third-party providers, sites and regulators.

We recently hosted a webinar on this topic and are hosting a hackathon in Spring 2020 to bring this initiative to life.
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Check out our top social mentions from the last three months

@OutsourcPharma: @transcelerate and its subsidiary BioCelerate launch new initiatives aimed at enhancing the research and development ecosystem, progressing its mission of getting innovative therapies to patients faster, says EVP. https://bit.ly/2Oiwoii

@transcelerate: Don’t miss our EVP Janice Chang’s article on why putting patients first matters and how cross-industry partnership & collaborative decision-making is the only way forward! Click to read: bit.ly/2Z6uF6h clinicaltrials clinicalresearch biopharma pic.twitter.com/2LcPwCz5k0

@transcelerate: Hot off the press—our latest edition of Pulse on Progress is LIVE! From newly published papers to brand new initiatives, this update has it all. Click to read right now: http://bit.ly/2ZjBNLY #TheMoreYouKnow #Innovate4Change

@ClinTrials365: How could eConsent and the “Clinical Trial Registry of the Future” revolutionize patient engagement? We spoke to @transcelerate to find out http://spr.ly/6017EAnNU #mhealth #healthcare #tech

@transcelerate: The use of digitaltechnologies is on the rise in clinicaltrials and TransCelerate’s Carrie Guglielmo and @ucb_news’s Laura Comer are tackling the necessity for continued eConsent implementation in this must-read article: http://bit.ly/2meUY7F

@transcelerate: @OutsourcPharma: @transcelerate and its subsidiary BioCelerate launch new initiatives aimed at enhancing the research and development ecosystem, progressing its mission of getting innovative therapies to patients faster, says EVP. http://bit.ly/2Oiwoii

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