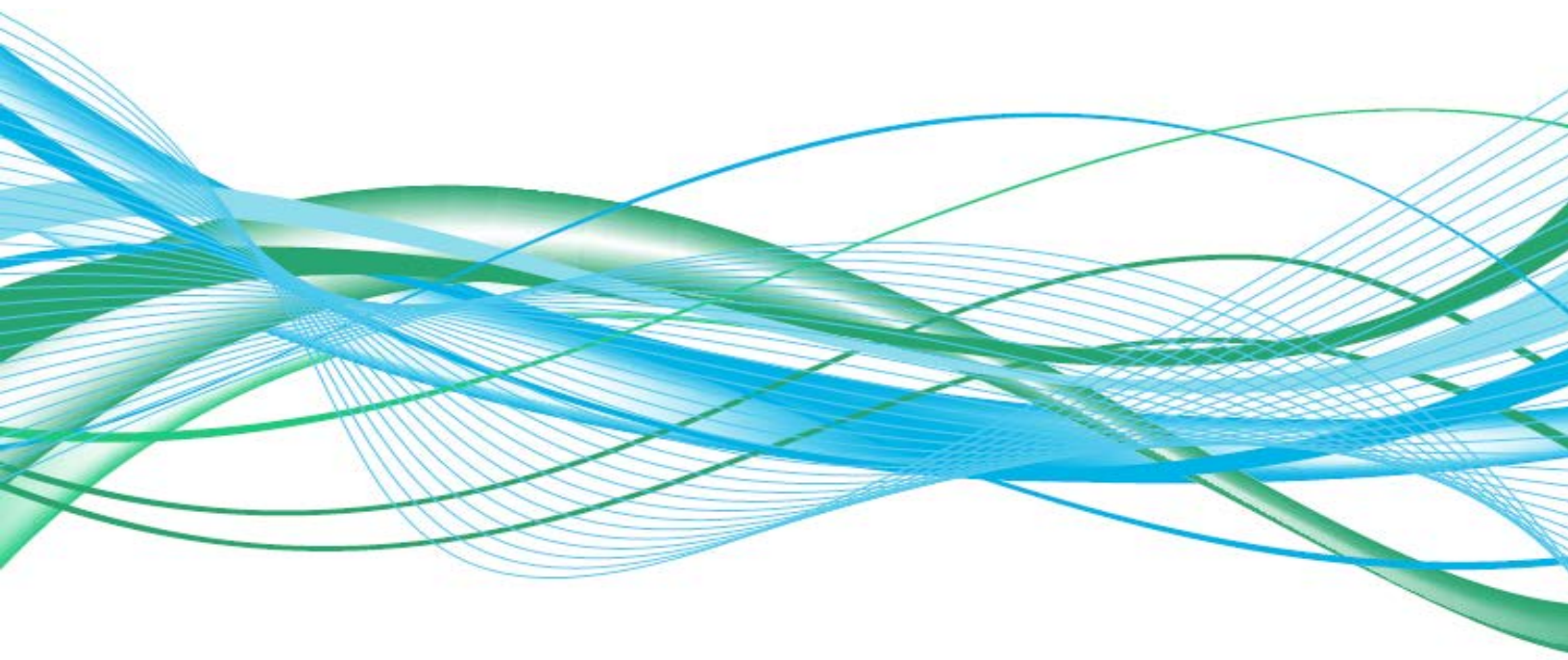
WHITE PAPER

Clinical Trial Transparency

The Technology Imperative



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MAKING THE COMPLEX SIMPLE

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Executive Summary

Clinical Trial Transparency is a broad term that covers the sharing and use of clinical trial data across global registries as well as other sponsored channels. Proponents of greater clinical trial transparency cite improved patient care, research advances and overall better healthcare systems as benefits. Sponsor companies are taking varying approaches to transparency, driven in large part by clinical trial registration and reporting regulations.

The combined effects of increasing complexity, shorter deadlines, and continued demands for greater transparency have created a perfect storm for clinical trial sponsors. From this storm, the technology imperative has emerged. As sponsors move forward in their clinical development activities, accurate and timely disclosure and results reporting is becoming a greater priority. Sponsors of all sizes are looking to mitigate non-compliance risks while improving efficiencies, with technology and repeatable processes playing a key role in this strategy.

This paper looks at clinical trial transparency and the driving forces behind it to better understand the role of technology in the execution of a solid clinical trial transparency policy.

Business Challenge

Clinical trial disclosure teams continue to work in a constantly evolving environment where they must plan for tomorrow's requirements today.

Evolving Requirements

Monitoring changing regulatory requirements and emerging registries with their unique requirements is a significant task. In addition, existing registries are continuously updating their technical requirements and disclosure rules. Sometimes new data is required or optional data becomes mandatory, sometimes the scope of disclosure increases, and sometimes the reporting deadlines shift. These changes can happen simultaneously in just one registry. In the case of U.S. registry, clinicaltrials.gov and the EU registry, EudraCT, new legislation promises additional data requirements combined with shorter reporting timeframes. Interpretation and implementation

of these new requirements is left up to the sponsor. Tracking and managing requirements such as these becomes an onerous task that simply never ends.

Compliance Risks and Implications

Sponsors continue to worry about compliance risks. Potential penalties in the U.S. include an initial $10,000 fine for non-compliance. The sponsor is then given 30 days to remediate the issue or face additional fines of $10,000 per day/per violation until the problem is resolved. A notice of non-compliance may also be posted on clinicaltrials.gov, which can affect the ability to enroll participants and damage a company's reputation. Additionally, the sponsor faces the loss of federal grant funding, as well as other civil and potential criminal penalties. Though the FDA has yet to enforce these penalties, inspections are likely to start following the implementation of the new disclosure rules in early 2017.

Risks are not only limited to direct penalties. Public perception of an organization that is seen as "trying to beat the system" can impact stock prices and have a far greater impact on the company's position in the marketplace. Even when a company inadvertently fails to disclose, the perception may be that the company is hiding something or that operational procedures are subpar. In the life sciences arena where credentials and trust are critical to attaining revenue goals, the public relations problem associated with non-compliance can create a rapid downward spiral.

Calls for Greater Transparency

Stakeholders from around the world are calling for greater clinical trial transparency. Initiatives such as AllTrials seek greater transparency than what is currently required by law. In fact, in July 2015, AllTrials brought together a collective of 85 pension funds and asset managers representing €3.5 trillion, calling on pharmaceutical companies to share their plans to register and report results for past, present and future clinical trials. These investors see greater transparency as adding to their due diligence efforts in providing a more accurate picture of an organization's current position in the market. This act represented the first time that transparency was directly tied to investment money. Previously, disclosure regulations were seen primarily as a compliance

concern with known financial risks in the form of potential fines levied by regulatory authorities. The addition of investment bankers into the transparency discussion adds the potential for a risk that is only quantifiable once it has already occurred and it may be too late to address.

The ICMJE (International Committee of Medical Journal Editors) adopted the WHO (World Health Organization) definition of clinical trials in 2007. This expanded definition requires registration of a clinical trial if the sponsor wishes to seek publication in an ICMJE journal. In this manner, the ICMJE is leveraging a key marketing tool that aids sponsors in accessing clinicians, consumers, and policy makers to motivate them toward greater transparency.

In addition to these organizations, others like Bioethics International are evaluating sponsor registration and results reporting to quantify their level of transparency. The COMPARE Project from the Centre for Evidence Based Medicine at Oxford University is monitoring clinical trials for switched outcomes. These organizations are representative of the increased scrutiny in the public realm that sponsors must undergo regarding their transparency efforts.

Technology Imperative

All of the activities and initiatives listed above are putting pressure on clinical trial sponsors to demonstrate a firm control of disclosure activities and "go above and beyond" in their approach to clinical trial transparency. In the current environment, just meeting the requirements of existing regulations is a daunting task. As we add new data requirements, shorter timelines and increased scrutiny, the need to employ an enabling technology is very clear.

Clinical trial transparency is an arena where efficiency and compliance must co-exist. One cannot be prioritized at the expense of the other. Efficiency will be required for compliance, particularly as complexity continues to grow. In 2016, the Tufts Center for the Study of Drug Development analyzed the costs to develop and gain marketing approval for a new drug and estimated the cost as $2.55 billion.[1] Automation of complex, time consuming, and costly tasks that reduce resource

[1] http://csdd.tufts.edu/news/complete_story/tufts_csdd_rd_cost_study_now_published

requirements, save time, and lead to greater compliance will continue to be key components to a sound approach. Disclosure systems provide the visibility necessary to manage global disclosure reliably and assure ongoing compliance with evolving requirements.

At its core, clinical trial disclosure is a content management challenge. Disclosure content typically goes through a rigorous review and approval process. As that process is occurring, some of the data changes, which may require an update or modification to portions of the disclosure content. And so the version control challenge begins. As the data moves through review processes the sponsor must ensure that the "correct version" is provided to all output channels, including registries, company sponsored website, collaboration sites, etc. This scenario can be likened to a stone being dropped in a pond and the resulting ripple effect. Sponsors are constantly trying to capture that ripple.

In the disclosure process, there are great opportunities to increase accuracy and decrease risks through automation. These include:

- Managing disclosure content in a single source system that can be accessed by team members for reuse around the world. This ensures harmonized disclosure across registries and increases the visibility into cross-functional disclosure processes.
- Integration into source systems to automate data entry and maintenance tasks, increasing efficiency and lowering the risk of human errors resulting from manual processes.
- Triggering reminders and alerts as regulatory deadlines approach to avoid missing compliance due dates. This puts the team in the driver's seat so they can prioritize disclosure activities.
- Roles-based access and permissions to help maintain the integrity of disclosure content.
- Automated workflows ensure that process participants are completing tasks on time while planning around potential bottlenecks.
- Dashboards and reporting to provide visibility into existing processes, allowing managers to address potential compliance issues proactively.

- Responding to request for clinical trial data from external stakeholders, automating the associated review and approval processes to provide transparency in the decision-making. The technology to manage these requests includes the requisite forms such as the data use agreements as well as the associated workflows and reports.
- Publishing data to the sponsor's own branded websites, leveraging the disclosure content that was previously approved for submission to global registries. This removes redundant approval processes and ensures integrity of the published data.

Key Elements

Clinical trial sponsors base their transparency policies on a few guiding principles:

- Preserving patient privacy while also sharing the information that the market expects.
- Protecting intellectual property while also encouraging great science.
- Disclosed data must be accurate, timely, and conform to regulatory requirements.

Technology can help to do this in a measured manner that provides controlled access. The technology that best fits this scenario should have four important attributes:

1. Platform Approach
2. Risk-Based Validation Approach
3. SaaS-Based Deployment Model
4. Content Management Foundation

Platform Approach

Clinical trial disclosure is an ever-evolving process that touches numerous functions and individuals across a typical life sciences organization. A platform approach ensures that the same foundation technology supports different aspects of the process. It also provides a significant benefit by offering a "one-source approach" to managing disclosure content. All the moving parts of the process including resources, content, standards, and requirements are all interacting within a controlled disclosure ecosystem.

Risk-Based Validation Approach

Risk-based validation of SaaS Solutions requires a commitment from the software vendor and the sponsor. This ongoing commitment is not only to provide the necessary documentation but also to look at system components objectively, and develop the appropriate tests and measures to ensure quality is built into the system from the start. As SaaS solutions gain in popularity, sponsors rely on risk-based approaches to validation to manage quality and minimize the costs of validating hosted solutions. A key to a successful risk-based approach to quality is working with a vendor that has deep and relevant experience, with an verifiable track record of successful implementations.

SaaS-Based Deployment Model

The life sciences industry is increasingly employing SaaS-based technologies to address business critical challenges, especially in areas like disclosure that are continuously evolving. Clinical trial disclosure is an organization-wide concern and supporting processes impact individual team members across various functions. A SaaS-based system provides web access without the traditional infrastructure burden, which translates into quicker ramp-up, broader access and greater flexibility as the team implements new capabilities.

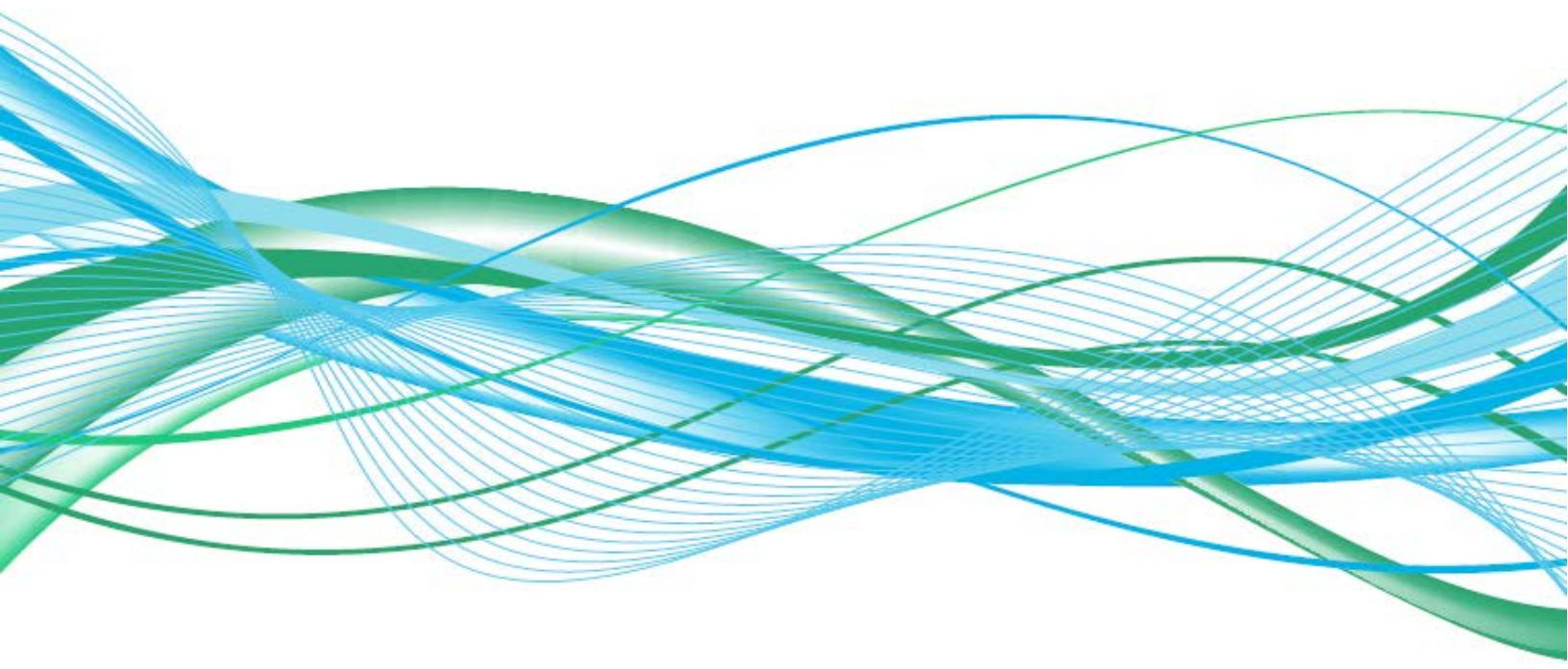
Content Management Foundation

Some of the biggest transparency challenges are those that relate to content management. Managing multiple versions of content, tracking who approved what version, as well as what data was disclosed when was it made public, are all content management requirements. Disclosure content requires a content management foundation to ensure integrity across versions, regardless of the output channel. Managing the content, supporting users and enforcing the disclosure process are key aspects of this content management foundation.

Conclusion

As clinical trial sponsors seek to expand their transparency efforts, it is important to recognize the role that technology plays in shaping a transparency approach that protects the disclosure process from manual errors, positions the team to respond quickly and accurately to disclosure

requirements and mitigates the risks of non-compliance. It is no longer a question as to whether technology should be employed to automate tasks across the process. Rather, it is a question about the degree to which it can be rapidly deployed to manage the complex process of disclosure and provide valuable insights to stakeholders across the organization.



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