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Clinical Data Transparency Is Big Challenge For Smaller Sponsors

by Thomas Wicks

Robust transparency, and perhaps even just compliance with evolving requirements of multiple regulators, requires commitment from the C-suite for companies of all sizes.

Biopharma companies with the most effective and robust clinical trial disclosure programs often have one thing in common: a leadership that recognizes the importance of transparency beyond mere regulatory compliance.

These companies – primarily some of the largest pharmaceutical firms such as *GlaxoSmithKline plc* – have a commitment at the executive level to, for example, publish their disclosure policies, making generous commitments to protocol registration, results disclosure, plain language summaries, and the sharing of a broad range of clinical documents. They invest as well in both tools and company policies to meet these commitments.

In contrast, smaller companies typically delay in investing in the focused systems needed for even the modest goal of regulatory compliance, let alone providing for a strategic view into disclosure activities. For example, they often are making do with manual, spreadsheet-type approaches rather than a centralized review and monitoring system. But repercussions of having less effective programs can go well beyond just regulatory penalties. (*See sidebar.*)

The Hidden Implications of Clinical Trial Disclosure Noncompliance

By Thomas Wicks

18 Mar 2021
Potential fallout from noncompliance goes well beyond regulatory penalties; adherence has improved but less so for smaller companies.

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Developing A Transparency Culture

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Publishing any clinical trial data requires effort and introduces some risks to the organization. There is often a concern about inadvertently releasing confidential company or patient health information, tipping off competitors, or jeopardizing the ability to file patents. The culture at many biopharmaceutical companies is to hold data very closely, especially data about unapproved products or indications. Kim Green, transparency expert and founder of ClaritiDox, said that "especially smaller companies focused on rare diseases or highly competitive therapeutic areas are particularly reluctant to share clinical trial results, especially if these are not promising."

Another factor undermining transparency is an exclusive focus on research, development and sales, limiting disclosure to the absolute minimum required by regulations. Ironically, seeking to disclose the least possible data required by law typically requires more effort to parse the regulations and question every requirement, and leads to companies erring on the side of nondisclosure.

However, a properly managed process easily mitigates the potential risks of disclosure. Such processes bring an organization into full compliance and enable it to leverage the data for valuable secondary uses, including patient engagement initiatives through intuitive trial-finder websites and streamlined recruiting efforts that rely on timely and high-quality trial, site, and status information.

Awareness And Coordination

Over the past two decades, mandatory clinical trial disclosure has evolved from providing summary protocols to publishing trial results and, more recently, the full clinical study report. (*See box below*.) In the coming years, trial sponsors will be required to make plain (lay) language summaries (PLS) of results available and eventually even anonymized individual patient data (IPD). For example, the EU clinical trials regulations (EU) No. 536/2014 requires PLS at the time of results disclosure for every trial registered on the new Clinical Trial Information System, while the EU policy 0070 will require the sharing of IDP in a future phase of implementation.

With a growing number of countries requiring the public availability of clinical data, maintaining compliance can be difficult. Although the company is ultimately responsible for compliant and consistent global disclosure, many organizations delegate local affiliates' responsibility. This delegation, however, means that there is little corporate awareness of what data are publicly disseminated or whether they are made public in compliance with local law.

While global disclosure regulations tend to have some commonality, typically requiring, at minimum, the registration of Phase II and III interventional trials around the time of study start, local variations make it more complicated. "Companies planning their first Phase I/II or Phase II

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trials are often unprepared for the new disclosure requirements and may lack internal expertise or regulatory writing experience," said Green. Adding to this complexity is that initial registration timing can vary, as do the frequency and types of data updates expected and whether results are mandatory.

A further difficulty is ensuring consistent public dissemination of information when every registry has unique data and local language requirements. In organizations without a central disclosure function, each affiliate, partner, or CRO makes editorial decisions to conform the data to the local registry standards. However, without a coordinated editorial approach, the data made public may be inconsistent. This lack of harmonization can raise questions from industry critics when, for example, one registry shows a different set of secondary outcomes or provides an inconsistent view of adverse events. Additionally, because data privacy laws vary across regions, local editorial decisions may inadvertently result in disseminating personally identifiable information in violation of privacy laws in another country.

Transparency Components

Elements of clinical trial transparency include the public disclosure of:

- Protocol summaries synopsis,
- Clinical results as or summary tables,
- Full protocol and statistical analysis plan (SAP),
- Complete Clinical Study Report (CSR), and
- Pending requirements: anonymized patient data, plain (lay) language results summaries.

Finally, even when the decentralized approach leads to compliance with local disclosure regulations, there is an increased risk of publishing company confidential information absent a central review and approval process. There are examples of the European Medicines Agency denying proposed redactions of sensitive information in submissions under its policy for publication of clinical data for products for human use because the information was already publicly available and at least one instance of a rejected patent filing due to such inadvertent disclosure of company information.

Systems And Data

Many smaller organizations have not yet implemented a specialized clinical trial disclosure system. Instead, they tend to rely on a manual approach, perhaps tracked through various spreadsheets. It can be difficult for companies to adapt to ever-changing policies or respond to tightened deadlines and more frequent update requirements with a manual approach. Spreadsheets and manual disclosure processes also make it harder to respond to inspections and rarely provide a global transparency perspective to company executives.

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Companies with smaller trial portfolios often lack a system to track the various dates, trial statuses, and metadata that must be disclosed to trial registries. Frequently, these data are managed by CROs or partner organizations and may not be aggregated in a central database or system.

In contrast, larger study sponsors are implementing guidelines and templates for documentation related to clinical data sharing and disclosure requirements, including protocols, clinical study reports (CSRs), and SAS datasets. Taking into consideration downstream data-sharing requirements facilitates efficient trial transparency and helps ensure global consistency of the data made public.

A Closer Look At Transparency

This is the second article in our series on clinical trial disclosure. Look for more coming soon and catch up on a recent perspective on regulatory *compliance among smaller and larger companies and the hidden costs of nondisclosure.*

The first step to addressing the challenges of regulatory complexity and evolving transparency expectations is to recognize that disclosure is not merely an administrative function. Executives leading regulatory affairs, clinical operations, and medical writing should collaborate with the chief medical officer to establish a transparency policy that aligns with patient engagement and corporate communication strategies. Understanding global requirements, which have changed substantially in recent years, is the foundation for establishing the processes and systems that will ensure compliance and avoid negative assessments by transparency advocates.

Thomas Wicks is chief strategy officer at TrialScope. He has more than 20 years of experience with performance and content management approaches in the life sciences, with particular focus on clinical trial transparency.