Purposeful Clinical Trial Transparency: Delivering Societal Value Beyond Compliance

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Disclosure: AI was used to create the first draft of this paper based on a presentation I authored and presented at the annual DIA Canada event in November of 2024.

Introduction

In the rapidly evolving landscape of clinical research, transparency has become more than a regulatory checkbox. Over the past decade, clinical trial transparency regulations, policies, and best practices have proliferated globally, driven by a growing recognition of the ethical imperative to share research findings with all stakeholders in a way that is useful to them. While compliance with these mandates is essential, it represents only the baseline. This white paper reasons that clinical trial sponsors should adopt a more purposeful approach to transparency, one that goes beyond mere adherence to regulations and actively seeks to maximize the value of clinical trial data for the benefit of society.

This perspective focuses on being purposeful with transparency policies and processes to invest in the activities that will enhance public health outcomes, foster trust, support equity, reduce research waste, and ultimately improve the lives of patients worldwide. We will explore the expanding landscape of transparency, detail the multi-faceted value proposition, address the costs and challenges, and offer concrete recommendations for sponsors looking to drive meaningful impact.

The Expanding Landscape of Clinical Trial Transparency

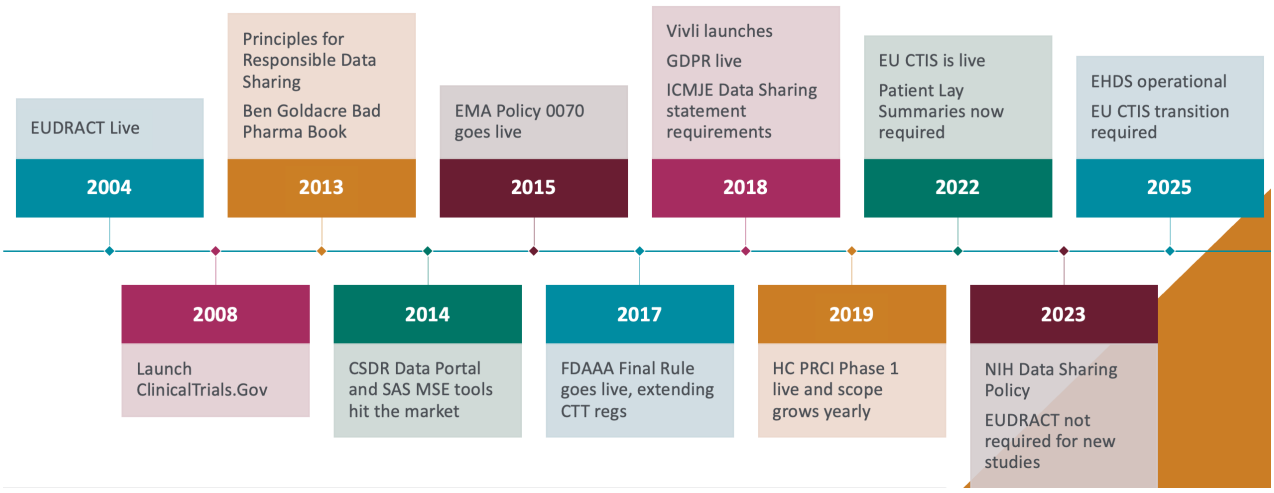
The clinical trial transparency landscape has become increasingly complex, multifaceted, and detailed. Regulatory bodies like the FDA in the United States and the EMA in Europe have established comprehensive requirements for the disclosure of clinical trial information. These requirements span various stages of the product development lifecycle, from trial registration through to New Drug Applications (NDA) to regulatory agencies. In addition to meeting the minimal requirements globally, several best practices have emerged that enhance science and support patients, such as sharing data sets and publishing easy to understand summaries of what happens in a clinical study.

Furthermore, the number of disclosure channels continues to expand, encompassing clinical trial registries, scientific publications, and clinical study data request systems. Disclosure involves multiple public disclosure

points throughout a study and product lifecycles. In this paper when we talk about the various disclosure channels, we are grouping them into four channels:

- **Clinical Trial Registrations and Results Posting** such as the US government clinical trials website[1] and the EU Clinical Trial Information System (CTIS)[2] .
- Clinical Trial **Plain Language Summaries** as defined in the EU Clinical Trial Regulation (EU) No 536/2014 Annex V[3].
- Anonymized full **Clinical Document Packages** such as those published under EMA Policy 0070[4] and Health Canada's Public Release of Clinical Information[5].
- **Clinical data set sharing** for secondary research purposes as defined by the Principles for Responsible Clinical Trial Data Sharing as published by EFPIA and PHRMA[6].

The growing number of disclosure channels, as demonstrated in the image below, creates a challenge: How much of this activity is genuinely generating value for public health? This paper contends that a more strategic and purposeful approach is needed to ensure that transparency efforts translate into tangible benefits for patients and society.



The Multifaceted Value of Clinical Trial Transparency

To move beyond basic compliance, sponsors must understand the full spectrum of value that clinical trial transparency can unlock:

- **Enhancing Public Health Outcomes:** Transparency demonstrates a commitment to science and the health of the public. By sharing clinical trial data, sponsors can reduce redundant research efforts and enable more comprehensive analyses, leading to improved treatments and prevention strategies.

Transparency supports access to and dissemination of clinical research findings globally, maximizing their impact on public health.

- **Patient Centricity:** Safe data sharing respects the invaluable contribution of patients to clinical research. By enabling the safe reuse of data gathered from a single study, sponsors can support additional research and accelerate the development of new therapies.
- **Boosting Journal Publications:** Data sharing or data access is increasingly required to publish in high profile scientific journals. Physicians rely on journal publications as part of their healthcare decisions treating patients.
- **Fostering Trust:** Surveys have indicated that the pharmaceutical industry has less public trust than do tobacco companies. In an era of declining public trust in the pharmaceutical industry, transparency can serve as a powerful tool for rebuilding confidence. By openly sharing clinical trial data, sponsors can demonstrate their commitment to ethical conduct and scientific integrity.
- **Supporting Equity:** Through transparency sponsors demonstrate they engage diverse groups and evaluate treatment across diverse populations, helping to address health disparities and promote equitable access to healthcare. Transparency initiatives enable the evaluation of treatment effects across diverse populations, supporting equitable access to healthcare.
- **Reducing Waste:** By sharing clinical trial information, the collective health research community can eliminate the need to re-run the same trials saves money and allows focus on answering subsequent research questions.

The Costs of Clinical Trial Transparency

While the benefits of clinical trial transparency are undeniable, it is important to acknowledge the associated costs. I had the opportunity to have a conversation with a patient advocate about transparency and the challenges for sponsors to balance all disclosure channels. The response was real and refreshing when the individual paused and reflected on the fact that it was not obvious that sponsors might have to choose where to invest in disclosure instead of doing it all. It's not obvious to many that each disclosure channel has a cost to comply with due to variations in formatting needs, distinct requirements, local laws, and other variances.

Key costs that need to be considered and managed:

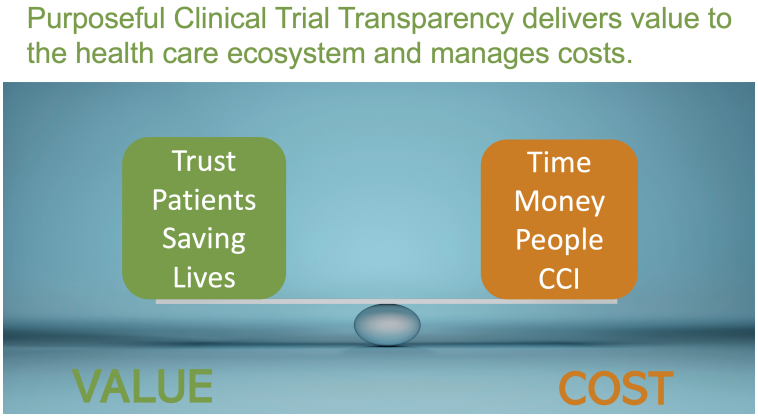
- **Operational Expenses:** Operational costs will accumulate as an organization builds processes to comply with all global disclosure channels. Some types of disclosure are more costly than others – for example safely publishing individual patient level data without contractual or security controls is of high cost. Anonymizing clinical trial data to protect patient privacy is a complex and costly process, particularly for

clinical study reports (CSRs) and individual patient-level data (IPLD). Redacting and Anonymizing CSRs is resource intensive.

- **Privacy Risks:** Sharing clinical trial data carries the risk of unintentional disclosure of patient identities or misuse of data, which could damage trust and undermine research efforts. Clinical trial sponsors rely on patients to conduct research. Sponsors must uphold commitments made to patients to ensure they feel confident in participating in clinical research going forward.
- **Data Sharing Infrastructure:** Establishing and maintaining secure data sharing platforms and processes can require significant investment. There are industry platforms available to meet these needs at a reasonable cost. These platforms, such as Vivli, are designed to support sponsors and researchers effectively whilst managing costs.

By understanding the totals costs, sponsors can make informed decisions about how to prioritize their transparency efforts and maximize their return on investment. Being purposeful with policies and processes is vital to support patients, inform the public, improve science, and drive discovery.

Sponsors must be purposeful as they establish their transparency policies. Will they aim for the minimum of compliance, or will they seek to use transparency as one of the pillars of building trust in their clinical trials and products?



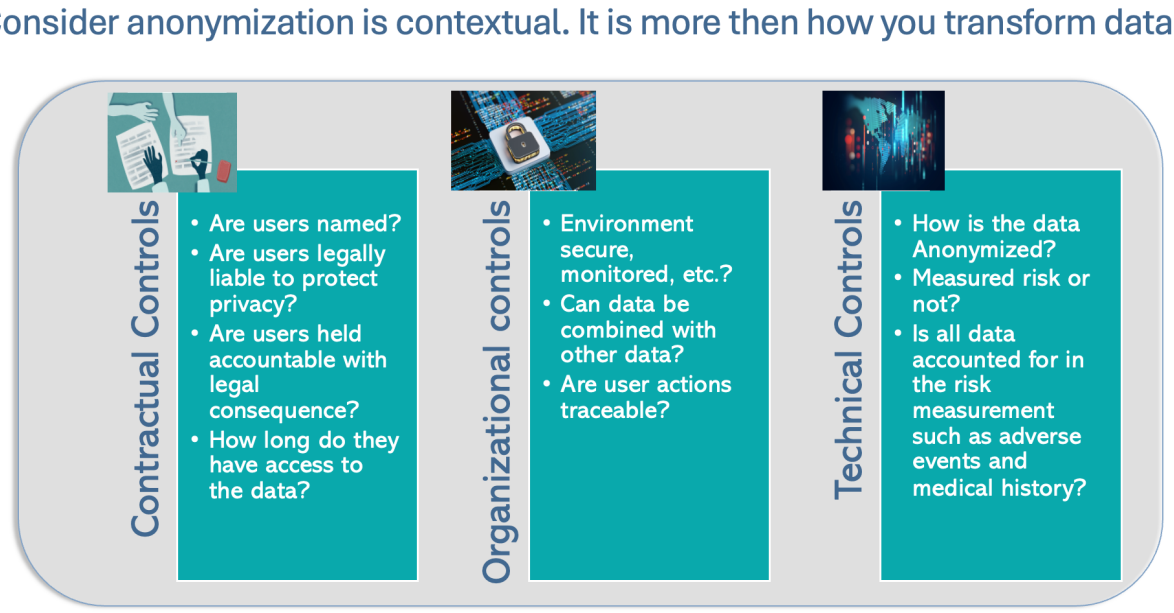
Clinical Trial Transparency requires getting the right balance between privacy and utility

To share data or documents, sponsors must first anonymize them. Anonymization is not a one size fits all exercise. Anonymization is a contextual process that requires careful consideration of the potential risks and benefits of data sharing in each situation. There are numerous types of controls available to sponsors when they

prepare clinical data for sharing under different policies and channels, and understanding these controls is vital. A few key questions sponsors need to understand to be successful:

- How can we support secondary research by sharing our clinical trial data safely and successfully?
- Is anonymization always done the same way, regardless of who we share with and where we are sharing the data? Consider clinical documents versus clinical data sets.

Implementing a carefully designed Anonymization process for each disclosure channel requires a thorough understanding of privacy laws such as the EU General Data Protection Rule (GDPR)[7]. Clinical research is global today and thus strict adherence to the strongest privacy laws must be respected by sponsors transparency policies. Anonymization is more than how you change or transform the data, also referred to as technical controls. Sponsor policies and processes must account for variations in the contractual and organization controls as well.



In different data sharing scenarios, sponsors can rely on higher or lower controls in each of the above areas. The right mix can enable sponsors to meet different data anonymization requirements and deliver on transparency commitments successfully in a value-added way. In the below table we demonstrate a couple different data sharing scenarios and how each type of control can be applied to drive different outputs. The scenarios where the Output is defined as High Utility represent examples of value-added transparency that is ultimately enhancing public health outcomes.

	Vivli Sharing (Secondary Use)	**HC PRCI Publication** (Secondary Use)	**Internal Data Reuse** (Secondary Use)	**Research Collaboration** (Secondary Use)	**Research partner during the study** (Primary Use)
Contractual Controls	• High	• Very Low	• Very High	• Very High	• Very High
Organizational Controls	• High	• Very Low	• Very High	• Medium (when using platform allowing data export)	• High (shared database inside Pharma using top notch security protocols)
Technical Controls	• Minimal Transformation • Reference Population	• High Transformation and/or Masking • Study Population	• Minimal Transformation • Reference Population	• Medium Transformation • Reference Populations	• Site Coded Data • No transformation because data is being analyzed as per the ICF to support study objectives
Output	Anonymized & High Utility	Anonymized & Low Utility	Anonymized & High Utility	Anonymized & High Utility	Pseudo-anonymized & High utility

Getting it right today and in the future, Privacy and Transparency

One thing to remember is that what's considered anonymized today, may not remain anonymized or unidentifiable tomorrow. These are tough considerations for sponsors as they build purposeful and effective transparency and disclosure policies.

The Yale Law Journal in 2004[8] and recently Faster Capital in 2024[9] both highlight how the "mosaic theory" of intelligence gathering demonstrates the importance of considering the cumulative effect of multiple disclosures on successful information gathering and human identification.

Applying this same theory to clinical data we can see that as technology and data access grow rapidly, this leads to more and more disclosures of the same patient data in different formats globally, which can be used to match locations and treatments in clinical trial datasets. Data marts continue to grow, making it easier to access, organize, and understand data trends. Large Language Models (LLMs) are increasingly used to make data combination easier.

To address these challenges, sponsors must adopt a holistic approach to anonymization and process management. This includes:

- **Assessing the Context:** Carefully evaluate the potential risks of each disclosure, considering the sensitivity of the data and the likelihood of re-identification.
- **Implementing Strong Governance:** Establish clear policies and procedures for data sharing, including data use agreements and security protocols.

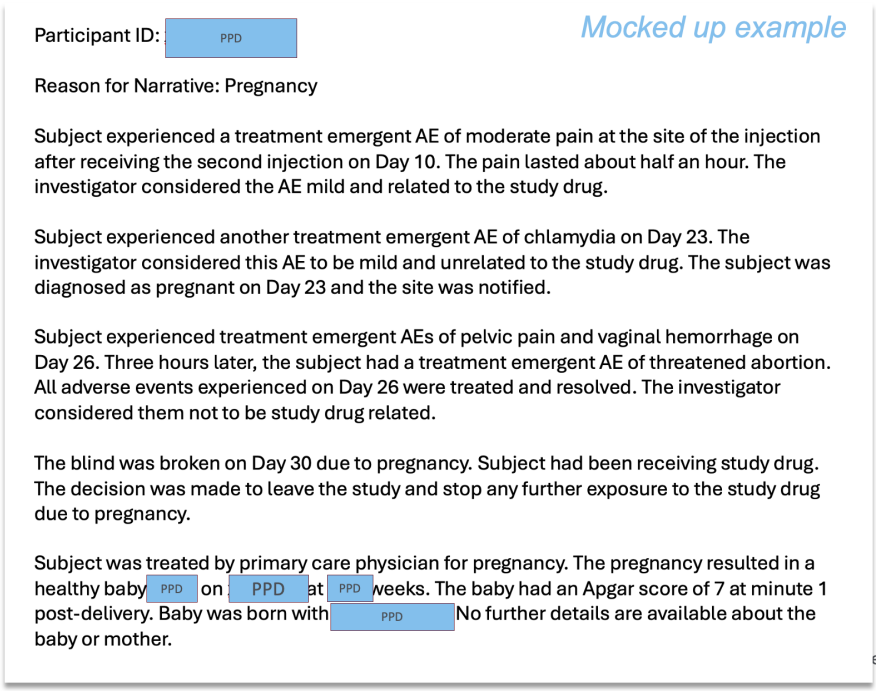
- **Engaging with Patients:** Seek input from patients on their privacy concerns and preferences for data sharing.
- **Staying Ahead of the Curve:** Continuously monitor the evolving data landscape and adapt anonymization strategies accordingly.

The Human Perspective of Clinical Trial Transparency, ensuring Privacy and Trust

Ultimately, clinical trial transparency is about people. It is about respecting the privacy of patients who volunteer to participate in research and building trust in the scientific process, whilst meeting transparency regulations and privacy laws globally. These two types of legislation are not always easy to reconcile. There's great debate about whether the patient level clinical trial data is truly personal and needs to be controlled or should be readily available to the public.

Is it really that personal? Consider the patient narratives in clinical study reports which are published in many EMA Policy 0070 and Health Canada PRCI packages. These narratives provide detailed stories of what happened in a clinical study for one real person. Such narratives include sensitive details of medical history, medical treatments, and medical outcomes often written for patients with the most notable and unique experiences in each clinical trial. This increases the likelihood that they can be identified due to the uniqueness of their experience. A detailed story of what happened in a clinical study for one real person. Such narratives are most challenging to anonymize.

Patient Narrative Example



Participant ID: PPD

Mocked up example

Reason for Narrative: Pregnancy

Subject experienced a treatment emergent AE of moderate pain at the site of the injection after receiving the second injection on Day 10. The pain lasted about half an hour. The investigator considered the AE mild and related to the study drug.

Subject experienced another treatment emergent AE of chlamydia on Day 23. The investigator considered this AE to be mild and unrelated to the study drug. The subject was diagnosed as pregnant on Day 23 and the site was notified.

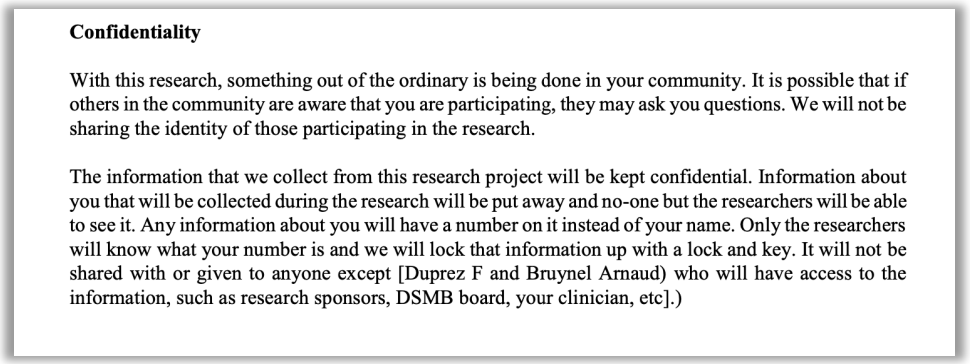
Subject experienced treatment emergent AEs of pelvic pain and vaginal hemorrhage on Day 26. Three hours later, the subject had a treatment emergent AE of threatened abortion. All adverse events experienced on Day 26 were treated and resolved. The investigator considered them not to be study drug related.

The blind was broken on Day 30 due to pregnancy. Subject had been receiving study drug. The decision was made to leave the study and stop any further exposure to the study drug due to pregnancy.

Subject was treated by primary care physician for pregnancy. The pregnancy resulted in a healthy baby PPD on PPD at PPD weeks. The baby had an Apgar score of 7 at minute 1 post-delivery. Baby was born with PPD No further details are available about the baby or mother.

Informed consent is a cornerstone of ethical clinical research, and sponsors have a responsibility to protect the privacy of patients who entrust them with their data. As demonstrated in the example below, Sponsors promise patients to protect their privacy when they agree to participate in a clinical trial, and patient trust is critical to enable clinical research to continue.

WHO ICF Template as found on clinicaltrials.gov



Confidentiality

With this research, something out of the ordinary is being done in your community. It is possible that if others in the community are aware that you are participating, they may ask you questions. We will not be sharing the identity of those participating in the research.

The information that we collect from this research project will be kept confidential. Information about you that will be collected during the research will be put away and no-one but the researchers will be able to see it. Any information about you will have a number on it instead of your name. Only the researchers will know what your number is and we will lock that information up with a lock and key. It will not be shared with or given to anyone except [Duprez F and Bruynel Arnaud) who will have access to the information, such as research sponsors, DSMB board, your clinician, etc].)

To date sponsors have been working hard to strike a balance in meeting privacy law and patient commitments, whilst publishing the required information under regulations such as EMA Policy 0070 and Health Canada's PRCI. Through careful implementation sponsors seek the best possible outcome, but let's be clear, there are no clear legal operational standards for sponsors. Each must figure out their approach based on their risk tolerances.

Of note is a 2006 Canadian court case - *HJ Heinz Co of Canada Ltd v. Canada*[10] -- The Supreme Court of Canada affirmed that personal privacy and information access are a balancing act. The Court's leading decision on Privacy and Access to Information makes it clear that Privacy is the top priority. "It is apparent from the scheme and the legislative histories of the Access Act and the Privacy Act that the combined purpose of the two statutes is to strike a careful balance between privacy rights and the right of access to information. However, within this balanced scheme, the Acts afford greater protection to personal information.**"** This statement was made about the interplay between the Privacy Act and the Access to Information Act in the decision document published by the court.

Purposeful Transparency in Action

To drive value with clinical trial transparency and disclosure activities, sponsors should focus on the documents and publications that truly help patients understand their options and researchers continue to learn more. We believe this requires investments in some of the areas of CTT that are not typically legally required in all jurisdictions but have a proven track record of helping society.

Plain Language Summaries: Plain language summaries (PLSs) of clinical studies started to appear at the conclusion of studies nearly a decade ago, and patients like them. These summaries provide an easy-to-understand summary of completed clinical research. Patient reviewers are typically involved. For more details on what is a Plain Language Summary and how to develop them effectively we recommend reviewing the Good Lay Summaries Practices Guidance[11]. Thousands of PLSs have been published to help the public better understand research and treatment options. A sample study overview is below. A great resource for the public to find hundreds of PLSs is the website www.Trialsummaries.com hosted by Citeline and used by numerous clinical trial sponsors globally.

Overview of this study

Why was the research needed?

Researchers are looking for a better way to treat migraine. Before a drug is available for all patients, researchers do clinical studies to find out how it works and how safe it is.

What treatments did the participants receive?

The participants in this study received LY3451838 or a placebo. A placebo looks like a drug but does not have any drug in it.

What were the results of this study?

The main question the researchers wanted to answer in this study was:

- Did LY3451838 reduce the number of days participants had migraine headaches?

No. Overall, the researchers found that the participants who received LY3451838 had about the same number of migraine headache days compared to those who received the placebo.

More details about the results of this study are included later in this summary.

What medical problems did the doctors report as possibly related to the study treatment?

There were 2.6% of participants who had medical problems that the study doctors reported as possibly being related to the study treatment. This was 1 out of 38 participants.

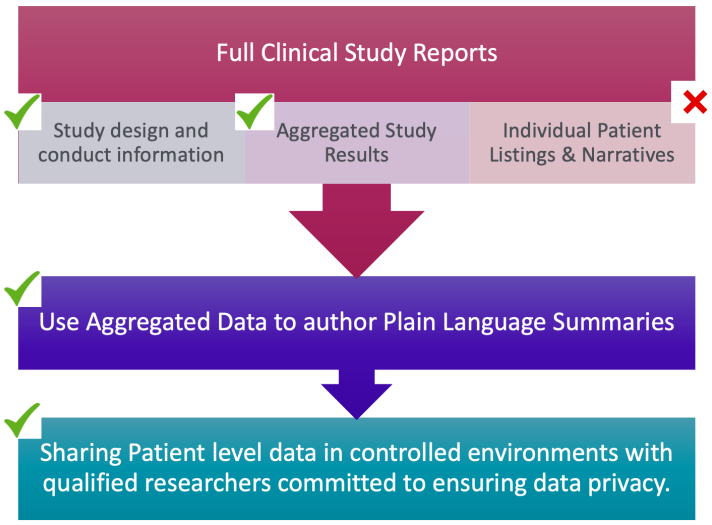
More details about the medical problems from this study are included later in this summary.

Where can I learn more about this study?

Controlled Data Sharing: Sponsors should implement a policy and process to share individual patient-level data with qualified researchers in controlled environments that include strong contractual and security controls. Controlled data sharing with researchers has yielded significant scientific insight as demonstrated by the number of publications. Controlled data sharing allows sponsors a chance to better meet the data utility needs of researchers. It is common for these data sharing platforms to publish statistics. By the end of 2024 there were over 600 publications cited by just four major data sharing platforms – Vivli[12], YODA[13], CSDR[14,], and Data Sphere[15]. It's clear that the data sets are being used to drive further research.

Clinical Study Report Sharing: Clinical study reports contain information about the study design, treatments, how data is collected and analyzed, and other information about the therapy being researched. Clinical study reports also include individual and aggregated results data. The publication of the body of the clinical study report, including all aggregated data such as the adverse events, helps communicate key information to the

public and create an environment of trust through transparency. However, the publication of the individual patient level listings and narratives should remain controlled, with Data Sharing Agreements (DSAs) and secure environments, to avoid risks of privacy breach for study participants.



Timely Study Registration: Tried and true, the first study registrations started in 2004 under the European EudraCT system. Shortly after the US followed with the launch of clinicaltrials.gov. Globally now there are many clinical trial registries. WHO recognizes 17 as acceptable locations for trial registration, but there are many more. It's considered a best practice and requirement in quality clinical research that a sponsor not only registers their trial but reports basic results. Compliant and timely study registrations bring trust to the health research ecosystem.

Conclusion: A Call to Action

Clinical trial transparency is more than just a regulatory requirement. It is an opportunity to deliver value to the health care ecosystem, improve public health, and build trust in the pharmaceutical industry. By embracing a purposeful approach to transparency, sponsors can unlock the full potential of clinical trial data and make a meaningful difference in the lives of patients worldwide. The time has come to move beyond compliance and embrace a future where clinical trial transparency is a catalyst for scientific discovery, improved healthcare, and a healthier world.

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