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Integrating Privacy By Design to Enable Innovative Clinical Trials and Post-Trial Data Sharing

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ABSTRACT

As clinical trial design evolves to incorporate newer technologies and innovative methodologies, identifying appropriate privacy measures for the safe collection and use of sensitive personal information has become a growing challenge. Often, privacy considerations are overlooked or are difficult to predict during the design phase of innovative trials, which necessitates pharmaceutical companies to employ reactive measures to address these concerns during the implementation phase.

Do the informed consent forms contain the appropriate language to protect human participant privacy while still enabling the expected or future uses required by goals of the study? Have the privacy considerations of innovative trial designs (cross-border transfer, linking to real-world data, data enrichment) been identified and accounted for to maximize usable data? Are there proactive measures in place to enable post-trial data sharing and re-use, including for transparency and publication purposes to make scientific results more widely available? These are some examples of the types of privacy considerations that sponsor organizations need to consider for innovative trials.

In this paper, we will explore guiding principles to enable success for innovative trials from a privacy and data enablement standpoint. We will discuss what privacy-by-design strategies can be integrated up front to streamline trial operations. We will also discuss how organizations can effectively achieve readiness for post-trial data sharing and re-use. These guiding principles will ensure that organizations maintain responsible data handling and protection practices to build trust between companies and study participants, while still enabling important research to be conducted in a safe and ethical manner.

INTRODUCTION

In the rapidly evolving landscape of healthcare research, innovative clinical studies have emerged as a vital force driving advancements in medical research and patient care. These studies represent a dynamic shift away from conventional methodologies, embracing novel approaches to study design, patient recruitment, data collection, and treatment evaluation, and hold the promise of faster drug development and more personalized treatments.

Innovative clinical studies come in various forms, each tailored to address specific research questions, patient populations, or therapeutic approaches. Examples of innovative clinical studies include adaptive trials, basket trials, platform trials, pragmatic studies, enriched studies, and virtual trials (including de-centralized clinical trials), amongst others. The traditional model of randomized controlled trials (RCTs) often follow a linear approach and are unable to capture the full range of characteristics of the target population. For this reason, innovative clinical trials often incorporate real-world data sources, to leverage the untapped insights across the entire target population. Largescale initiatives such as Patient-Centered Outcomes Research Institute (PCORI®; http://www.pcori.org) in the USA and Innovative Medicines Initiative (IMI; https://www.imi.europa.eu/) in the EU have realized this and are seeking to maximize this potential. American Society of Clinical Oncology (ASCO®) has stated; “When trial data inform our

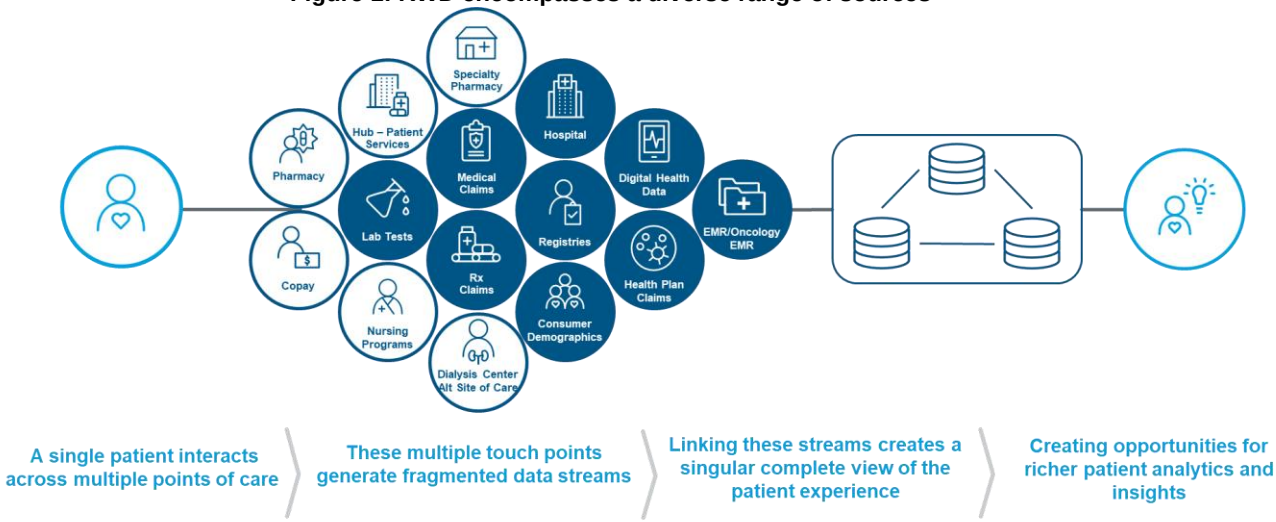
decisions, we tap into only 3% of the cancer patient population.…To improve care for every patient, we need insights from the other 97% of people receiving cancer care."[1]

As clinical study design has evolved to incorporate newer technologies, innovative methodologies, and sensitive real-world data sources, identifying appropriate privacy measures for the safe collection and use of sensitive personal information has become a growing challenge. Often, privacy considerations are overlooked or are difficult to predict during the design phase of innovative trials, which necessitates pharmaceutical companies to employ reactive measures to address these concerns during the implementation phase.

REAL-WORLD DATA IN INNOVATIVE CLINICAL TRIALS

Real-World Data (RWD) is the empirical data derived from everyday clinical practice, patient experiences, and healthcare systems. It provides a lens through which we can observe how medical interventions and treatments perform in the real world, outside the controlled environment of traditional clinical trials. RWD encompasses a diverse range of data sources from across the patient's health care journey (Figure 1). Some examples include electronic health records (EHRs), claims data, patient registries, wearables, and patient-reported outcomes.

Figure 1: RWD encompasses a diverse range of sources



RWD is generated from each interaction point with the healthcare system. These multiple touch points generate fragmented data streams, giving an incomplete picture of the patient as a stand-alone data source. However, if these data sources are linked, a comprehensive and complete picture of the patient experience can be attained, creating opportunities for richer patient analytics and insights.

The use of RWD in innovative clinical trials, offers a wealth of opportunities to transform healthcare in profound ways. When used in concert, RWD and innovative trials create a virtuous cycle of discovery, refinement, and validation. Key benefits of using RWD in clinical trials are summarized below.

- **Pre-Trial Insights**: RWD can inform the design of innovative clinical trials by providing critical insights into disease prevalence, treatment patterns, and patient characteristics. This allows researchers to refine trial protocols, identify relevant endpoints, and target specific patient populations effectively.
- **Adaptive Decision-Making**: The flexibility of innovative trials aligns seamlessly with the ever-evolving landscape of real-world healthcare. As new insights emerge during a trial, adaptive trial designs can pivot to optimize treatment strategies, dosages, or even trial endpoints, maximizing the chances of success.
- **Enhanced Patient Recruitment**: RWD aids in patient recruitment by identifying eligible participants from real-world healthcare data. This streamlined approach not only expedites trial initiation but also ensures that enrolled patients are representative of the broader patient population.
    - As an extension to this, **bias can be removed** in studies and **novel questions** can be addressed related to aspects that are not answerable by study data alone. Questions about factors correlating with dropouts and or non-enrolment, for example become possible with RWD linked into trial data. This might lead to planning trials covering more diverse populations as one benefit.
- **Improved Data Collection**: By leveraging **historical data**, a complete and accurate picture of a patient's history becomes available. For example, in a trial, collecting medical history information from a patient relies

on their memory. By linking in RWD, the patient's actual medical history can be tied in to answer those questions required for a full understanding of trial results without relying on potentially faulty memory.

- **Post-Market Surveillance**: After regulatory approval, RWD can continue to play a pivotal role in post-market surveillance. It allows researchers and healthcare stakeholders to monitor the long-term safety and effectiveness of treatments, identifying rare adverse events or subpopulations that may benefit most.
    - Looking at the future, if RWD is linked to trial data and patients continue to be tracked and linked to the study in their long-term health care journey, those real-life long-term safety concerns for the trial can be more easily managed, analyzed, and tracked.
- **Healthcare Integration**: The insights gained from RWD-driven evidence can directly impact clinical practice. As innovative therapies emerge from clinical trials, healthcare systems can more seamlessly integrate them into routine care, benefiting patients across the healthcare continuum.

PRIVACY CONSIDERATIONS IN INNOVATIVE CLINICAL TRIALS

While innovative clinical trials hold much promise in terms of their immense potential, organizations pursuing greater sophistication of trials have experienced novel privacy considerations as part of the process.

- **Data Sources**: Innovative clinical trials often incorporate RWD sources, such as electronic health records (EHRs) and wearables. These sources introduce complexities in data privacy management. Many RWD contain **sensitive personal information** which has been de-identified upfront prior to use in innovative studies.
    - In that regard, patients in a trial might be heavily incentivized to give broad coverage **consent**, including linking their trial data to all and any RWD that might be available about them. However, the owner of the RWD (if external) may not have collected or anonymized the data under this broad consent framework. This might pose a further challenge trying to have the study consent apply to RWD collected outside or prior to the study.
- **Data Linking**: While the RWD may have been anonymized prior to use in studies, linking with data collected during the trial or with other RWD sources may 'reverse' the applied anonymization; the risk of reidentification of the combined dataset may be higher due to sensitive information collected as part of the clinical trials.

PRIVACY-BY-DESIGN: GUIDING PRINCIPLES FOR INNOVATIVE CLINICAL TRIALS

To address these considerations, a set of fundamental principles need to be defined to enable privacy-by-design for innovative clinical trials. Utilizing a **proactive approach** is at the core of this concept; defining and integrating privacy considerations from the very outset of trial planning and design, rather than treating privacy as a reactive measure to be employed during the study execution phase.

Empower the team: Privacy-by-design encompasses not only processes and technology, but also the people. This includes assigning the right roles and responsibilities, starting with leadership i.e., someone accountable. It is important to ensure that the leadership and the team have the necessary skills and knowledge to identify and address privacy considerations that may arise during innovative clinical studies. Basic SOP training that covers the standard principles and procedures of data handling can be supplemented with more advanced trainings on disclosure control, data security, data protection law. For example, individuals can get training specifically for anonymized data assets, on what can and cannot be done with anonymized data, and the challenges of linking to external datasets.

Proactively evaluate the study design for privacy considerations: The study design should be evaluated early in the trial lifecycle to ensure privacy considerations are addressed appropriately and in a proactive fashion. This evaluation can encompass the following aspects –

- Data sources: Some of the questions that need to be asked about data sources include - what are the external RWD sources being utilized for the trial and where are they found? How will the data be used?
- Contractual agreements: Contractual agreements need to be considered to understand allowable options and necessary controls for linkage.
- Applicable privacy legislation: Applicable privacy legislation and Institutional ethics and review guidelines need to be considered for the data. Note that regional data protection regulations (such as GDPR in EU) may be supplemented by additional guidance/requirements from local bodies (such as data protection authorities within each Member State in the EU). For multi-country clinical trials, cross-border transfers may invoke additional privacy considerations.

Implement utility-preserving privacy protection approaches: Considering the outcomes of the evaluation from above, organizations can then better strategize the appropriate data linking strategy and implement privacy-protective measures accordingly.

- Strategize the data linking method: Integrating multiple datasets from multiple sources generates incremental information about any given patient and creates an elevated degree of identifiability through data linking. In these cases, undertaking a privacy-impact assessment for the combined dataset (especially when external RWD sources are being linked) can identify what further anonymization is required to remain privacy and contractually compliant.
- Risk-based Approaches vs Masking: Rules-based or masking approaches are often detrimental to the analytical value of the data or otherwise fail to adequately protect the participant privacy. On the other hand, use of risk-based approaches affords flexibility and scalability to handle more complex data (e.g., linked data covering multiple RWD sources and data spanning multiple jurisdictions), stricter privacy regulations and deidentification guidelines, and sophistication in evolving threat and attack vectors.

Promote transparency: Researchers and sponsors should ensure that the right level of communication with stakeholders is achieved; study participants should have a clear understanding of how their data is being protected, used, and shared, to understand the risks as well as the benefits (i.e., it is important to highlight benefits when describing use/reuse of health data) associated with the study. This can be a very simple statement in the informed consent form.

POST-STUDY DATA SHARING

Responsible data protection and management practices are now adopted by the pharmaceutical industry, including a commitment to make scientific results more widely available for secondary research after the study has been completed. This is to align with best practices outlined in data protection regulations and standards. With the increase in transparency initiatives in the past 2-3 years, post-study data sharing can now be considered part of the study lifecycle (Figure 2). Post-study data sharing requires the data to be de-identified prior to sending to data recipients.

Figure 2: Post-study data sharing as part of the study lifecycle

IMPACT

Implementing privacy-by-design into innovative clinical trials has several benefits for researchers and sponsor organizations. These advantages are described below.

- **Safe Data Enablement**: Privacy-by-design enables faster access to safe data to be utilized for innovative clinical trials, with minimal interruptions during study execution. By catching privacy considerations earlier in the study life cycle and addressing them as part of the study design phase, interruptions during the study execution phase are minimized.
- **Ensure Compliance**: Organizations are able to achieve demonstrated compliance with privacy laws such as the General Data Protection Regulation (GDPR) in the EU and Health Insurance Portability and Accountability Act (HIPAA) in the US.
- **Build Trust**: When participants trust that their data is handled ethically and securely, they are more likely to contribute to research efforts, leading to a wealth of data that can drive medical breakthroughs.
- **Enhance Reputation**: Incorporating privacy-by-design principles enhances the ethical reputation of research institutions and sponsors. Ethical conduct in clinical trials not only benefits participants but also serves as a competitive advantage, attracting collaborators, funding, and top-tier talent for future trials.
- **Patient-Centered Care**: Privacy-by-design aligns with the broader shift toward patient-centered care. It empowers individuals to make informed decisions about their data and treatment options, putting patients at the center of healthcare decision-making.

CONCLUSION

The fusion of RWD with innovative clinical trials represents a transformative force in modern healthcare. These complementary approaches create a symbiotic relationship where real-world insights inform and enrich clinical trials, while innovative trial designs accelerate the translation of discoveries into tangible benefits for patients. This synergy holds the potential to reshape the future of medicine, driving precision healthcare, optimizing treatment strategies, and ultimately improving patient outcomes on a global scale. Privacy considerations remain an essential facet of this transformative journey, requiring continuous vigilance and ethical diligence to balance data-driven progress with the protection of patient rights and data privacy. Privacy-by-design enables ethical and responsible healthcare research, particularly in the context of innovative clinical trials. As technology evolves and healthcare research advances, the protection of patient privacy remains a dynamic challenge. The guiding principles outlined in this paper provide a roadmap for researchers, institutions, and stakeholders to uphold the highest standards of privacy protection while advancing medical knowledge and improving patient outcomes.

REFERENCES

1. American Society of Clinical Oncology (ASCO). CancerLinQ. Access at: <https://cancerlinq.org/>

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