Paper ML04

Responsible AI in Protocol Design for Use in Digital Data Flow

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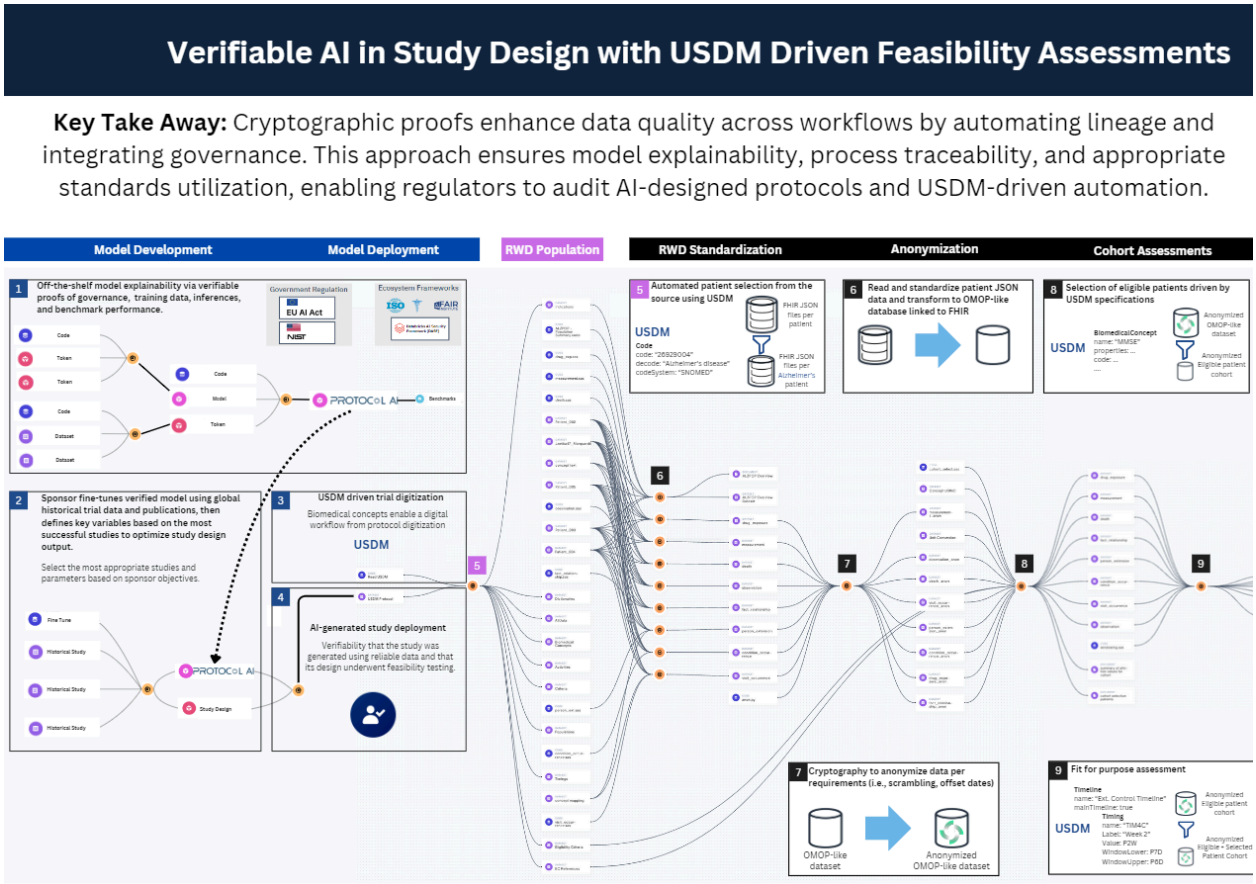
ABSTRACT

CDISC USDM can hold study design information in a structured format. This facilitates several impacts downstream in protocol amendments, cost assessments, and EDC set-up. Historical trials structured with USDM formatting can serve as training datasets for an LLM to build new trials, leading to faster study designs that have traceability to ensure the ethical design and connection downstream into the analysis.

Curated from hundreds of existing protocols and trial design documents, this presentation describes a use case in Alzheimer's trial design. Based on a retrieval-augmented generation (RAG) model, we aim to demonstrate the study protocol generated conforms to USDM standards, considers market access, and provides the probability of trial success. For this we will present a framework for implementing verifiable controls in training, constructing, and maintaining large language models (LLMs) for clinical trials, focusing on bias prevention and enhancing trial success.



INTRODUCTION

The advent of mainstream generative AI marks the beginning of a new technological era. Much like the personal computer and the Internet revolutionized access to and creation of knowledge fifty years ago, AI is reshaping this dynamic by introducing ubiquitous augmented intelligence. This evolving relationship between humans, machines, and information brings both opportunities and challenges. For businesses seeking to harness AI's full potential, responsible and strategic use is essential to maximize its benefits while addressing the associated risks. The pressing concern for industries isn't AI becoming sentient or uncontrollable, but rather its potential to create confusion, inefficiency, and disruption if mismanaged.

As we look to use AI in critical processes such as protocol and study design, how do we ensure the reliability, explainability and responsibility in the use of AI models?

RESPONSIBLE AI

Part of the journey to responsible AI are easy-to-use tools that help make your AI models transparent and collaborative. Cryptographic integrity is foundational to interoperability and transparency in any process. There are five key areas to consider when implementing any technology, but particularly AI models.

- Reproducibility: Regulations must ensure that AI models are transparent, standardized, and verifiable, producing consistent results across different runs.
- Fairness: Regulatory bodies must enforce measures to detect and mitigate biases, promote diverse data sources, and establish ethical guidelines to prevent discrimination.
- Reliability: Ensuring consistent and accurate performance requires quality assurance, continuous monitoring, maintenance, and risk management.
- Ethical Considerations: Regulations must address patient privacy, informed consent, and transparency, holding developers accountable for errors.
- Security: Data privacy can only be fully guaranteed with properly managed ownership of data flow and model deployment and usage.

AI STUDY DESIGN

Clinical trial protocols are critical documents that determine the success or failure of a trial. Developing a protocol is a complex process, as it involves multiple stakeholders, each with specific requirements. AI is a promising technology that can facilitate this complexity, accelerate trial initiation, and increase the likelihood of success. However, any AI solutions applied in this process must meet key features of responsible AI to address stakeholder requirements and ensure appropriateness for clinical trial protocols.

In this use case, we utilized Protocol AI™, an evidence-based, transparent solution that generates digital protocols in machine-readable USDM format (JSON). By following the key principles of responsible AI, we ensured transparency and traceability in the study design process, in addition to providing added value. This approach enables all stakeholders to clearly view every activity during the study design, meeting stakeholder requirements and ensuring traceability by users or regulatory bodies.

Once the study has been designed and protocol created and exported in a machine readable USDM format JSON file, we use those information, tags, biomedical concepts to drive the creation of required submission data. Whether that be utilizing real-world data or merely the normal set of data for clinical trials; the underlying code, data and processes are governed by tamperproof controls baked into the processes and demonstrated through clear lineage and traceability.

Any changes made in the protocol design can now be tracked, and the impact assessed to the downstream activities, patient counts. For example if you alter the inclusion / exclusion criteria, how do you know what the impact will be downstream? Once the AI model is connected through cryptography to the ongoing workflow it becomes clear what the impact is, and any changes are verified, tracked and clear for anyone to see.

As part of the Protocol AI model, a tamper-proof manifest is created to bolster trust in the model and transform attestations into an immersive blueprint that provides a real-time visualization of the model's entire lifecycle.

- Registration & Documentation: Capture critical statements about data, model, compute, governance, and transformations.
- Integrity & Trust: Digitally sign each statement to cryptographically establish attributability and tamper-resistance of all inputs, compute, and outputs.

- Verifiability: Use graph data structures to establish chains of lineage for added transparency.
- Federated Collaborations: Registration statements can be produced by many parties, and composed together to describe collaborative processes. These statements can also optionally be anchored on public ledgers, fostering a decentralized approach to AI advancements and added dimensions for transparency and trust.

Making the AI in protocol design responsible:

- Clarity in AI Creation: By labeling AI-generated content and providing metadata for authentic content, we're fostering an environment where origin and authenticity are clear BUT always up to the user on how to control.
- Ethical Foundation in Training Data: Steering clear of problematic data, our tool encourages transparency and ethical practices in AI information supply chains for training and inference..
- Streamlining Verification: In line with emerging standards, our tool simplifies the process of verifying credentials, which is crucial as risk multiple with the mainstreaming of AI.
- Empowering Content Creators: By automating digital signatures, we make it easier for creators to claim and protect their work without having to go to a centralized registry.
- Future Proofing: Create a framework for downstream use of AI in the clinical data workflow to trace lineage but also to establish clear governance.

In the age of AI, there is no more important metric for enterprises than trust. Organizations that operationalize AI trust, transparency, and security will achieve a 50% improvement in adoption and user acceptance.

As companies race to establish credibility in their AI tools, there are an increasing number of standards they must meet to be considered trustworthy. These standards come in three distinct forms:

- Government legislation, such as the EU AI Act
- Risk management frameworks, such as Databricks AI Security Framework
- Responsible AI frameworks, such as the Responsible Artificial Intelligence Institute's Framework
- Internal Policies, Standard Operating Procedures (SOPs) that align with or combine standards 1-3 to streamline processes and minimize compliance risks

Earning high marks from these frameworks is a mission critical business practice, but the current compliance journey is complex, non-linear, and necessitates significant resources.

That's why we have developed a novel methodology that transforms this painstaking process into an automated workflow with verified integrity. We do so by working from the bottom up — we start at the level of a framework's "controls," or rules.

Our novel approach revolves around the atomization of each control in a given framework.

We then automate the reconstruction of an AI model's lineage and traceability for AI models and data, from EHR to submission. Where real-world data plays a role in informing the study design, we trace back to those specific uses of data.

USDM DRIVEN PROCESS

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CONCLUSION

In an AI-driven world, ensuring compliance, governance, and data lineage is crucial for safeguarding your AI investments. By leveraging cryptographic techniques, businesses can create transparent, secure, and scalable AI systems that comply with regulations like the EU AI Act, ICH guidelines and internal SOPs. As organizations navigate the complexities of AI adoption, cryptography offers the assurance needed to innovate responsibly, enabling a future where AI is both trusted and transformative.

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ChatGPT 4.0 assisted with some of the text
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RECOMMENDED READING

https://www.ema.europa.eu/en/documents/scientific-guideline/reflection-paper-use-artificial-intelligence-ai-medicinal-product-lifecycle_en.pdf
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