ONC Blockchain Challenge – Blockchain Clinical Trials

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Summary

This whitepaper shows how blockchain implementations can be used to improve the efficiency and quality across clinical trials in the following areas:

1. Safety reporting
2. Trial data integrity
3. Consent management
4. Computable regulatory compliance

Leveraging the blockchain's capabilities, such as an immutable ledger, hash functions, and the nature of a distributed, trustless system, allows for increased transparency throughout all phases of clinical trials. This is accomplished without sacrificing the privacy of patients or risking loss of intellectual property.

A blockchain implementation can help accomplish several of the objectives set out by US government agencies, such as FDA, ONC, and CTTI, a public-private organization.

Background

Clinical Trials

Clinical trials are studies frequently used to determine the impact of a given intervention, such as a medical product. This whitepaper will assume a context of pharmaceutical clinical trials, however, the blockchain technologies discussed can be applied to other study contexts with little to no change in implementation.

There are four human clinical trial phases which are summarized below. For the purposes of this whitepaper, no assumptions are made as to the phase of the trial.

Phase I	Assessment of safety and evaluation of side effects.
Phase II	Assessment of efficacy and impact of the drug in question.
Phase III	More robust assessment of clinical effectiveness. FDA marketing approval may be granted upon completion.
Phase IV	Post marketing surveillance, often comparing one drug against another.

Table 1: Clinical trial phases

Blockchain Clinical Trials

Clinical trials are costly and time intensive processes in a highly regulated environment. In the current state, high degrees of trust between multiple parties are required for successfully executed trials. Some of the relationships are detailed below.

Patient and study conductor	The patient trusts the study conductor not to publish their personal data and preserve their consent.
Study conductor and regulatory agency	The regulatory agency trusts the study conductor to provide complete and accurate information, such as results, regardless of outcome.
Regulatory agency and public	The public trusts the regulatory agency to accurately approve pharmaceuticals and publish results when applicable.

Table 2: Trust relationships.

These trust concerns are addressed as blockchain is powered by a trust-less system. This means that no central authority is required to ensure appropriate behavior. Instead, all actors in the system can put their faith in the decentralized structure and feel comfortable that the resulting actions are valid.

Regulation: Clinical Research Associates and FDA

Clinical trials are embedded in a highly regulated environment. Regulation is a vital part of ensuring that only safe and effective drugs are introduced to the market. In the United States, clinical trials must conform to FDA standards and ICH-CGP (clinical good practice).

Clinical Research Associates (CRAs) play a key role in confirming that studies follow the stated protocol and that regulatory hurdles are appropriately met. CRAs have several demanding and time intensive tasks that involve verifying consent and protocols, two areas that can be made more efficient through the implementation of blockchain.

Alignment of Blockchain with Government Goals

FDA objectives span a wide range of topics and include improving the efficiency and quality of clinical trials. The comprehensive report of goals can be found in the FDA Strategic Priorities.[1] The implementations discussed in this whitepaper will improve the efficiency of trials in areas such as data integrity and regulatory compliance, as well as improving the quality through consent management and safety reporting.

The Clinical Trials Transformation Initiative (CTTI) is a public-private organization formed by the FDA and Duke University. CTTI has laid out specific goals each year through its annual reports and projects. Among the most recent goals are improved informed consent[2] and safety reporting systems.[3]

[1] www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/UCM416602.pdf
[2] https://www.ctti-clinicaltrials.org/projects/informed-consent
[3] https://www.ctti-clinicaltrials.org/who-we-are/annual-reports

The consent ledger, detailed in the Solution section, works to address several of the specific policy and technical components from the ONC's Interoperability Roadmap.[4] While a case can be made for how blockchain can address several of the initiatives detailed in the roadmap, this whitepaper will focus on three of the primary areas:

1. Verifiable Identity and Authentication of All Participants
2. Consistent Representation of Authorization to Access Electronic Health Information
3. Consistent Understanding and Technical Representation of Permission to Collect, Share and Use Identifiable Electronic Health Information

Solution

Safety Reporting

An immutable ledger can be built to track adverse-event reporting by establishing each submitted report as a transaction in a block.

1. An adverse event is reported to the FDA Adverse Event Reporting System (FAERS)
2. The report is run through a SHA hashing algorithm
3. The resulting hash is used as the private key for a cryptocurrency address
4. A pairing public key is generated by a wallet application.

This means that anyone with the report can repeat step 2 and verify the effectively-notarized report.

The transaction can either be between two placeholder parties to simply notarize the report submission, or, with further implementation, between the FDA and the clinical trial sponsor. The latter serves as a notification system for reporting and improves interoperability by standardizing the dissemination of adverse events to responsible parties with a clear, auditable transaction history.

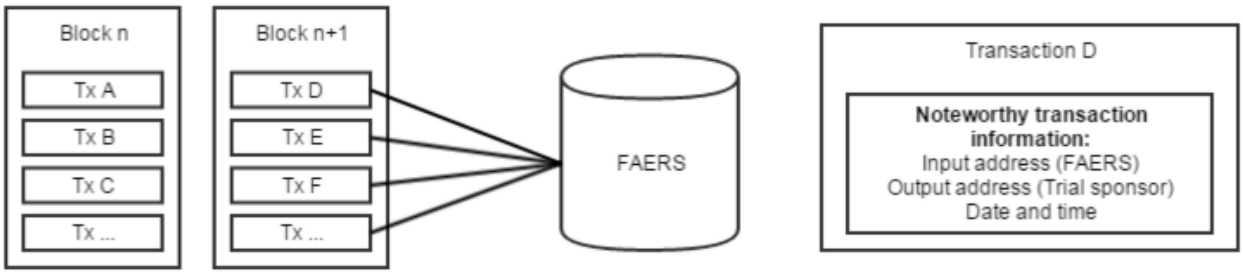

Figure 1: Blockchain adverse event reporting implementation diagram.

Trial Data Integrity

When clinical trial data has been collected, integrity can be preserved by generating a hash of the data file and storing the result on the blockchain. Similarly to the previous safety reporting implementation, this ensures that data is accurate

[4] https://www.healthit.gov/sites/default/files/hie-interoperability/nationwide-interoperability-roadmap-final-version-1.0.pdf

both quantitatively and within the time bounds of the clinical trial. It can be easily audited at any time by anyone with the original data file.

It is important to understand that the trial data itself is not stored on the chain and can remain in the trial's database. The entire process can be conducted without having to expose any data, sensitive or other, and will not risk compromising the privacy of patients and study participants.

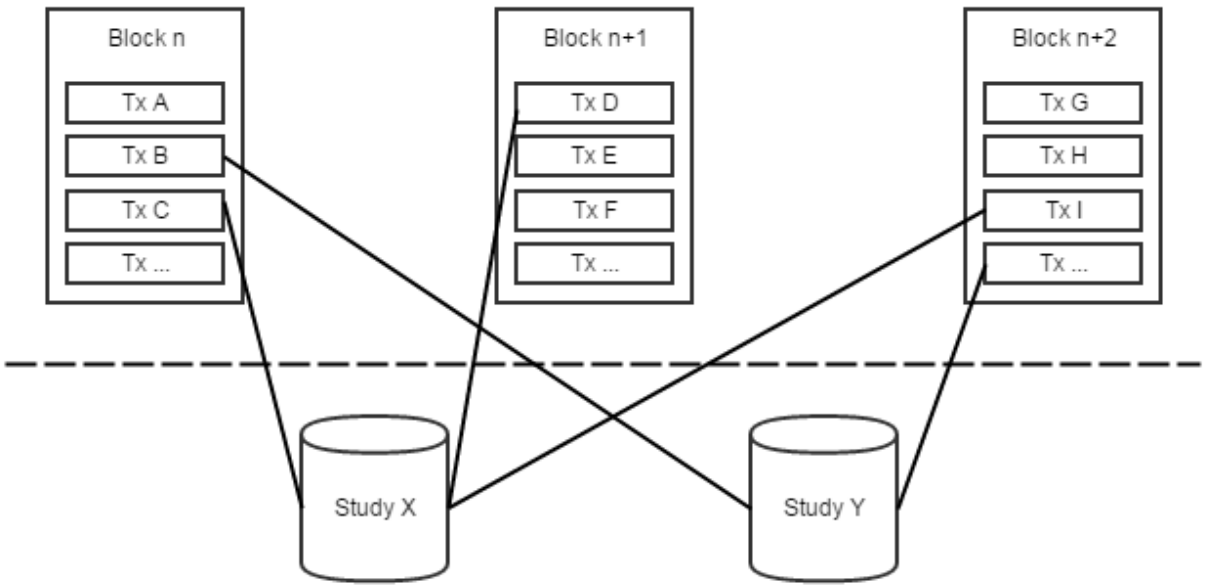

Figure 2: Blockchain data integrity diagram.

Figure 2 shows how Study X and Study Y databases can remain independent and secure while publishing only the hashes of their data files to the blockchain.

Consent Management

A blockchain can facilitate the management of informed consent. Storing consent decisions on the blockchain provides study participants with an immutable ledger of their consent decisions and choices that can be audited in the future and referenced by the clinical trial operators should the participant's decisions change over time.

In addition to a ledger, blockchain provides a robust identity that can be applied to the data owner, the study participant. The resulting output of this combination is a tamperproof chain of custody where the participant or patient is the sole owner. This is a powerful capability that becomes increasingly applicable as clinical trials move towards mobile technology and can enable patients to share data between studies and research organizations.

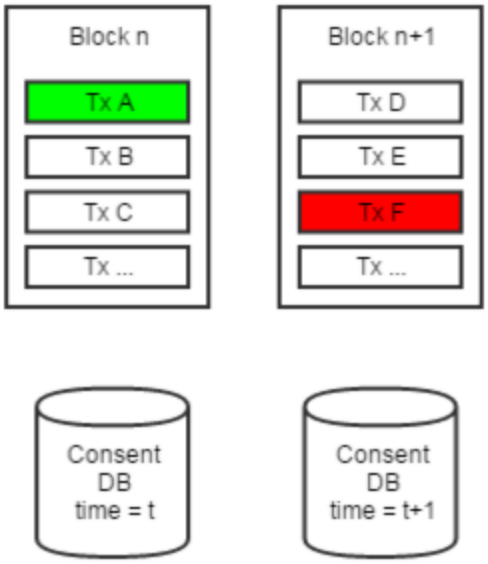

Figure 3: Consent management diagram.

Block n shows Tx A at time t, which represents a consent decision where the patient opted-in to a study. Later, at time t+1, the patient opted-out, which is represented by Tx F. These decisions can be easily identified by a machine to determine the current state of the consent choice and perform an audit if necessary.

Regulatory Compliance

The application of consent management extends beyond data ownership and stewardship, it is also an integral part of the regulatory process. CRAs spend significant time here and it could be relieved by a blockchain implementation.

In addition to boosting management efficiency, the ledger-driven change of custody allows for efficient auditing with complete accuracy and integrity.

Conclusion

Blockchain applications extend far beyond the realm of Bitcoin and other cryptocurrencies. Highly regulated environments should capitalize on the technology's capabilities of immutable ledgers, powerful auditing, data integrity, and chain of custody, all of which are achieved without a central trusted entity. Clinical trials are an excellent example of such an environment and the opportunity for increased efficiency and quality ultimately leads towards healthier patients and populations.