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Evaluating How Blockchain Can Transform The Pharmaceutical And Healthcare Industries

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ABSTRACT

The purpose of this paper is to explain why and how Blockchain Technology is relevant for the pharmaceutical and healthcare industries. Moreover, that this is the time for action. Some of the key driving forces include;Federal/state regulations for industry interoperability and accountability; worldwide demand for patient oriented healthcare; cross jurisdiction and nature of industry; supply chain fraud eroding industry profitability, decreasing patients' trust, and compromising patient's health; opportunities to reduce the inefficiencies of traditional R&D process; unique ability to effectively negotiate the tension between patient data privacy and data sharing; rapid improvements of Blockchain Technology. It is a technology infrastructure, software and cultural movement towards more accountable transactions and decentralized processing. Subtly, it is also a movement towards greater, secure and near real-time machine to machine transactions, this perhaps representing the greatest transformational benefit. In addition, this paper will provide some relevant use cases and how to get started.

INTRODUCTION

Define blockchain and summarize its advantages over legacy technologies. Explore and propose three high-level use cases including an in-depth exploration of two tailored use cases for future proof-of-concepts for the healthcare and pharmaceutical industry on supply chain using smart contracts and patient data access and transparency. Includes a list of prerequisites for blockchain exploration and adoption in our industry.

WHAT IS BLOCKCHAIN

Blockchain is a type of Distributed Ledger Technology (DLT) that can record any transactions of value and share it across a peer-to-peer network. Blockchain can be a private platform with vetted participants or a public open network, such as Bitcoin, where anyone can participate in the maintenance of the ledger. Bitcoin has played a significant role in popularizing blockchain technology and illustrates the problem blockchain originally set out to solve—no central authority—as envisioned by Satoshi Nakamoto's seminal 2008 paper[5]. In the present day, blockchain application has evolved into a platform for enabling decentralized computation across many industries such as food supply chain, government (e.g. Estonian's EHR/EMR, US FDA's RAPID), energy and utilities, consumer retail, pharmacy retail and others.

Within a blockchain each node contains a full, replicated copy of the global ledger; it uses an algorithm called a consensus model to prevent synchronization issues between nodes, including the "double spend" problem. Using Smart Contracts, blockchain can support a vast array of use cases that apply far beyond the finance sector, including healthcare, energy, industry, and research by providing a mechanism that allows untrusted entities to interact and collaborate.

KEY BENEFITS

The key benefits are its inherent traceability, trust, security, and provenance. Blockchain represents the expansion of a distributed database, with the unique capability to fully automate transactions and instantly update an audit log. With medical data transactions, a blockchain can deliver cost-effective improvements that are impossible with existing technology. Unlike with legacy systems, the technical feasibility of a solution is not so much dependent on the data being handled, but rather on the underlying governance protocols. Ultimately, the goal of each protocol is to achieve consensus, but there are varying degrees of portability, accessibility, and immutability core to the blockchain application. To properly review protocols in the context of use cases, permission and transaction speed are two important additional considerations. There are many protocols out in the market such as Ethereum, Hyperledger, IOTA, R3 Corda, OpenChain, and others.

HOW BLOCKCHAIN WORKS: FOUNDATIONAL PRINCIPLES

a. Digital trust and consensus models:

The underlying structure of a blockchain is rooted in the desire to validate and synchronize data that is spread across a decentralized network of computers creating a 'digital trust by design'. A blockchain typically consists of a network of computers containing a shared ledger comprised of transaction data that has been broken into pages, called

blocks. Each block is linked to the previous block using a cryptographic hash function, thus forming a chain, and ensuring that the chain of blocks cannot be corrupted as new blocks are created. As new transactions enter a blockchain network, a consensus model is used to determine which next set of validated transactions will comprise the next block. Proof of Work (PoW) and Proof of Stake (PoS), also known as mining, are geared more towards public networks that yield a cryptocurrency that has value. While Proof of Authority (PoA), used for private networks where a subset of the network nodes are selected as authorities and determines the next block.

b. Authentication:

In blockchain, identity is established using a pair of numbers called a key-pair, which consists of a public key and a private key. The private key is secret and known only to the owner, while the public key (or an address derived from it) is visible to others on the blockchain. The ownership of a private key is what defines identity on a blockchain. Before an individual submits a transaction into a blockchain, they must sign the transaction using their private key. This signature is what enables the blockchain to verify the authenticity of the transaction. It is possible for one private key to be associated with multiple public keys.

c. Immutability:

Every node in the blockchain maintains a fully replicated copy of the ledger. To ensure that the ledger being distributed across the network is the verified version, a mechanism to resolve conflicts between multiple ledgers is required. each block of transactions contains a reference to the block before it; this linkage is encrypted using a hash function to establish a "chain" of blocks. Using a consensus model, the network of nodes determines the next valid set of transactions (block) that should be adopted blockchain network-wide.

PROS/CONS OF BLOCKCHAIN VS. STATUS QUO

PROS OF BLOCKCHAIN	CONS OF BLOCKCHAIN
• **Increase efficiency across the industry by establishing trust among peers (less repetition of work, such as data entry, data cleaning, etc.)** • **Full audit trail (ability to track the source of information)** • **Disintermediation reduces the number of required intermediaries between parties. It shifts the responsibility of validation from a central authority to the distributed network** • **Faster transactions in specific use-cases** • **Lower transaction costs by eliminating third-party intermediaries and overhead costs for exchanging assets** • **Transparency and auditability of signed transactions allowing for more transparency and full disclosure of the information** • **Permanent and immutable/indelible records** • **Clearing and settlement with smart contracts to manage claims in a transparent, responsive, and "irrefutable" manner; ability to enforce claims by triggering payments automatically when certain conditions are met and validated.** • **Reduced counterparty risk by revealing trusted data to another counterparty ahead of trade time to provide greater transparency** • **Protect information database against failure or attack as data is kept decentralized between parties**	• **Limited scalability**: blockchain versions today, like Bitcoin and Ethereum, can only process a small fraction of the transactions per second that traditional companies like Visa process. In order for blockchain to become mainstream, it must solve scalability concerns. It is taking longer and longer for a transaction to be validated by consensus and added to the chain (especially in a public chain). • Lacks ease of use: understood by a small number of experts. Requires end user friendly interfaces as with any other web applications. • Behaviors and culture change that resists new technology adoption • Unknown long-term return on investment • No standardization and validation • Cost of storing data for indefinite period • No data deletion allowed, only updates of data. Potential impacts on GDPR for personal data. • Processing power limited for public blockchain, especially in PoW • Private key management is currently quite complex and non-intuitive, leading to potential loss of digital identity on the chain and possible loss of access to own data

SWOT ANALYSIS

Strengths: Trust, security, transparency, full audit trail	Weaknesses: technical immaturity, not all data is digitalized, scarcity of skills, replaces part of current applications, APIs to be developed
Opportunities: empower patients and increase trust, accelerate drug development, improved treatment and care, reduce fraud	Threats: industry not ready and regulations not in place, complex processes, lack of knowledge, long-term ROI, change management, no standardization

WHAT PROBLEMS ARE WE TRYING TO RESOLVE?

We have identified several different areas where blockchain can be harnessed to provide or support solutions in the pharmaceutical and healthcare industry. High-level examples of how blockchain could be applied to our industry

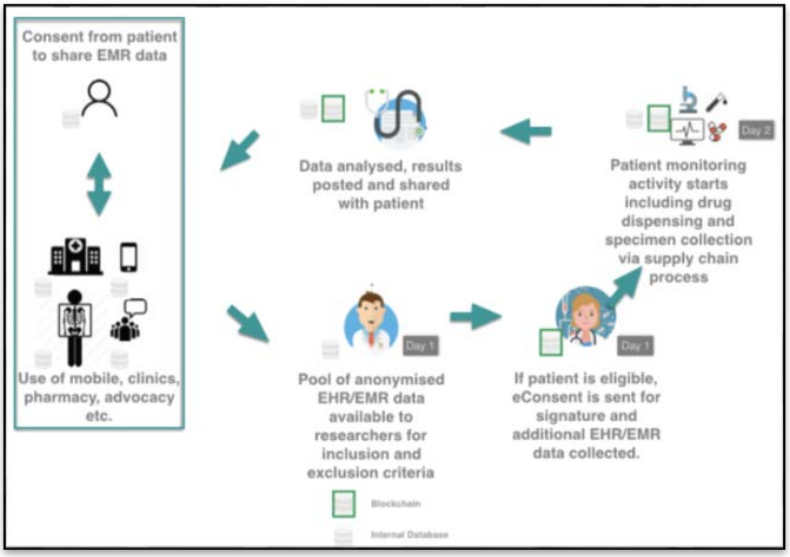
include the following:

- Empower patients to control and access their data (EMR/EHR, Health Apps, Advocate groups, etc.) and decide who and what data is shared peer-to-peer
- Incentivize and reward patient data sharing, while ensuring trustworthiness and control over the data stream
- Protocol algorithms allow system agnostic real-time data sharing and availability during public health emergencies across various healthcare systems
- Address inefficiency of drug development process for patient populations with high unmet patient needs by bringing new drugs early to market and using patient health data consented for:
    - Real World Evidence (RWE) analysis
    - Safety/Efficacy assessment
    - Recruitment into clinical trials
    - Research of the disease and other unmet needs particularly rare diseases
- Provide a longitudinal view of the patient's health journey by enabling permissioned access to patient information for healthcare professionals to better assess patient's health, identify the best course of treatment, and better understand the patient's disease
- Enhance the drug supply chain process by ensuring the validity and distribution from raw materials to production as well as the controlled distribution of end-product to pharmacies and hospitals (tamper-free and according to drug specifications)
- Provide a mechanism for real-time, secure, transparent, and auditable collaboration in clinical research amongst a group of peers
- Provide a mechanism for secure, efficient, and transparent recruitment of subjects for clinical trials, with ability to digitally streamline the process
- Improve data integrity of clinical trials with full audit trail of each record (raw data) to mapping into standards and removing the need for manual quality checks.
- Data transparency for patients, healthcare practitioners, and regulatory authorities to access information in real-time, enabling faster submission for drug applications
- Compliance with data privacy and permissions such as GDPR
- Compliance with the US FDA's DSCSA (Drug Supply Chain Security Act), and Drug Quality Supply Act in the US and Falsified Medicine Directive in the EU
- Oversight of vendor and third parties' deliverables in clinical trial/research with nearly real-time data, thus establishing robust processes quickly and efficiently

General Use Cases for Blockchain in the Pharmaceutical and Healthcare Industries

ACCELERATING PATIENT RECRUITMENT FOR CLINICAL TRIALS BY ACCESSING EHR/EMR

Clinical trial recruitment is a common challenge, especially for special patient populations like pediatrics and patients with rare diseases. Recruitment can take up at least one third of the total clinical trial duration. In addition, approximately 20% of sites recruit no patients. This adds additional cost to the conduct of clinical trials, delaying the right treatment access for patients. On average, it takes 14 years for new drugs to reach the 1st market (cost of over 1 billion USD). These timeframes and costs have not improved in over a decade.

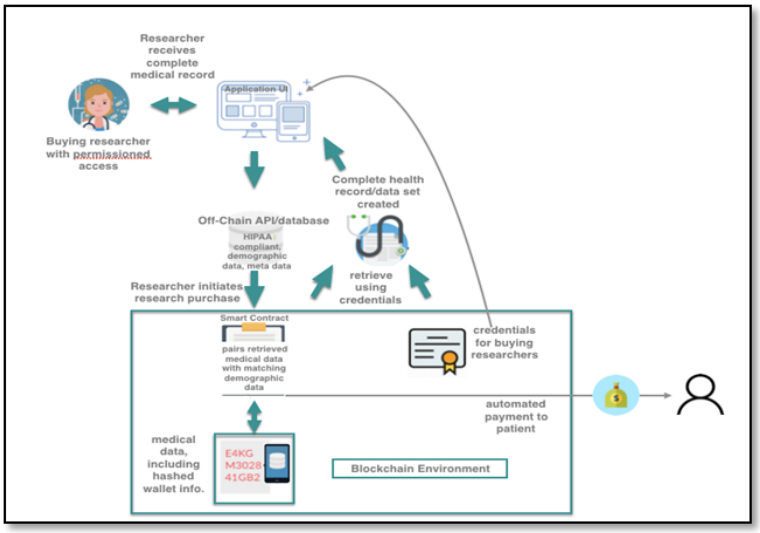


In the figure above, if a patient is interested in participating in a clinical trial due to unmet needs (e.g. no adequate or available treatment) and owns their data, he or she could contribute a set of EHR/EMR (using FHIR standards) data anonymized through the blockchain. As a result, this allows researchers to access the information and verify the

inclusion and exclusion criteria. The researchers or investigators (e.g. virtual sites) would have access to a pool of data and any patient who qualifies could be requested to provide additional data and to e-sign the e-Consent. In the best possible case, the recruitment for a given trial could be completed in the space of **one day** with a substantial amount of the data already collected, allowing clinical trial to begin on Day 1 or Day 2. The patient data would be shared from a public or private blockchain (on-chain) to a private clinical trial permissioned blockchain with investigators, the sponsor (pharmaceutical company), vendors, central laboratories, etc. where the data can also be shared through internal systems/databases (off-chain). Taking into consideration the data integrity, interoperability, near real-time access, additional security, and other benefits blockchain can provide in comparison to the available systems, this means that the drug can potentially be available 3-5 years sooner than a traditional drug development process.

INCENTIVIZING PATIENTS AND ENABLING THE ACCESS OF PATIENT DATA FOR CLINICAL RESEARCH

Studies have consistently shown that as many as 87% of patients are motivated to share their health information to help other patients and contribute to research. Accessing EMR data has been challenging as patients are seldom the true proprietors of their personal health data. Therefore, health data mining and the sale of health records comprise a multi-billion-dollar industry whereby intermediary companies purchase patient and provider data from commercial pharmacies, insurance companies, and EMR systems. These data are usually anonymized, analyzed, and resold for research purposes such as for clinical trials, RWE studies, etc. The patient in turn has neither control over the future use of their medical information, nor any direct knowledge of the individuals and companies handling their data. In fact, despite signing consent forms, most patients may be completely unaware that their data are sold and resold.



Blockchain technology enables an open source platform by storing HIPAA-compliant demographic data off-chain, allowing pharmaceutical researchers to directly purchase anonymized data from patients per above figure. When the purchase of a full dataset is initiated, the Smart Contract matches the demographic data to its corresponding medical data. This process thereby links the demographic dataset and the hashed medical dataset for use in addition to initiating payment into the patient's wallet (e.g. using health tokens or ether). The pharmaceutical researcher then decrypts the combined health record for analysis. By using the blockchain as the central hub in this sample architecture there is a lowered risk of a large-scale HIPAA violation even if the off-chain database were to be compromised. While such an exchange has the power to both reduce the cost of research and return ownership of health data to patients, its implementation will be dependent upon the presence of an interoperable EMR system. Using blockchain technology, this type of formerly unachievable data exchange may become a reality in the near future, thereby bolstering the notion that even anonymized data still belongs to the patient.

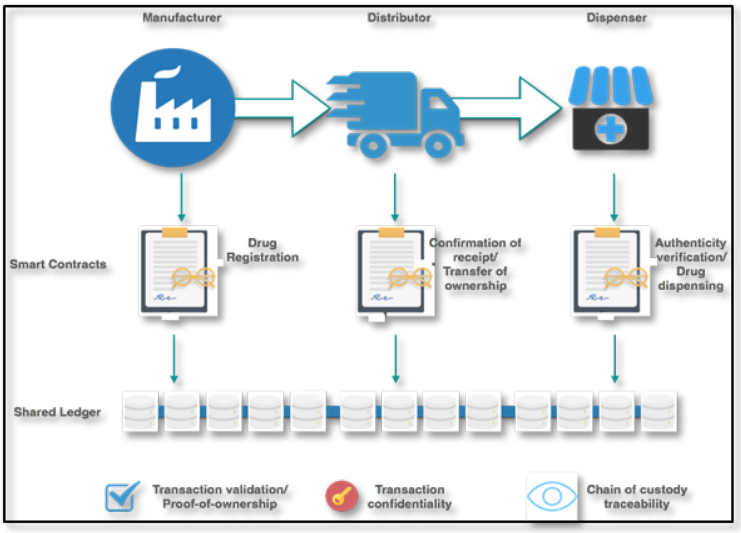
TRACEABILITY ACROSS THE DRUG SUPPLY CHAIN

We have seen the drug distribution network grow immensely in scope and complexity while lagging behind other industries in its ability to simplify and secure the process. Amongst other issues, current supply management systems lack visibility (transfer of ownership) to track the authenticity of the medicine from manufacturers to the patient.

Globally, counterfeit drugs sales amounted to $75 billion in 2010 according to World Health Organization (WHO). This 90% increase in fraudulent drug sales over 5 years leading to approximately 100,000 deaths worldwide. In Asia, Africa, and South America, counterfeit drugs comprise between 10-30% of total medicines sale. Despite massive seizures, a single Interpol operation in 2015 seized $81m worth of counterfeit medicines, arrested 150 people and removed 2,500 fraudulent websites. The issue of counterfeit drugs is pressing, poses a risk to patients, and has a

large economic impact.

Governments around the world are tightening the supply chain integrity to slow down the global flow of counterfeit medicines. The European Commission and European Parliament produced the Falsified Medicines Directives published in 2011, stipulating that pharmaceutical drug supply chains serialize their products for track-and-trace by Feb 2019. The US Congress introduced the Drug Quality and Security Act (DQSA) in 2013, giving the industry until 2023 to build an electronic, interoperable system to identify and trace certain prescription drugs as they are distributed in the US30.



Blockchain can help to resolve current challenges in the supply chain, by providing traceability until the point of delivery per above figure. Blockchain can provide the immutable and interoperable shared ledger using Smart Contracts, updated, and read by all participants in the drug supply chain, creating the ability to monitor the journey of the product through serialization from manufacturers, distributors, re-packagers, and wholesalers before reaching patients; creating full visibility throughout the drug supply chain process. The immutability of the blockchain limits the possibilities for fraud and increases the overall trust in the product and the supply chain. It allows the quick identification and removal of contaminated drugs and can improve the management of shelf-life and waste of expired products.

RECOMMENDED USE CASE 1 AND 2 FOR PROOF OF CONCEPTS

USE CASE 1: CAPTURING EFFICIENCY AND ENSURING QUALITY IN THE SUPPLY CHAIN USING SMART CONTRACTS

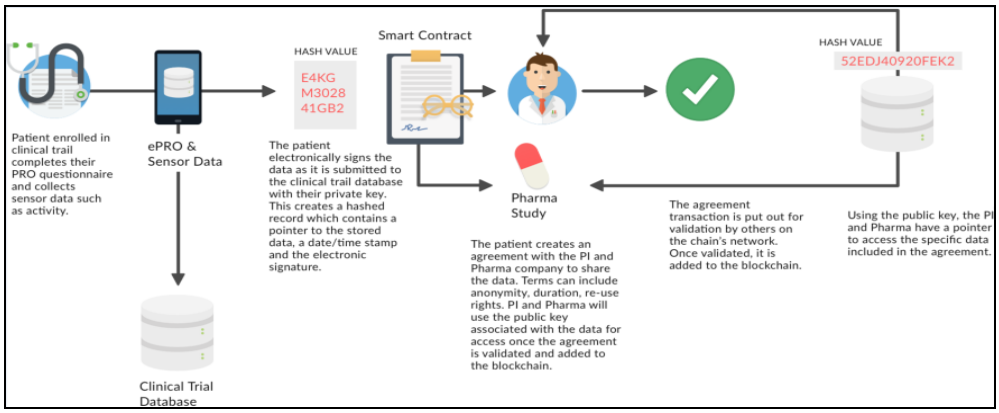
Using a blockchain-enabled management tool, companies can perform end-to-end tracking in the supply chain. Assets, such as raw materials, Active Pharmaceutical Ingredients (API), and packages, can be digitally inventoried, and a decentralized immutable record of all transactions created, allowing end users (anyone who has access to the blockchain key) to track these assets from sourcing to delivery.

To unlock the full power of blockchain, the technology should be forward deployed to contractors and subcontractors to ensure the integrity of the whole supply chain. For example, everything from shipping containers to truck deliveries could be equipped with sensors that transmit business-related data (such as temperature- cold chain) to a platform using the Internet of Things (IoT). The data is visible to all personnel with key access and can be analyzed in real-time. If the quality of the containers (as judged by the analysis data collected by sensors) falls below an acceptable threshold, indicating a potential breach of contract, the Smart Contract can be triggered, and the system will automatically deliver an insurance proposal, penalty to freight forwarder or distributer centers, and order of product replacements.

Because of the enhanced transparency and automation, communication or data transfer errors can be greatly reduced. Companies and contractors can streamline their processes on data validation, drug accountability/inventory management, labelling, and audit through the use of distributed ledger technology. In addition to increasing efficiency, blockchain also helps to enforce contractual terms in a timely manner.

USE CASE 2: PATIENT DATA ACCESS AND TRANSPARENCY

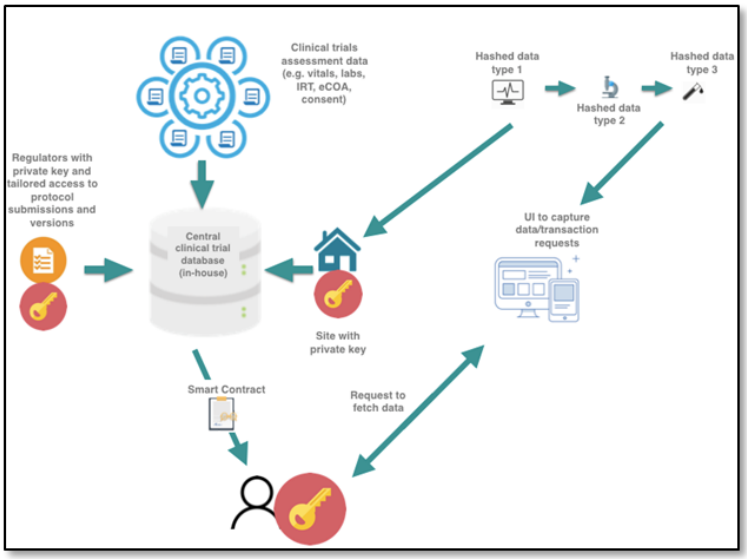
This use case enables patients to join the blockchain network at specific time points on their clinical trial patient journey to access their data directly such as through activity monitors or indirectly through third-party lab databases.



This solution enables patients to control access and also receive full disclosure of their own data at will. This would be a private network for patient data transactions and a public network recommended for the incentivized use of tokens.

The pharmaceutical and healthcare industries have historically struggled to increase support from the general public (patients) to join clinical trials. This is largely due to low levels of trust regarding the transparency of drug safety. A recent survey conducted in 2017, by HealthUnlocked on 126 patients confirmed a strong interest for patients with chronic diseases to access and share their data. This survey showed motivations for wanting to share data include having the ability to help others through research using their data while accessing reports on data transactions conveniently using Apps.

The evolution of traditional site-based trials to remote or virtual trials (such as “Remote”) can greatly benefit from blockchain for patient eligibility, consent, distribution of investigational drug, and remote assessments to meet regulatory requirement. This enhanced model would enable the prospective collection of data points from potential patients even before a clinical trial starts. This would provide not only eligible patients to enroll from Day 1, but also a large amount of study data already collected and cleaned. A patient eConsent process on a rolling basis would allow patients to provide multiple permissions for use the of their data (across multiple trials).



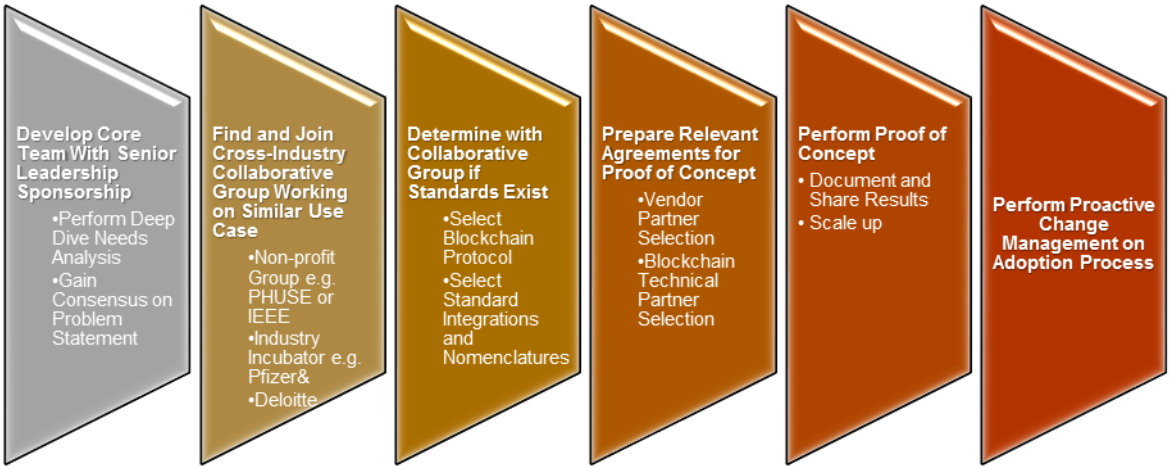
The explosion of wearables, sensors, and genomic screening have accelerated the gathering of patient data in recent years. Sensors are becoming smarter and cheaper than ever, while genomic screening costs are plummeting. Furthermore, cloud architecture and analytics provide a solid foundation for data sharing and data processing.

Wearables companies like Fitbit have started regulatory filling processes with FDA to enable consumers ownership over their own health. According to Gartner, by 2020 40% of employees will be able to cut their personal healthcare costs by wearing a fitness tracker. Other companies like Apple have started offering access to remote clinical trials through its Research Kit, simplifying the process for both recruiters and participants.
Blockchain is a clear enabler in this overall ambition, with 2 basic roles: first, it allows patients to grant permissioned access to their data; and second, in a complementary process, Smart Contracts automate compensation for data

purchase through tokens dispensed into patients' smart wallets.

For patient data in a clinical trial, we propose starting with the metadata level of data and defining the critical and valuable data (assets) that will enable a significant benefit to the clinical trials cost, patient safety, and data integrity. Examples include electronic PROs or CLINROs data, EMR/EHR, imaging, and blood tests including genetic sampling.

IMPLEMENTATION FRAMEWORK FOR PROOF OF CONCEPT



GETTING PHARMACEUTICAL INDUSTRY READY FOR BLOCKCHAIN: NEEDS, RISKS, BARRIERS, AND PRIORITIES

Pre-requisite	Recommended Actions
Understanding regulations and compliance	It is critical to understand regulatory compliance such as GCP, and data privacy laws (HIPAA, GDPR). Due to lack of regulations and standards on this new technology it's essential to collaborate within the industry and regulatory agencies. How can we give access to authorities for auditing transactions? Clinical trials audits typically include these contracts and payment systems which would also need to be visible and accessible by regulators when requested.
Talent	Adopting blockchain will require a rare breed of cryptographers and blockchain-literate subject matter experts to develop this new technology to ensure a smooth implementation.
Pick the correct use case	Blockchain is not the solution for every business problem. Start by identifying the needs that the current system is not able to support, then customize your best blockchain use case solution with a clear value proposition. Integration with existing systems and processes should follow. Clearly understanding your reasons for exploring blockchain and the desired outcomes of all parties will help steer proof-of-concepts effectively and support decisions to stop, go, or grow them. This should in turn avoid premature ends or sunk cost reasoning.
Create the right network	A cross-industry collaboration with regulators will accelerate adoption. Join or create a consortium of necessary participants in exploring and applying blockchain. The network structure should formalize some of the stakeholder management and communication essential for successful technology adoption.
Strategic alignment	Consider your strategic focus (ROI and trade-offs) and choose the best-fitting use case for your organization by measuring KPIs against time, cost, quality, and reputation.
Effective risk management and avoidance	Adopt a collaborative approach to risk management by performing a risk assessment plan. Ensure the right level of stakeholder engagement and right skill sets for implementation. More importantly, conduct pilots and proof-of-concepts in small iterations to address all possible issues and streamline processes before scaling up. The inter-dependent nature of blockchain means that risks to one party may be applicable to others or may carry knock-on risks. Execute a bold proof of concept (PoC) as this will identify real-life risks and opportunities to maximize the potential of this technology.
Exit strategy	In a distributed smart contract network, consider how easy it will be to change models, if necessary, since information is shared. What if parties decide to return to a centralized system? This should be detailed in a charter to which all parties consent as part the agreements. Legal clauses in this consideration should be added to contracts.

Change management plan	It is essential to prepare the organization for the paradigm shift. Identify your stakeholders and blockchain champions to drive for quicker adoption of the new technology across the organization. This collaborative approach will require mutual recognition and transparency of interests among all participating stakeholders (Fig. 3).
Industry standards	Standardization is critical to enable blockchain-to-blockchain integrations, especially in the flow of assets/transactions from one network to another, and even more so when there are multiple networks and/or consortiums. Such interoperability minimizes the cost of implementation in the long run.
Reputational damage	Ignore the 'wild-wild-west' reputation of bitcoin that affects the reputation of the agnostic blockchain protocol. Instead concentrate on understanding and explaining the qualities of blockchain that will have benefits in pharma.
Cost	Proof of concept in start-ups is expected to reduce the cost of infrastructure; remember to hire and train talent with the right skill competencies. Participating and collaborating in a consortium will leverage the implementation of existing blockchain platforms to optimize cost. While the time and cost may be greater than creating your own vanguard, the consortium approach ensures no one member bears all the costs of PoCs, you gain insight from diverse perspectives, and you cover several prerequisites by necessity. Once established, it is expected that there will be significant cost efficiencies to scale up the solution. Multiple single-player solutions would be unappealing for some companies that would need to deploy various APIs for the different e.g. supply chain blockchains. Clarification is needed on who pays for the transactions and maintenance of the network. In terms of the additional code, it needs to be taken into account how this becomes applied to the enterprise systems and if this will be fully integrated and not hosted.
Architecture	Being in a heterogeneous environment, we need to deal with off-chain transactions to avoid problems of reconciliation and duplication. This will support blockchain as a single source of truth as adoption increases.
Governance model	As with all software; there will always be bugs; if a smart contract does not form as required, additional tools may be employed to resolve any dispute. We will need to gain consensus on these tools as adoption increases.
Other digitized tools	Cloud-computing and IoT will enhance the digitization of physical assets into data points for example in supply chain, allowing for real-time analysis of supply chain activities.
Vendor selection	There has been increased activity by large pharmaceutical companies partnering with blockchain experts to deliver proof-of-concepts of smart contracts with payments solutions. Choosing the right vendor to understand the user stories (business processes) and have the right capabilities will be critical to implement blockchain successfully.

CONCLUSION

The conclusion summarizes your paper and ties together any loose ends. You can use the conclusion to make any final points such as recommendations predictions, or judgments.

We acknowledged that through joint collaboration we will see quicker adoption of blockchain in piloting robust use cases and processes supporting its implementation. It is an exciting time for this technology to demonstrate its benefit and potentially transform the pharmaceutical industry. The argument that blockchain is simply another database can be dispelled when one understands that blockchain's benefits reside in its unprecedented provision of transparency, immutability, and efficiency, while bolstering trust and reputation. These benefits enhance access to data and can increase the volume, veracity, validity and velocity at which patient data becomes available for research and patient care. Technologies to analyze and visually report on these types of data assets also need to mature to maximize blockchain's full potential.

Adoption of blockchain technology by the healthcare and pharmaceutical industries will undoubtedly require efforts across industry and interests; however, we believe that this paper can provide a launch point from which we all, as industry collaborators, work to bring forth one of the most promising technological paradigms of our time.

ACKNOWLEDGMENTS

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