BLOCKCHAIN
for Pharmaceutical Engineers

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This article discusses how blockchain technology may disrupt the way we collect and manage data within regulated processes. The first section is a nontechnical summary of blockchain's features, including a description of what it is (and what it is not). This sets the context for the next section, in which we discuss several blockchain use cases currently being piloted by life sciences companies. In the final section we explain how you and your organization can leverage blockchain technology.

If you haven't heard of blockchain yet you probably will soon. The technology behind the cryptocurrency craze has been gaining momentum since early 2016 and shows no sign of slowing down. Blockchain is now making its way into life sciences companies across many different operational disciplines. *PE* magazine published a feature article in the July-August 2018 edition titled "Blockchain: The Next Disruptor in Clinical Trials." [1] While this is certainly a great use case, it is only one of many that are being pursued within the industry. Before we look at blockchain applications in life sciences, let's begin with a primer on what it is.

BLOCKCHAIN

What It Is

To many people, blockchain and cryptocurrency (bitcoin being the first and best known) are synonymous. The former, however, is the underlying technology and the latter is an application of that technology. While the two are related, it's important to understand that the volatility of the cryptocurrency market does not mean that blockchain technology is volatile. It is still evolving, though, and as with many new technologies there is currently much hype and speculation about how it will change the world. This initial excitement and speculation will fade as the technology matures. But blockchain is a fundamentally new way of sharing and trusting information, a new communication protocol for exchanging data between computer systems. If successful, it will become the foundation for many technologies, in much the same way as TCP/IP (Transmission Control Protocol and Internet Protocol) did when it was introduced in the 1980s, allowing for the development of the now-ubiquitous Internet. [2]

What do pharmaceutical engineers need to know about blockchain? That depends on a lot of factors, many of which are still being explored by the communities who are evolving blockchain protocols. But there are a few fundamental concepts that are likely here to stay, and they will shape the way we redefine our processes to capitalize on this technology. To put this in context of a pharmaceutical manufacturer let's consider the simple distribution model in Figure 1.

In this example we can think of each transfer of the finished good as a transaction on the blockchain. To manage and track those movements we will use foundational blockchain elements:

Transactions: Blockchain networks are peer-to-peer transactional systems. This means they track exchanges between parties that use the network as a medium of exchange. Among other things, this allows transactions to be time-stamped based on the network protocol (i.e., outside the control of any one individual). While blockchains are considered databases and some additional information can be included in each transaction, they are not large data stores, nor are they organized in typical relational tables with rows and columns.

Distributed ledger technology: All blockchains are a form of distributed ledger technology (DLT)—but not all DLTs are blockchains.

- The "ledger" part of DLT is simply an ordered listing of transactions, not unlike your credit card statement. As we'll explain in more detail later, these ledgers are "append only"; new records can only be added to the end of the ledger, and once added cannot be changed.
- "Distributed" means that instead of having one source maintain your list of transactions (e.g., your credit card company) many sources maintain the list.
- "Technology" refers to the protocol that defines how the distributed ledgers will be kept in sync. It does this through a mechanism called "consensus." Different DLTs have different ways of reaching consensus.

DLTs create a redundant and resilient network that no longer needs a central authority to maintain the integrity of a transaction list. Of course, it also introduces concerns around how public this information is and who can see what; people do not make it a habit of publishing their credit card statements, for example. This is where cryptography comes in.

Cryptography is at the core of blockchain functionality. It is both how we secure transactions (using public and private keys) and is a part of how we make sure that only authorized individuals can view certain information about transactions.

One of the most utilized tools in cryptography is hashing, in which an algorithm (a piece of computer code) generates a unique identifier for just about anything digital. A hash of the letters "ISPE" using an SHA256 algorithm looks like this:

```
E7AE003CF0974DEC21E4BB10C0EB3ECD1B-
C389471C8CDA83798AA825C51C04B9
```

Hashing is one-way encryption; if you have only this hash there is no way to figure out what it means. If you were given "ISPE" and knew the algorithm that was used, however, you could reproduce the same hash. Most hashes are very sensitive. Even a minor change in the original input produces an entirely different hash ; for example, the hash of "ISPe" using the same SHA256 algorithm:

```
481A9F91046AEF67E2D2407C05C3E6EE-
C52894108794324A2B2A1DBF0CBBB880
```

There is currently a lot of development around privacy within blockchains, and this is an area that is expected to generate significant advances in the near future.

Hashing of hashes: One thing that sets blockchain apart from traditional distributed computing systems is the concept of "hashing of hashes" to make an immutable chain. Blockchains group transactions into "data blocks" based on when the transaction was posted. Once verified, a hash of each transaction is generated to prove that the data was not altered. The blockchain protocol then combines each transaction hash into a tree structure (allowing us to search the blockchain faster) and creates a hash of all the transaction hashes it contains. When the next block of transactions is created, the hash of the previous block is included in the overall block hash, effectively "chaining" the blocks together. Because a change in the source data would result in an entirely new hash, changing a past transaction would invalidate the hash of that block and invalidate the hash of every block that occurred after it. This is known as being "tamper evident" and it leads to the next blockchain element.

Immutability: Once a transaction (and any data associated with it) is stored in a blockchain, it cannot be altered without others knowing about it (since the ledgers are distributed). Any change will be evident, since records can only be appended to the end of the blockchain. Rewriting history would require a massive coordinated effort to change all of the ledgers simultaneously. This does not mean that transactions posted in error cannot be corrected; it just means they must be reversed by a subsequent transaction, and there will always be a record of that reversal. It would be better to prevent those mistakes by implementing rules or controls on your blockchain. This is where smart contracts come into play.


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Smart contracts are pieces of logic—business rules—that can be deployed on a blockchain. They act as an "account" where transactions can be sent when certain conditions are met (defined by the contract logic). They can generate "events," which are typically another transaction. Most blockchains that support smart contracts deploy them in a way similar to posting a transaction—that is to say, once the contract code is written and posted to the blockchain it cannot be changed. In life sciences companies, many controls that exist in our systems could be pushed into smart contracts. This would allow rules to apply across disconnected systems. A smart contract might prevent inventory movement once the expiry date has been reached, for example. The expiry date could be set by the manufacturer but the inventory might be managed by a wholesaler or dispensary. Accomplishing this in today's world would require a set of interfaces or electronic data exchanges.

Tokenization: Transactions within a blockchain are often an exchange of value between two accounts; to keep track of that value blockchains use tokens. "Fungible" tokens, used in cryptocurrencies and mobile pay phone apps, can represent a utility or can simply be a store of value; they are non-unique and interchangeable. Of particular interest to life sciences, however, companies are "non-fungible" tokens (NFTs). These represent unique assets such as serialized unit of a drug or a uniquely identified medical device. NFTs can be created, transferred, associated with other another, and consumed (destroyed). Product provenance can be captured on a blockchain by tracking the movements and changes to an NFT. The "tokenizing" process creates and maintains the tokens on a blockchain;

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this is likely where a lot of effort will be placed as companies begin to use blockchain as an exchange medium for assets. You can see how this works by tracking the asset on the blockchain in Figure 2.

What It Isn't

Having noted some of what blockchain is, here are a few things that it is not.

Blockchain is not a silver bullet, nor is it a unique stand-alone solution. Blockchain will most likely be a backbone that connects systems or business partners, but existing systems will still play a role and will need to be integrated into the blockchain to trigger events or record important information. Leveraging blockchain may introduce additional data-sharing requirements to store and secure off-chain data.

Blockchain is not bitcoin. Bitcoin is the longest-running blockchain experiment, a cryptocurrency that uses a blockchain network to pass value between accounts. It is unlikely that the first production use of blockchain in life sciences will be tied to bitcoin or any other cryptocurrency.

Blockchain is not an application. While it is possible to build a new breed of distributed applications on top of a blockchain, the blockchain itself is not an application—it is a protocol-based network. Many blockchain network protocols such as Ethereum (an open blockchain platform), allow smart contracts to be executed within the network itself. Because the network can execute logic it can be thought of as a virtual world computer, though this still would not be an application.

Blockchain will not store all your data. This must be underscored when considering use cases for blockchain. Though it is a distributed database, it is not a database in the traditional sense. It is designed to store a ledger (or an ordering) of transactions, each one being only a few bytes of information. Most blockchains incentivize users to keep transactions as small as possible. When transactions become too large, or when there are many transactions, latency is introduced into the blockchain (making it less functional). As technology advances, current scalability issues will be addressed, but the underlying principles of small data will still be applied. This means that blockchain integration points will not look like the electronic data interfaces currently utilized in life sciences companies today.

POTENTIAL USES

While there are many fascinating predictions on how blockchain can be applied within the life sciences (a quick Internet search of "blockchain for pharma" will provide enough reading material for several days), the following features will probably drive the first production uses of the technology.

Anti-censorship and data integrity: This is blockchain's *raison d'être*—the purpose for which it was created: the need for records that cannot be manipulated or repressed.

Chain-of-custody, asset tracking, and immutable audit trails: This can be serialization, but that will likely just be a byproduct of a network that can track the exchange of assets between parties. The reliability and transparency of that tracking will change the way we account for the value of our assets, determine legal ownership/custody, and calculate tax due to movements between tax jurisdictions (just to name a few).

Proof of existence: Time stamps certify events on the blockchain in the order in which they occurred—if an asset were posted 100 blocks back, you would know that the asset had to have been in existence at that time.

Connecting the Internet of Things without integrating it all. Blockchain is both a network and a database. This means that it can be used to store and share data from many sources, including IoT sensors and existing systems, without needing to "connect" those sources in a traditional sense. As pointed out above, blockchain is not meant to store big data, so designs must specify what is captured and posted.

Data privacy and authentication: Blockchain goes beyond two-factor (username/password) authentication, providing a good mecha-

Figure 1: Simple distribution of a finished good

nism to store consent, or grant/revoke access. Interesting solutions are being built on top of blockchains that will allow people to better control their personal data. These solutions also offer a reliable way to track how organizations manage personal data, something that will be useful in supporting compliance with data privacy regulations.

USE CASES

A recent article published by McKinsey & Company [3] identified the strategic importance of blockchain by industry. Several of the health care use cases discussed have also been topics of discussion in recent GAMP® Community of Practice (CoP) forums.

Health care research: As medical information begins to be stored on blockchains in the form of transactions associated with individual patients and treatments, a rich and reliable data set will emerge that may change the way new drugs or incentives for preventive care are researched. This new way of recording history may also challenge many of our existing policies for data management.

> *Currently, blockchain is a double-edged sword. The features it is known for are also problematic for trading partners. For example, immutability is beneficial but can also go against a company's data retention policy where data owners have the right to delete their records. Visibility is key and so is privacy. Conversations between industry stakeholders and blockchain platform developers will be pivotal to work out balance between the need and the possible."*
>
> —Bob Celeste, Founder, Center for Supply Chain Studies

Identity and data security: With the potential of managing medical records on a blockchain come risks associated with data privacy and security. Several initiatives currently underway are exploring blockchain as a means to govern information exchange, verify digital identity, and authorize (or revoke) access to use personal data. This places the ownership (and control) of information back in the hands of the individual and may play a key role in connecting our ecosystem in a secure manner.

Blockchains will change the way we trust and share data between business partners

Blockchain is both a network and a database

Blockchain also holds great promise for the healthcare industry, in addressing current challenges like interoperability of data systems and data security. [4]

—Vas Narasimhan, CEO Novartis

Drug supply chain: With serialization and unique device identification major factors in the pharmaceutical industry, certain distributed ledger solutions offer a tremendous benefit in proving the provenance of the drug supply chain. Many of these also incorporate IoT devices to register environmental factors that might affect drug stability during transportation and storage.

We are looking to use the unique capabilities of blockchain technology to create a permissioned distributed network for the Pharma industry that will deliver a step function improvement in prescription medicine security. We believe the ability to curtail diversion and counterfeit is possible by creating a confidential chain of ownership as drugs change hands. It is exciting to work with industry leaders who are actively experimenting to see what this technology can do.

—Susanne Somerville,
Head of Pharma Solutions, Chronicled

Clinical trials: From managing patient registries to securing trial protocols and results in an immutable manner, blockchain use cases in the clinical trial space are plentiful. Blockchains can bridge communication, trust, and privacy gaps between contract research organizations, sponsoring organizations, and regulators.

Blockchain will do for a network of companies what the ERP did for an individual organization. In life sciences this is about creating both fluidity and traceability within R&D and our drug supply chain; this will help keep patients safe while making the approval of new drugs more efficient.

—Paul Brody, EY Global Blockchain Leader

While there is much potential around the development of use cases that capitalize on blockchain, solutions for some of the industry's more intractable problems are still a few years away. As the technology is still evolving, it is crucial to capture the use cases now; this will help refine and incorporate requirements into open-source standards that will shape future blockchain transactions. One such standard is Ethereum Request for Comment (ERC)-721, [5] which defines a standard for transmitting NFTs (e.g., serialized drugs and devices) on an Ethereum blockchain. This touches on another interesting change that blockchain is introducing to life sciences companies—the application of open-source development to solve industry-wide problems.

There is a lot of power in open-source development, each successive application is built using the lessons learned from others within the community—this lets us avoid making the same common mistakes and lets us move faster with better quality. The trade-off is companies will need to be comfortable sharing their code and be willing to incorporate designs from the broader community.

—Will Entriken, Blockchain Developer

OPENING THE BLOCKCHAIN DOOR

So where will this lead the life sciences industry? Blockchains will change the way we trust and share data between business partners. This in turn will change the way that we ensure the integrity of that data when making decisions. From a regulatory perspective, companies will have to understand what that means and be able to explain it to regulators. As more and more control points are pushed into the blockchain via smart contracts there may be "business rules" set by external upstream suppliers that are enforced by internal systems. (Consider, for example, the expiry date example from the perspective of the wholesaler.) To understand and capitalize on these changes it is important to experiment with blockchains and "get your hands dirty" in these early days. The community of developers is hungry for use cases and practical applications of blockchain. The life sciences are rife with such use cases.

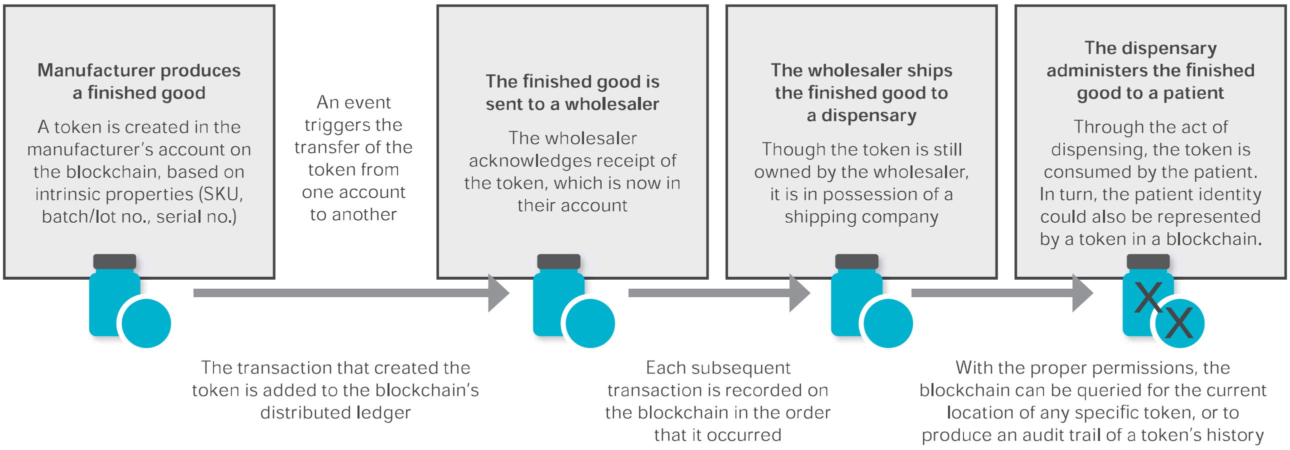
HOW TO GET STARTED

1. **Learn the ropes.** It's likely that your organization, or one of your business partners, is already running a blockchain pilot. The protocols themselves are generally free to download and many create easy-to-install test environments that come complete with step-by-step tutorials. The blockchain community tends to be a collaborative one; it may be as easy as reaching out.

2. **Educate yourself.** There are lots of great online do-it-yourself tutorials out there, though many will quickly take you down a technical track. Service organizations increasingly offer blockchain education sessions or sponsor workshops to help identify and design use cases.

3. **Build an application.** This may not be everyone's forte, but there is no better way to learn about what the technology is capable of than to try to make it do something. Whether you initiate a proof of concept within your organization, join an existing one, or even just experiment on your own, getting familiar with the nuts and bolts of blockchain now will serve you well in the future.

Figure 2: Distribution of a finished good tracked by a tokenized asset



4. **Join the GAMP Blockchain SIG!** Many of the authors of this article meet monthly to discuss the latest trends and developments and hear from industry speakers about their exciting projects. Through our CoP website we are also building an inventory of great reference articles and case studies within the life sciences.

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