

CA GOV OPS BLOCKCHAIN WORKING GROUP

BLOCKCHAIN APPLICATIONS IN PHARMACEUTICAL SUPPLY CHAINS

By Radhika Iyengar and the Office of Ian Calderon, CA State Assembly Leader
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I. Introduction¹

The global pharmaceuticals industry is big business, valued annually at \$1.2 trillion. Pharmaceutical companies spend tens of billions of dollars and go through an arduous process to produce and commercialize prescription drugs. According to the World Health Organization, the counterfeit prescription drug trade is 10% of the global market.

Fake drugs for every therapeutic treatment exist, with a majority of falsified drugs targeted to chronic illnesses, antibiotics, antivirals, as well as alimentary drugs such as cholesterol and diet pills. In the US, we are also seeing demand for opioid drugs, particularly those with fentanyl, a synthetic opioid. According to the Centers for Disease Control (CDC), fentanyl-related overdose fatalities are rising exponentially – from 2013 to 2016 fatal overdoses involving fentanyl have doubled each year, leading to tens of thousands of deaths.

With the mega billion-dollar global counterfeit drug market annually, there is a clear motivation in the pharma sector to fight counterfeiting. What is also at stake are human lives, with adverse reactions and effects to these fake drugs leading to illness and hospitalization and fatalities. In emerging markets, 10-30% of prescription drugs are counterfeit, and in certain parts of the world, up to 50% are fake. Issues range from tampered drugs to drugs with incorrect, often toxic, ingredients or incorrect proportions of ingredients.

Most of the counterfeit drugs are being produced in China and India but sold worldwide. A very relevant example of this type of fraud is the China vaccine scandal of 2018 where a government vaccination program was found to have administered hundreds of thousands of faulty vaccines to young children. In the US, the DEA (Drug Enforcement Agency) continues to conduct raids of fentanyl opioids. Various studies have shown that most of these opioids in the US are coming from China. In April 2019, China acknowledged the severity of the crisis and issued a ban on all fentanyl-related substances.

Today, pharma supply chains are becoming increasingly complex and globalized with the increased demand for more affordable drugs. “Since the 1990s, the pharmaceutical industry has increasingly used factories in lower cost economies to manufacture their products; according to the US Government Accountability Office 40% of finished medications are now made outside of the US.” Furthermore, with nearly 90% of the pharmaceutical drug ingredients being sourced outside the US, the impact on generics is significant.

With the increased demand for generics which are more affordable, there is a greater responsibility to safeguard consumers in the US as well as to make the supply chains more transparent in the case of drug recalls. An unprecedented number of recalls of various generic drugs like blood pressure medications such as Losartan (one of the 10 most prescribed drugs), Valsartan, and Irbesartan. These recalls have taken place since July 2018 because the detection of carcinogenic impurities. ²

<https://www.fda.gov/drugs/drug-safety-and-availability/fda-updates-and-press-announcements-angiotensin-ii-receptor-blocker-arb-recalls-valsartan-losartan>

There is also a rising awareness of the impact of counterfeit drugs on public health, and FDA regulations are forcing the pharmaceutical industry into compliance. In the US, the Drug Supply Chain Security Act (DSCSA) was passed in 2013 to require electronic serialization and traceability of all pharmaceutical drugs from manufacturer through distributor to consumer. The DSCSA was passed to safeguard the safety of prescription drug supply chains. Product information, manufacturing information, logistics routes and other key information must be shared with all supply chain partners involved in the delivery of the particular drug to the patient. The first critical milestones were reached in November 2019, with full compliance expected in 2023.

To assist with achieving compliance with the DSCSA, the FDA began a pilot project program in May 2019. The FDA selected 20 participants as part of the pilot program to evaluate and explore different methods of achieving compliance. Blockchain technology provides an immutable, shared source of truth and, when combined with serialization and smart sensors, can provide an effective method of establishing a safer and more secure drug supply chain.

Of the 20 participants in the pilot program, the FDA selected at least seven participants that are using blockchain-based technology platforms working to provide compliance with the DSCSA. These include projects with MediLedger, the IBM/KPMG/Merck/Walmart consortium, UCLA Health, Rymedi, The Optimal Solution, TraceLink, and IDLogiq. These initial pilots showed positive results and suggest that a blockchain-based solution will enable compliance with the Drug Supply Chain Security Act (DSCSA) while improving operations and reducing the supply of counterfeit drugs.

In Europe the Innovative Medicines Initiative (IMI) is the world's largest public-private partnership between the European Union and the European Federation of Pharmaceutical Industries and Associations (EFPIA) providing funding to health research directives, particularly to develop better and safer medicines. The IMI is allocating 8.3 million Euros to a Blockchain Enabled Healthcare initiative now known as PharmaLedger (see Section III below). The goal of the initiative is to create a common blockchain-based framework for the European pharmaceutical ecosystem enabling collaboration on common issues such as mitigating counterfeit drugs and improving shared data access.

The IMI Blockchain Enabled Healthcare initiative includes Europe's most prominent pharma companies including Novartis, Janssen | Johnson & Johnson, Bayer, Sanofi, Novo Nordisk, Pfizer, AstraZeneca, and AbbVie. A major push is in the counterfeit drugs battle, spurred by the Falsified Medicines Directive (FMD) regulation passed in 2011 to ensure the authenticity of medicines. The regulation specifies that only licensed pharmacies and approved retailers can sell pharmaceuticals, including online. Compliance is being enforced as of February 2019 to have 2 safety mechanisms placed on the packaging of every pharmaceutical drug, a unique identifier and an anti-tampering device.

As discussed in the Food and Ag section of this report, at the root of global pharmaceutical fraud is a supply chain transparency and product authenticity problem. The blockchain ledger can provide end-to-end transparency for drug production and distribution, including visibility into every stage of the supply chain. Blockchain technology not only improves the traceability of prescription drugs in the supply chain, it can also ensure that international standards are upheld, such as GDP (Good Distribution Practices), ensuring the integrity and quality of the medication for the end user. Additionally, it will also be much more difficult for bad actors to tamper with the process or for pharma companies themselves to market fraudulent products. It is for this reason that the blockchain community in China has called for placing all vaccine data on a transparent blockchain system.

With regulatory tailwind, the deployment of blockchain-based solutions has the potential to protect consumer safety and public health, enhance consumer trust in pharmaceutical drug supplies, as well as bring operational efficiencies to pharmaceutical companies. Some might wonder whether the benefits outweigh the risks or costs. While we are still in early days for implementing blockchain solutions, early results from pilots in 2019 provide support for optimism.

For example, the MediLedger Project, which comprises 25 major pharma manufacturers, distributors, logistics partners and other stakeholders, was approved by the FDA for a pilot in 2019. The MediLedger pilot project final report noted “The working group considers that consortium-based software development has proven to be more cost efficient, have higher quality, and show a quicker time to value than traditional unilateral development efforts. Within the consortium, all members share in the development effort to include costs, requirements and testing. The output is a single code base that can be deployed by each company with a high degree of interoperable certainty.” (MediLedger DSCSA Pilot Project Final Report, February 2020)

Some critics have questioned whether privacy and confidentiality can successfully be maintained. The use of permissioned blockchain systems and zero-knowledge proofs (ZKP) have produced early promising results. MediLedger, as well as other blockchain solutions, utilize ZKP to preserve privacy and confidentiality while still providing transparency along the supply chain.

NOTE: There are other use cases for improved drug discovery and development processes, and clinical trials. These, however, are not in scope of discussion in this section.

II. Who or what is impacted?

Since blockchain is an ecosystem-spanning technology, the impact of compliance with the DSCSA is extensive. Any and all CA stakeholders that are part of the drug supply chain will be impacted. The main concerns with pharmaceutical supply chains, as we have discussed, is drug traceability, compliance and early detection of issues such as contamination, adulteration, honest reporting of drug manufacturing processes or issues with drug shipments.

In October 2019, California Congresswoman Anna Eshoo and Congressman Adam Schiff held a joint hearing on how to better protect the drug supply chain. Congresswoman Eshoo indicated that there are shortages of life-saving medications and a reliance on subpar manufacturing, which has led to recalls of contaminated products.

Concerns over contamination have been a major issue since health officials have recently overseen recalls in 30 countries of blood-pressure medications made with tainted ingredients. [Congresswoman Eshoo](#) wrote in a Washington Post Op Ed “the supply chain already poses a significant public safety issue to the quality deficiencies that keep arising in the manufacturing of drugs overseas.” The only time consumers find out they’ve consumed a contaminated active ingredient pill is when there is a recall and crisis.³

Blockchain technology can provide game-changing solutions in each of these areas. To solve problems like product shortages, contamination, false labeling, and inventory management in existing pharma supply chains, stakeholders can either join an existing blockchain consortium or create their own.

Because they are ecosystem-spanning, consortia include competitors who are now placed in a unique and unprecedented position of being required to share information with their consortia partners. This model is a paradigm shift and requires a new mindset to be deployed successfully. Finding common ground with competitors is a new type of thinking required in blockchain consortia. Stakeholders will have to develop the right mindset to participate in blockchain-based systems. As noted in the MediLedger pilot, above, there are benefits such as significantly improved efficiency and greater interoperability which can be very attractive to participating members.

Additionally, [according to KPMG](#), blockchains can serve as the “ledger of truth” for sharing complex information with regulators, pharmacy benefit managers, contract manufacturers, physicians, patients, academic researchers and R&D collaborators, among others. For California, there are other stakeholders including the CA State Board of Pharmacy, CA-based pharma manufacturers, distributors/retail pharmacies, hospitals/clinics, and consumer or patient advocacy groups.⁴

One of the highest priorities in any system is patient safety. Safeguarding patient safety is currently motivating all stakeholders to successfully solve systemic supply chain issues in the US. Certainly, as we are writing this report in the midst of the Coronavirus pandemic, patient safety is at the top of our minds. Anything that can mitigate health risks to patients is always important; during a public health crisis, it is of critical importance. Being able to effectively track drug provenance and medication supply chains becomes paramount in a crisis. Safe treatment and sufficient supply are tremendous responsibilities, and a top priority, for the government and regulatory bodies.

Well-managed pharmaceutical supply chains ensure that medicines are accessible to all. When people need their prescriptions, they should be assured that their medications will be available to them. Transparency across pharma supply chains ensures movement visibility of prescription drugs along the chains to prevent product shortages. Supply chain visibility also helps pharmacies and other distributors better manage their inventories to keep up with demand.

Consortia entail other considerations such as new technology platforms and governance. These elements are likely to require new thinking for most drug supply chain stakeholders. Training is likely to be needed both for blockchain in general but also on specific platforms. On the technology front, the concept of decentralization will be new and unfamiliar territory. Current models are all centralized, and as we move into decentralized models required in blockchain-based supply chain implementation, companies will be required to learn how to migrate to decentralized frameworks, build consensus across these decentralized frameworks and employ governance standards.

Governance presents a non-technical challenge, one that many experts believe to be perhaps more difficult to master than the technological issues. Good governance is a strong success factor in blockchain networks. Since blockchain networks are decentralized, there is no single leader. This means the members must agree on a framework for how they will work together and resolve issues. In essence, consortia governance standards lay out how issues are navigated and resolved. This includes numerous considerations, for example what information is to be shared, how privacy is maintained, key member eligibility criteria, and member accountability, among many others.

There are currently a number of existing pharma-specific consortia. These consortia are listed in the next section of this paper under key deployments.

Existing consortia and their frameworks present excellent starting point for anyone wanting to learn about consortia and best practices. Additionally, the IEEE P2145 Blockchain Governance Standards Working Group is assembling a best-practices approach including developing lexical standards for governance to provide guidance to companies and consortia.

III. Solutions and Compliance

Key Deployments

The key consortia for combating drug counterfeiting include (all are in development):

- **MediLedger** is focused on pharmaceutical drug compliance with the DSCSA. It was accepted into the FDA pilot program in 2019. MediLedger was started in 2017 and includes 25 members that span many major pharmaceutical companies, retail pharmacies, and medical distributors such as Pfizer, Amgen, Genentech, Lilly, Gilead, Novartis, Sanofi, GlaxoSmithKline (GSK), Walmart, Walgreens, McKesson, Cardinal Health, Amerisource Bergen, FedEx, and others. ChroniCloud is the main technology partner. Product authenticity is required under the law by November 2019 for saleable returns, a \$6 billion market in the US. The network plans to launch just prior to the deadline. MediLedger is built upon Parity Ethereum, which is a permissioned version of Ethereum for enterprise environments). It will use zk-SNARKs for privacy.
- **IBM/KPMG/Merck/Walmart** consortium is focused on compliance with the DSCSA. It was accepted into the FDA pilot program in 2019. The pilot is focused on traceability of vaccines and prescription medicines within Merck's supply chain and is using IBM's Hyperledger Fabric permissioned blockchain framework. The application will enable end customers to scan a QR code at pickup to see the provenance and authenticity of the product by providing information such as manufacturing site and duration on store shelves. The pilot project results will be available in Q4 2019.
- **Rymedi consortium** was selected by the FDA in 2019 to take part in the DSCSA pilot program. It is focused on data transparency and integration in health system transfers from manufacturer to pharmacy through to patient medicine use, with the purpose of providing real-world evidence and traceability. It is being deployed with various health systems in North Carolina, Indiana and Tennessee, and includes Good Shepherd Pharmacy and RemediChain, Rymedi, Temptime/Zebra Technologies, Indiana University Health, WakeMed Hospitals and Health, the Center for Supply Chain Studies, and the Global Health Policy Institute. While Rymedi is providing the blockchain platform to integrate upstream supply data, Temptime/Zebra Technologies is providing temperature monitoring targeted to specialty medicines.
- **IMI Blockchain Enabled Healthcare** is an EU-based initiative focused on developing a blockchain technology framework to address issues of drug counterfeiting, secure health data sharing, and more efficient clinical trials. It will address issues such as digital identity, off-chain storage, security, and scalability. The initiative is a public private partnership that includes 8 large European pharma companies including: Novartis, Janssen | Johnson & Johnson, Bayer, Sanofi, Novo Nordisk, Pfizer, AstraZeneca, and AbbVie in partnership with UCB Pharma. It will also include other members of the ecosystem including academia, health authorities, clinical research, hospitals, supply chain partners, patient representatives, and blockchain SMEs. The

consortium is to be funded with 18 million Euros and is planned for launch in Q4 2019.

· **PharmaLedger** is a healthcare consortium that brings together 29 partners from 10 EU Member States, including 12 large pharmaceutical companies, technology SMEs, universities and research institutes, leading clinical trials companies, supply chain partners, patient representatives, and leading healthcare service providers. This is a European initiative sponsored for 3 years by IMI and EFPIA under the Horizons 2020 program. Large members include Novartis (Pharma Industry lead), Abbvie, AstraZeneca, Bayer, Boehringer Ingelheim, GSK, Janssen Pharmaceuticals, Merck, Novo Nordisk, Pfizer, UCB Biopharma. Members of the Advisory board include HL7 International Foundation.

The PharmaLedger project is creating a blockchain-based framework for the efficient and secure digitization of the healthcare industry. The goal of the project is to provide a trusted platform with a focus on governance that will support the design and adoption of blockchain-enabled healthcare solutions that accelerate delivery of transformational innovation and benefit the entire ecosystem, from manufacturers to patients. Key use cases include supply chain, clinical trials, and healthcare data. The platform approach is different from the use-case driven approach of the other three consortia discussed.

IV. Recommendations for California

Compliance will be the biggest driver for many CA stakeholders in the pharmaceutical industry. As we've noted above, many California pharma companies as well as their partners, such as distributors and retail pharmacies, are already part of blockchain networks focused on drug traceability, provenance, and safety. This is a good starting point and a foundation that California can build off of to provide a broad range of valuable blockchain-based solutions for the industry and for residents.

To provide the greatest value, we recommend developing a pilot program that brings together a broad group of CA partners, including CA government, pharma manufacturers, distributors, retail pharmacies, technology companies, healthcare providers and payers, patient advocacy groups, universities and other research facilities. This can be thought of as an approach that is a blend between PharmaLedger and the private-sector focused US consortia. The US consortia are very good at delivering a solution for a specific well-defined problem, while PharmaLedger is focused on transformational change across multiple use cases.

This recommended 'CA Pharma consortium' will reference the broad PharmaLedger approach, focusing on a robust platform and governance model that can be used across multiple use cases – including supply chain, clinical trials, and health records. As discussed previously good governance is the cornerstone to successful blockchain networks. Additionally, including key members of the pharma sector, healthcare community, patient advocacy groups, technology companies, universities, and research organizations will ensure that drug development and clinical trial use cases will also be covered and will comply with product manufacturing and delivery modalities. Similar to other consortia like MediLedger, it is recommended that a 'CA Pharma Consortium' includes distributors and retail pharmacies, to ensure that the "last mile" in the pharma supply chains are secured.

V. Resource Links

1. <https://www.pharmasalmanac.com/articles/why-the-industry-is-moving-toward-blockchain-technology>
2. <https://eshoo.house.gov/media/press-releases/eshoo-holds-hearing-address-broken-global-pharmaceutical-supply-chain>
3. [https://pharmaphorum.com/views-analysis-market-access/the-challenge-of-transparency-in-the-global-supply-chain/\)](https://pharmaphorum.com/views-analysis-market-access/the-challenge-of-transparency-in-the-global-supply-chain/)

Endnotes:

¹ Enterprise Blockchain Has Arrived, by Radhika Iyengar and Jordan Woods, copyright 2019