

UCLA-LedgerDomain: DSCSA Solution Through Blockchain Technology

Drug Tracking, Tracing, and Verification at the Last Mile of the Pharmaceutical Supply Chain with BRUINchain

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ABSTRACT

As part of the FDA's DSCSA Pilot Project Program, UCLA and its solution partner, LedgerDomain, focused on building a complete, working blockchain-based system, BRUINchain, which would meet all the key objectives of the Drug Supply Chain Security Act (DSCSA) for a dispenser operating solely on commercial off-the-shelf technology. The BRUINchain system requirements include scanning the drug package for a correctly formatted 2D barcode, flagging expired product, verifying the product with the manufacturer, and quarantining suspect and illegitimate products *at the last mile*: pharmacist to patient, the most complex area of the drug supply chain.

The authors demonstrate a successful implementation where product-tracing notifications are sent automatically to key stakeholders, resulting in enhanced timeliness and reduction in paperwork burden. At the core of this effort was a blockchain-based solution to track and trace changes in custody of drug. As an immutable, time-stamped, near-real-time (50-millisecond latency), auditable record of transactions, BRUINchain makes it possible for supply chain communities to arrive at a single version of the truth. BRUINchain was tested with real data in a real-world setting at one of the busiest pharmacies in the United States.

In addition to communicating with the manufacturer directly for verification, BRUINchain also initiated "sad path" reporting, which culminates in the origination of a Form 3911 to FDA. During the study, a 100% success rate was observed across scanning, expiration detection, and counterfeit detection; and paperwork reduction from approximately 1 hour to less than a minute. Based on this performance, DSCSA compliance for the 4.2 billion prescriptions dispensed each year is estimated to cost dispensers at least 17 cents per prescription, and potentially much more depending on regulatory interpretation and speed of verification. The study concludes by touching upon policy considerations aimed at addressing these challenges while enhancing the detection and removal of potentially dangerous drugs from the drug supply chain to protect U.S. consumers.

ACKNOWLEDGEMENTS

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1. INTRODUCTION

1.1. BACKGROUND

Enacted in 2013, the Drug Supply Chain Security Act (DSCSA) outlines steps to build an electronic, interoperable system to identify and trace certain prescription drugs as they are distributed in the United States by 2023.¹ The DSCSA is intended to enhance FDA's ability to help protect consumers from exposure to drugs that may be counterfeit, stolen, contaminated, or otherwise harmful. This law sets forth requirements for multiple stakeholders along the pharmaceutical supply chain, from manufacturers, repackagers, and wholesale distributors to dispensers.²

By allowing for more rapid tracing and potentially even allowing for real-time tracking, the system will also improve detection and removal measures: "The ability to track and trace finished prescription drugs plays a significant role in providing transparency and accountability in the drug supply chain."³ To facilitate the development of the 2023 system, the FDA established the DSCSA Pilot Project Program, which prompted the study outlined in this paper.⁴

UCLA Health consists of five distinct facilities and over 200 clinics, with roughly 20,000 employees serving nearly 600,000 unique patients per year comprising over 2.5 million patient visits. The UCLA Health Pharmacy supports all these facilities with three hospital pharmacies, an infusion pharmacy, two research pharmacies, and five retail/specialty pharmacies staffed by over 300 employees.⁵ As one of the nation's leading dispensers and a blockchain solutions provider with extensive healthcare experience, UCLA and LedgerDomain decided to take on the challenge of applying DSCSA requirements to the last mile – a pharmacy in a large hospital setting – a highly complex area of the drug supply chain.

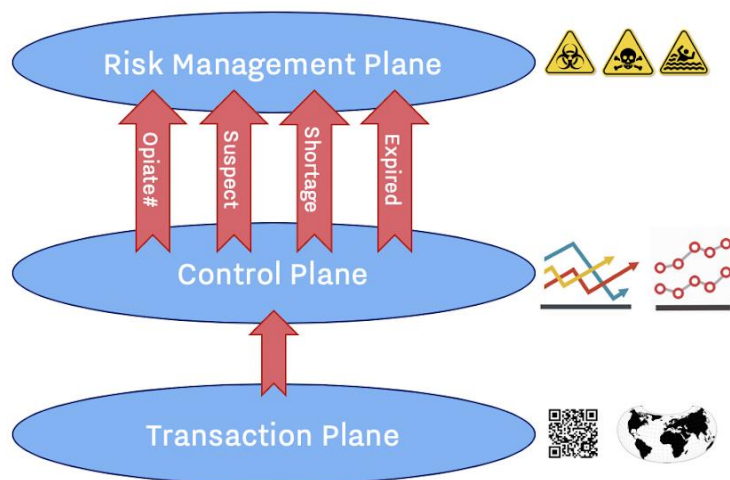
Both UCLA and LedgerDomain are members of the Linux Foundation and the Hyperledger Project, and are active in advancing the use of blockchain to drive pharmaceutical supply assurance directly to patients. UCLA and LedgerDomain are also both charter members of the Clinical Supply Blockchain Working Group, an initiative formed along with Pfizer, Biogen, GSK, Merck, UPS, IQVIA, and other healthcare leaders. In 2019 the group published results from Project KitChain, a collaborative model for immutable digital recordation and inventory and event tracking in the pharmaceutical clinical supply chain.⁶

1.2. PILOT PROGRAM OBJECTIVES

The objective of the study was to focus on the enhanced requirements for package-level tracing and notification that go into effect in 2023 to comply with the DSCSA. In particular, UCLA and LedgerDomain (collectively referred to as the team hereafter) focused on the verification system requirements under section 582 of the FD&C Act⁷ and the existing protocols around

Form FDA 3911, which is used by manufacturers, repackagers, wholesale distributors, and dispensers to notify FDA and all appropriate immediate trading partners within 24 hours after determining a product is illegitimate or has a high risk of illegitimacy.⁸

As part of this endeavor, the team also aimed to learn about the challenges of implementing an interoperable system on a larger scale, identify projected costs, and articulate potential soft costs and benefits encountered that might be worthy of further study. The logical components of such a system are depicted to the right.



In supply chain systems, transactions are captured as events in the “transaction plane.”

These events are aggregated into trends in the “control plane.” Exceptions and problems are then surfaced to the “risk management plane.” In the legacy relational database world, the transaction plane was often termed the online transaction processing (OLTP) database,⁹ while the control plane was termed the online analytical processing (OLAP) database, or data warehouse.¹⁰ With an integrated system, not only can a single expired unit simply be blocked at the transaction plane level, but multiple blocked transactions of this expired drug can rise to the level of a risk management issue.

There are security tradeoffs made with relational database implementations of such multiplanar supply chain systems. In these implementations it is typical for each transacting party to manage its own database systems: there is no shared global database representing the single source of truth describing the flow of items through the supply chain. Maintaining a private database allows each party to minimize the security threat surface to which they are exposed while ensuring data integrity, as a global relational database would require each party to trust all other parties in the supply chain with the integrity and security of their data.

However, this privatization of truth comes at the expense of the supply chain’s resilience to common attack vectors such as man-in-the-middle or spoofing.¹¹ Without global and persistent visibility into the state of the supply chain, duplicate “spoofed” counterfeit drugs cannot be identified; counterfeit or defective lots cannot be tracked, traced, and recovered; and malicious “men in the middle” cannot be identified by the signature transaction patterns they leave across multiple points in the supply chain. Modern blockchain systems are aimed at eliminating the need to trade data integrity and privacy for global visibility and interpretability,¹² contributing to the inspiration for the BRUINchain study.

The questions this pilot aims to answer are:

- **Barcode reading error rates.** Is commercial off-the-shelf hardware capable of delivering highly reliable scanning of typical drug packaging? Can the team shed some light on the number of scans per dose and the time required to scan (including failed scans due to damaged packaging or other reasons)?
- **Interoperability implementation and implications.** Can the application and backend be configured to identify expired, duplicate, unverifiable and damaged products, and alert the relevant stakeholders?
- **User satisfaction ratings by role.** Can UCLA's pharmacy technicians, pharmacists, and prescribers master this technology and incorporate it into their daily routine?
- **Simulated counterfeit and expired lot metrics.** How robust would the system be in checking for counterfeits (e.g. duplicates or faulty barcodes) and expired product?
- **Paperwork reduction.** Can the team validate the generation of Form FDA 3911 notifications and evaluate the enhanced timeliness and reduction in site burden achieved as a result?
- **Cost, quality, and speed of product tracing information.** How fast and accurate might the solution be within a real-world context?
- **Real and imputed costs to implement.** Can the team gather enough data to generate an estimate of likely cost that would be helpful to policymakers?

1.3. PILOT SCOPE

The last mile in the pharmaceutical supply chain is a complex environment, as drugs are moved from shipping containers and pallets to individual packages and amber bottles with several degrees of separation from their point of origin.

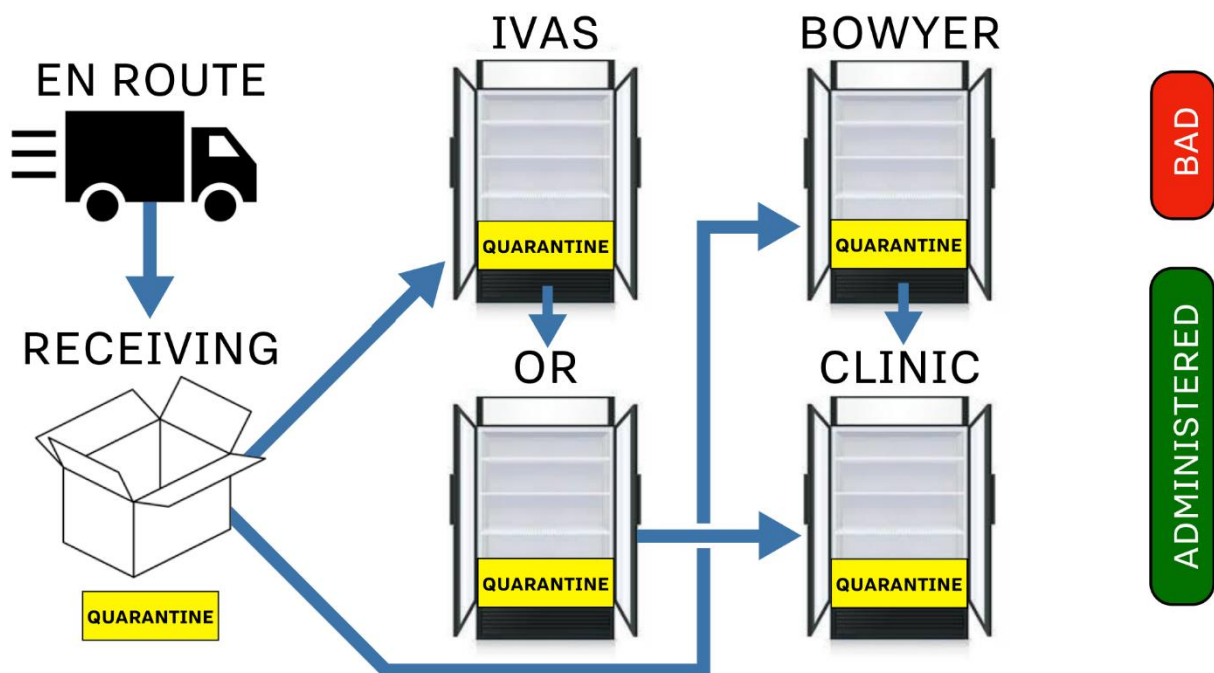
The keystone of this project is BRUINchain, a blockchain-based mobile solution and notification system designed to track and trace changes in custody of drug within a “dispenser” organization using FDA-stipulated barcodes.¹³ Changes in custody were translated into the application with real-time reporting of inventory counts and locations within the UCLA Pharmacy system. The following checkpoints were built into this system to prevent distribution of suspect product to patients: (1) verify that the information on the scanned barcode matches the human readable label; (2) verify that the product is fit for distribution, i.e., not past its expiration date; (3) obtain verification from the manufacturer; and (4) visual inspection of the product.

Based on earlier learnings from a pilot application designed for the clinical supply chain,¹⁴ system requirements included notifications; i.e., (1) automated product tracing notifications to key stakeholders and (2) notifications for suspect product with key information that mapped to the existing Form FDA 3911. For this pilot project, the team assessed BRUINchain system requirements for a successful implementation on a larger scale, including identifying, flagging,

and preventing the distribution of suspect and illegitimate products, and evaluating the enhanced timeliness and reduction in paperwork that might be achieved.

To fully test the system's track-and-trace capability, the team decided to select one study drug and have BRUINchain track its journey from the point UCLA received the drug in its receiving dock to being dispensed to the clinic/patient. *While to some observers this may encompass greater scope than that warranted by the DSCSA, a closer examination of UCLA's workflow revealed that different UCLA colleagues were performing different DSCSA-mandated checks.*

SPINRAZA®¹⁵ (referred to as study drug hereafter), a Biogen product, is a treatment for children and adults with spinal muscular atrophy (SMA). Infantile-onset SMA (Type 1) results in early mortality.¹⁶ This was chosen as the study drug for its ideal tracking characteristics. It is packaged as single-dose medicine with a GS1 barcode on the outer packaging (see image).¹⁷ In this particular situation, Perry Shieh, MD, administers all of the study drug in the UCLA system. Because Dr. Shieh, not the pharmacy, opens the carton, the team decided to track the drug all the way to the prescriber/ clinic in order to incorporate visual inspection of the vial as part of the BRUINchain process.



Most importantly, however, the study drug has a complex workflow at UCLA Health. After UCLA receiving takes custody of the drug, the study drug may be forwarded to a variety of pharmacy locations, including the Intravenous Additive Service Pharmacy (IVAS), the Operating Room Pharmacy (OR), the Bowyer Infusion Pharmacy (Bowyer), and outside the pharmacy, Dr. Shieh's Clinic; all depending upon a variety of important variables. This complex real-world setting, depicted above, was an ideal use case for the BRUINchain application.

As part of exploring DSCSA requirements for verification of drug as a legitimate product, the team coordinated with the study drug's manufacturer on a potential solution. This culminated in the development of an automated verification system (supported by the Oraculous notification service), involving queries of serial and lot numbers between the UCLA Pharmacy and the manufacturer's serialization team.

It is important to note that the implementation of the BRUINchain pilot study (section 2.4) was conducted as a parallel system to existing systems of record in an active pharmacy at UCLA Health. In this way, the team met its goal of getting real data in a real-world setting.

2. PILOT PROJECT

2.1. PARTNERS AND ROLES

UCLA Health Pharmacy's William Chien was the system owner and manager, providing LedgerDomain with workflow requirements to design the system. Dr. Chien also recruited and managed technicians and pharmacists to test the solution and provide feedback.

UCLA Health also acted as the prescriber. Dr. Shieh personally retrieved the medicine at the relevant UCLA pharmacy or received into his clinic directly from a specialty distributor, Accredo, via pre-dispensed distribution (also known as "white bagging") and administered to the patient.

LedgerDomain designed, coded and tested the BRUINchain iPhone application, and supplied the DocuSeal framework, the Oraculous notification service, and Selvedge blockchain application server, as well as hosted the Hyperledger Fabric backend.

2.2. DESIGN REQUIREMENTS

2.2.1. WHY BLOCKCHAIN?

Blockchain is an *immutable, time-stamped, near-real-time, auditable record of transactions*, thereby making it possible to enhance privacy and security across a range of collaborative applications.¹⁸ Unlike a centralized relational database, no single user or organization can access the full record of transactions within the blockchain. Unlike in a relational data model,

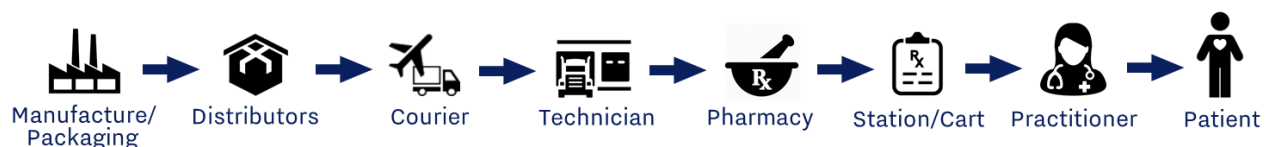
blockchain communities converge on a *single version of the truth* through the application of consensus algorithms. Once consensus is achieved, that single best version is *committed* to the blockchain.

This consensus is particularly important in the drug supply chain, as this single version of the truth cancels out double counting and surfaces possible instances of counterfeiting, diversion, spoofing, or man-in-the-middle attacks. Each event within the blockchain occurs when relevant parties agree to cryptographically sign a transaction. This agreement, in turn, adheres to an associated “smart contract.” Once this transaction has met those conditions and is committed to the blockchain it is both binding and irrevocable.

After a transaction is struck between two parties, each will have keyed access for later decryption and analysis, as might a regulator or auditor. Thus the team saw blockchain as a potential “honest broker” that would allow hundreds of competing pharmaceutical and biotech enterprises and their vendors to work collaboratively and communicate with hundreds of wholesalers and tens of thousands of dispensers.

The data privacy and security requirements associated with healthcare¹⁹ demand a shared-permission blockchain-based system; i.e. a system where membership and participation in the network is controlled rather than open to the public. Hyperledger Fabric components were chosen as a scaffolding for the pilot, as well as a Fabric-based framework that allowed for off-chain private storage combined with blockchain-based authentication.²⁰

2.2.2. COMMERCIAL PHARMA SUPPLY: SIMPLIFIED STAKEHOLDER ROLES



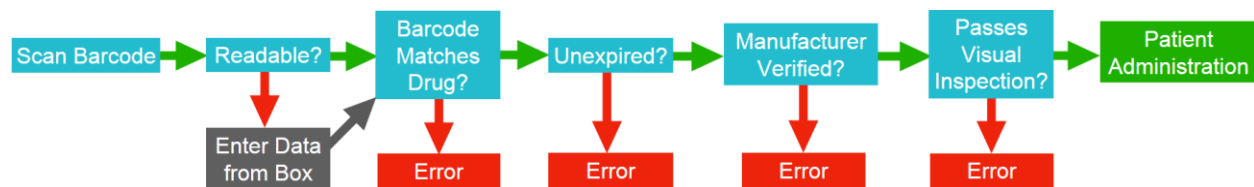
The goal of the DSCSA is interoperability among thousands of companies that make up the pharmaceutical supply chain, including manufacturers, repackagers, wholesale distributors, and dispensers. Even within these four categories, one can identify numerous organizational and individual roles; between the distributor and the practitioner at UCLA there are shippers, technicians in the pharmacy receiving department, and stations/carts within the pharmacy itself. A key goal of BRUINchain was to provide a real-time system that allows all its internal stakeholders to interact in a manner appropriate to their privileges.

Under DSCSA, dispensers are required to be able to trace and verify drugs. The drug barcode may be used to pull the relevant data fields, but the question in the pre-2023 environment is from which external party might BRUINchain electronically poll to trace. This presented an additional challenge: how BRUINchain might communicate without compromising its security

envelope. To address this challenge, LedgerDomain designed a novel approach which leverages the blockchain concept of an oracle,²¹ detailed in section 2.4.1.

2.2.3. PROCESS FLOW

A key goal of the BRUINchain application and process is to surface and report problems. In the pilot, the team defined the ideal supply chain workflow as the “happy path,” and possible failure states as “sad paths.” A package that (1) has a valid barcode with a GS1 Global Trade Item Number (GTIN) that matches the expected value, (2) is unexpired, (3) is verified by the manufacturer, and (4) passes visual inspection has fulfilled the happy path.



At the last stage of the drug’s route through the pharmacy, Dr. Shieh scanned the package with his iPhone to take custody on behalf of the clinic prior to administration (of the drug) and retirement (of the unique Asset ID within the blockchain system). However, if it fails any of these tests at any of the pharmacy locations (detailed in section 1.3), the package has taken one of the sad paths. Again, in UCLA’s current workflow, the study drug is delivered to the prescriber as a sealed package, and the prescriber performs the unsealing and inspection, thereby fulfilling the final requirement.

Of the four types of problems that are identified by a dispenser locally, each requires a slightly different approach. If a medicine is expired, the transaction is flagged: there may be no external reporting necessary.

In the case of the barcode failing to match the medication, or a visual inspection failure, the dispenser is required to escalate the situation and stand ready to file Form FDA 3911. The BRUINchain application automatically generates the XML-formatted dataset for the filing of a 3911 and asks the user to take a photo supporting their issue. Both documents are encrypted, timestamped, and stored in a secure archive, mediated by DocuSeal.²² At UCLA, the policy is for the user to surface these issues to William Chien, system owner. Dr. Chien then confirms the issue and submits the email if necessary, in addition to any steps stipulated by UCLA Health.

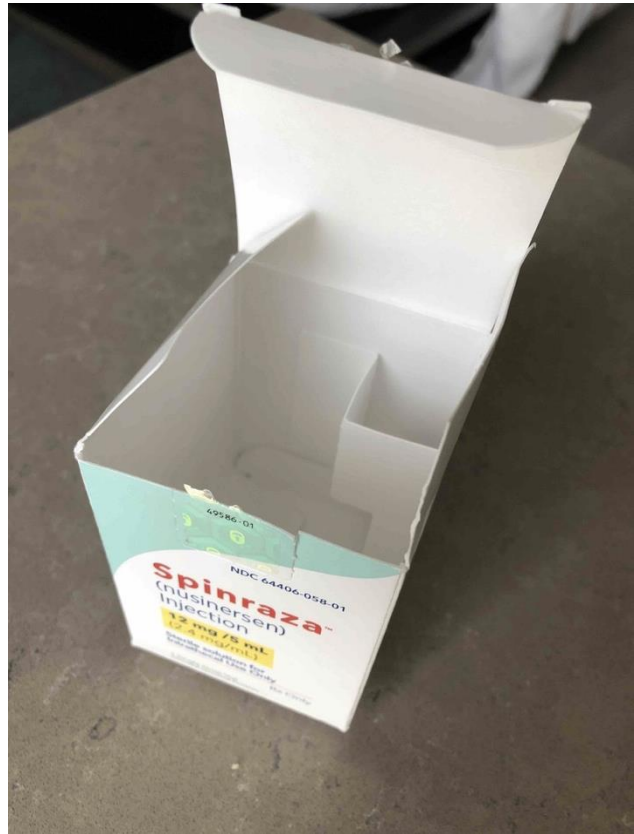
Finally, if there is a problem in verification, the BRUINchain system will have already provided the manufacturer with all of the fields necessary for the manufacturer to file a Form FDA 3911. Below is a sealed document from the blockchain of a simulated issue, including a photograph that supports the issue and is sealed to the blockchain as well. (Note that for security purposes, all study drug serial numbers have been obfuscated except for the last four digits; barcodes and contact information have also been obfuscated.)

```

<bruinchain-doc-problemreport>
  <Asset-
  Id>[REDACTED]</
  Asset-Id>
    <GTIN>00364406058011</GTIN>
    <SN>[REDACTED] 6540</SN>
    <Expiration-Date>01/2021</
  Expiration-Date>
    <Lot-Number>SH0305</Lot-Number>
    <Problem-Description>package
  was empty when opened</Problem-
  Description>
    <Reported-By>William Chien</
  Reported-By>
    <Reported-By-
  Email>[REDACTED]</
  Reported-By-Email>

  <Timestamp>1578839700193180007</
  Timestamp>
    <Timestamp-Human>Sun, 12 Jan
  2020 14:35:00 UTC</Timestamp-
  Human>
</bruinchain-doc-problemreport>

```



It should be noted that quarantine is an intermediate step within the BRUINchain system; human review is required to determine whether the drug is illegitimate, or whether it has been quarantined due to user error or other factors. In the event of a quarantined drug, a sticker or tape (as shown below, alongside the quarantine bin) is to be affixed to the package until resolution of its status. If a quarantined medication is deemed illegitimate, it is flagged as “bad” within the BRUINchain workflow, potentially resulting in a report to FDA via Form FDA 3911.



2.2.4. DATA STANDARDS

Under the FD&C Act, manufacturers are required to “affix or imprint a product identifier to each package and homogenous case of a product intended to be introduced in a transaction into commerce.”²³ This must take the form of a 2-dimensional data matrix barcode for packages,²⁴ with data containing the product’s National Drug Code (NDC), unique alphanumeric serial number, lot number, and expiration date. The barcode must be “on a data carrier that conforms to the standards developed by a widely recognized international standards development organization.”²⁵

For the BRUINchain pilot, it was determined that this barcode would set the stage for intake into receiving for further evaluation as to expiry, storage condition, tampering, and barcode verification. The barcode on the study drug is based on the GS1 standard. GS1, which develops and maintains global standards for efficient business communication, has published a material identification standard for both commercial and clinical pharmaceutical supplies.²⁶ (In GS1-compliant barcodes, the National Drug Code is concatenated within the GTIN.)

The data standards used in the BRUINchain pilot further include: a concept of network time and time-stamping; FDA Form 3911 specified problem-handling fields; user ID, email, and location; quarantine and retired statuses; and verification statuses.

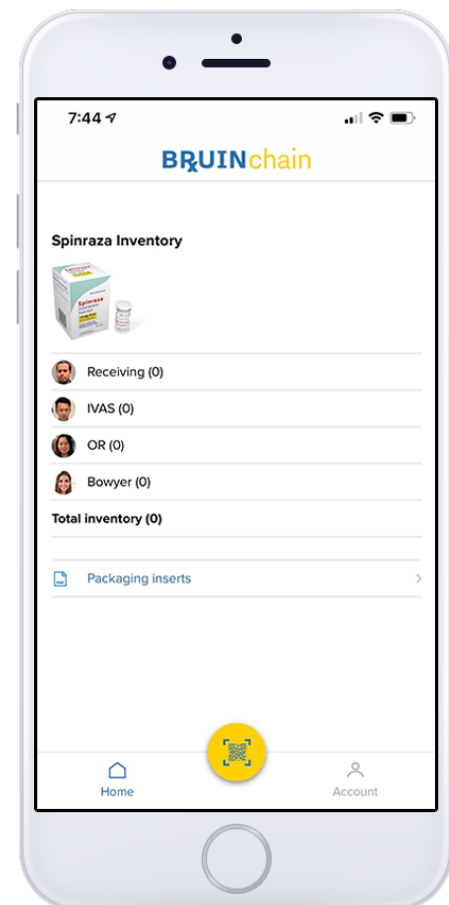
2.2.5. TECHNOLOGY

The BRUINchain system has five major components: a frontend mobile application (also called BRUINchain), an application framework encompassing smart contracts and application logic (DocuSeal), a notification and verification service (Oraculous, which is detailed in section 2.4.1), a blockchain application server (Selvedge) and a backend blockchain (Hyperledger Fabric).

The first thing presented to the member is a modal login screen (member email and password). Once logged in, the full application UI is presented.

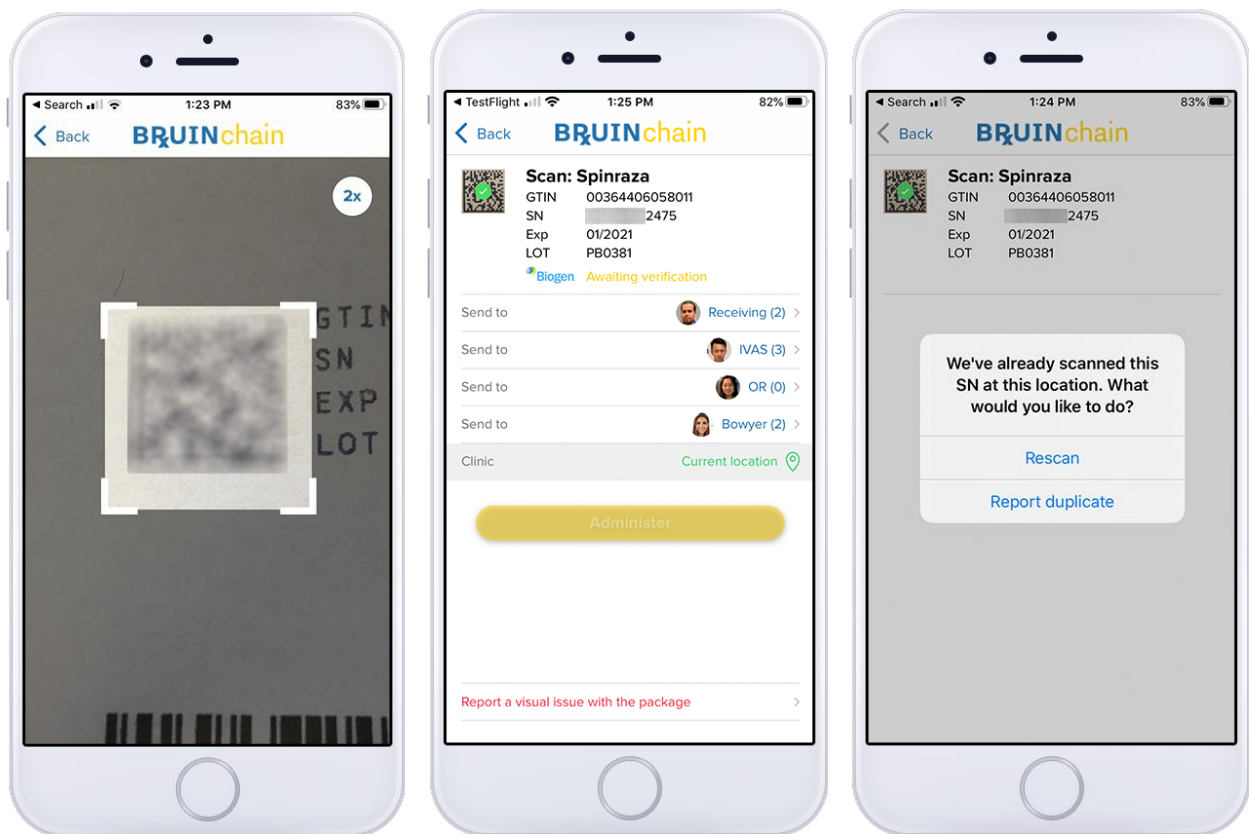
Account actions. All members can change their first name, last name, and avatar; change location; or logout. Admins additionally have the ability to invite a new member (sending an email that grants the recipient access to the application) and purge the blockchain of data to reset for testing.

Distinct roles. There are four roles: Receiver, Pharmacist, Manager, and Prescriber. All have the ability to log in and



perform their roles. Only a Prescriber can administer; only a Prescriber or a Receiver may receive. The Manager has extra privileges.

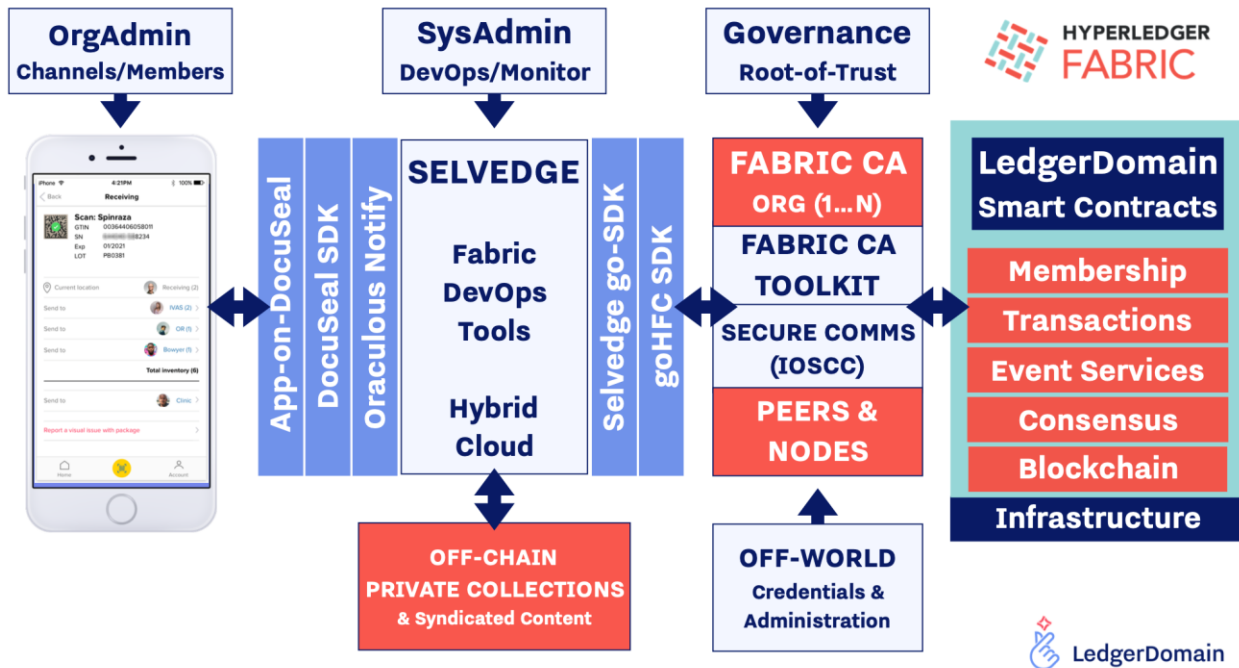
Scan. The logical custody is keyed off the scan, which is checked for expiration date and validly formatted drug barcode. In addition, the barcode is checked against the register of verified (but not retired) barcodes: if the barcode is not already verified, the verification procedure is automatically initiated by the Oraculous notification service. Once scanned, the application displays the elements of the barcode (GTIN, serial number, expiration date, and lot number) in a human-readable format. Users can then compare the information on the screen against the human-readable information on the package.



Confirming Modals. Users have the ability to flag units that do not pass visual inspection and start an exception report. If the application detects a duplicate scan, the users are asked to confirm whether or not they believe they scanned the same box twice (“rescan”). Any of these routes can turn from the “happy path” to the “sad path,” which eventually leads to quarantine and potentially to “bad status” and Form FDA 3911 for resolution.

BRUINchain Architecture

Real-world custody locations, advanced workflows and multiple roles & exception handling



2.2.6. SECURITY, PRIVACY AND DATA RETENTION

For security reasons, the team does not intend to detail the security envelope, any encryption at-rest, or in-transit protocols. FDA staff may arrange for a private briefing under NDA for themselves or their designates at U.S Commerce Department’s National Institute of Standards and Technology (NIST).

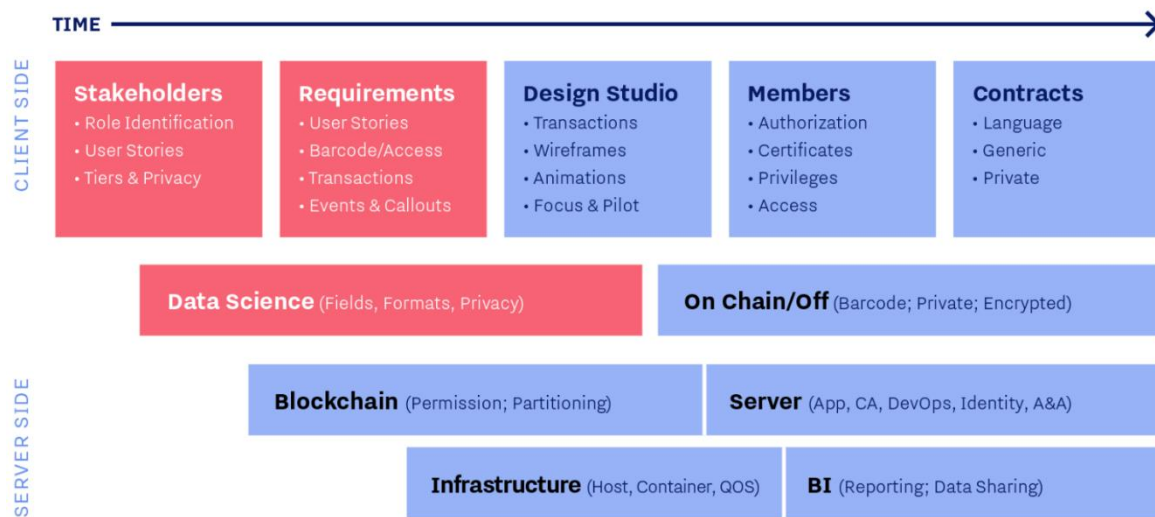
For this pilot, the BRUINchain application remained private amongst a few participants at UCLA Health and *handled no patient data*. It should be noted that no scanned packages had any PII/PHI, except for the white-bagged units in section 2.4.2, which were handled exclusively by UCLA personnel.

The team performed multiple cycles of by-invitation only testing. At the end of each cycle, personal and personally identifiable information such as names, email addresses, and IP addresses were discarded.²⁷ In addition, the application was distributed via the Apple TestFlight sandbox and was thus not exposed to the general public in the App Store.

2.3. DEVELOPMENT AND TESTING

This phase of the pilot project comprised (1) gathering of requirements and confirming target drugs and partners; (2) specifying and building the blockchain application; and (3) testing in controlled environments, referred to as UCLA User Site and LedgerDomain Developer Site.

During this phase, existing workflows were mapped, and possible paths to DSCSA compliance were workshopped. These were then built as process flows within the system’s roles, privileges, and smart contracts. This culminated in the happy and sad paths workflow (shown in section 2.2.3). The team’s methodology in testing the counterfeit sad path was to flag everything that was not the study drug and generate a modal warning.



2.3.1. UCLA USER SITE TRAINING AND TESTING WITH BRUINchain

Training was self-guided with LedgerDomain personnel as coach. Trainees from the UCLA Pharmacy staff typically spent 15-20 minutes getting familiar with the BRUINchain application, roles, and locations. Eighteen minutes was the training time mean.

The first set of testing was to gain insight into barcode reading error rates. User 1 performed test on two (2) non-study drug packages and two (2) study drug packages. All barcodes were successfully read and packages were correctly identified as non-study drug vs. study drug.

User 2 performed the next test on ten (10) study drug packages and on randomly selected non-study drugs. All barcodes were successfully read and packages were correctly identified as non-study drug vs. study drug.

A second set of testing was performed to quantify the amount of time to scan barcodes. UCLA Pharmacy staff typically work with rolling carts, which contain a range of 25 to 50 scannable units per cart. Four carts were randomly selected and their contents were scanned and timed. In total, the four time-measured flights involved 197 units scanned in 27:50 minutes (11.8 seconds per package). Zero failures were encountered during scanning.

2.3.2. BOARD GAME TEST, LEDGERDOMAIN DEVELOPER SITE

For this phase, a “board game” simulation mat of the UCLA pharmacy workflows was used to test inventory counts and location of drug. Training and testing were done with naive LedgerDomain colleagues playing different roles (receiving tech, pharmacist, and prescriber) on seven (7) discarded study drug packages traveling from receiving to clinic.

Trainees performed test scans on the study drug. Scanning was 100% successful, and inventory tracking was 100% accurate.

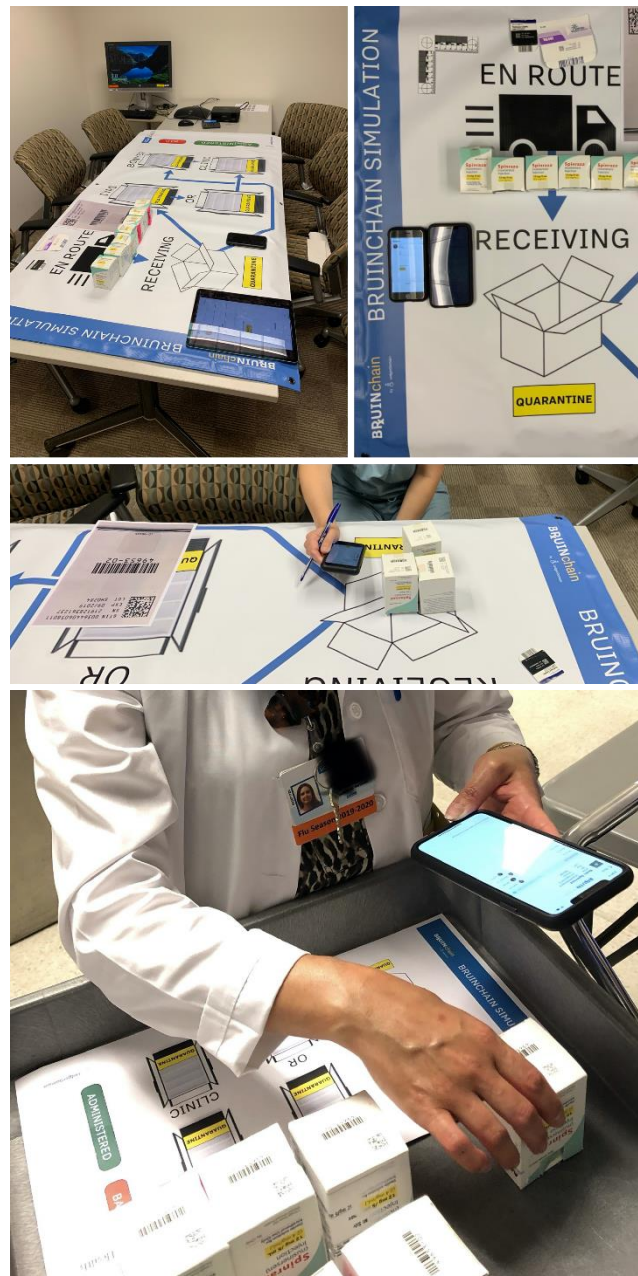
2.3.3. BOARD GAME TEST, UCLA USER SITE

Training and testing were done with group of UCLA pharmacy staff in a conference room setting on seven (7) discarded study drug packages. This session was used to test inventory count, location of drug, and “sad path” of expired drug.

Training was self-guided with LedgerDomain personnel as coach. Trainees typically spent twenty minutes getting up to speed (20:25 and 19:00). Once trainees pronounced themselves comfortable, the trainees worked together to push the seven packages through the board game supply chain. The total time was 45 minutes to individually train and to work together as a team. During this round, BRUINchain successfully flagged expired drug barcodes and generated modal warning screens to indicate expiry.

The next training and testing session was conducted with Dr. Perry Shieh, prescriber, on seven (7) discarded study drug packages. Dr. Shieh was readily able to receive, transfer, and simulate administration of the drug. Ambient lighting was poor and scanning was slow, but accurate.

The last training and testing session conducted with UCLA was done on ten (10) discarded study drug packages (two of which were expired) in the infusion



pharmacy, in which the workflow includes affixing patient names and subsequently dispensing either directly to nurses or through a Pyxis™ interface. User 3 was readily able to receive and transfer the drug on the BRUINchain application.

Training took 18 minutes in total, while provisioning the application on the iPhone took an additional 10 minutes and scanning 33 packages across a variety of bins took 4:58min or 9.0 sec/package.

2.3.4. VERIFICATION OF DRUG WITH MANUFACTURER

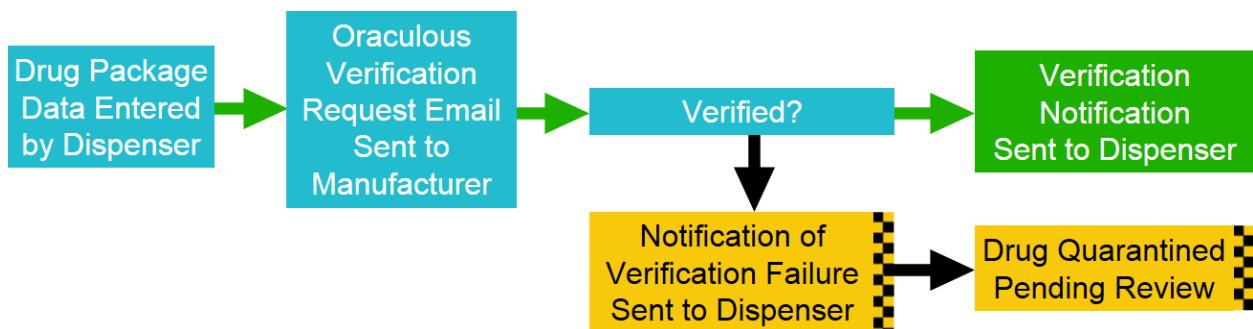
As an initial test, the team successfully verified 11 out of 11 study drug barcodes with the manufacturer’s serialization team through a manual process (i.e. emailing parsed barcodes for review).

2.4 BRUINCHAIN PILOT STUDY

2.4.1. BRUINCHAIN IMPLEMENTATION, SOFT START

The goal of the soft start was to confirm UCLA’s forecasted activity for the week of December 16-20 (“Live Test”) and to verify all on-hand study drug three days prior through the BRUINchain system. This enabled the team to pre-verify the study drug and avoid quarantine scenarios, while also gathering further feedback from the manufacturer. William Chien scanned all five units on hand.

The BRUINchain system automatically generated a notification to the manufacturer’s serialization team through the LedgerDomain Oraculous Notification Service. The process was fully automated in-bound and out-bound for UCLA users on BRUINchain. The Oraculous service allowed for manual verification on the manufacturer side. This notification and associated verification involves the following flow:



The first five notifications were successfully verified by the manufacturer. The “not verified” functionality was also tested, although it should be clear that this was strictly a test of the software, not a real event. *Per the team’s custom, BRUINchain security policies will not be*

explicitly laid out in this publication. Policy considerations merit the attention of FDA security professionals and the team stands ready to privately brief under NDA.

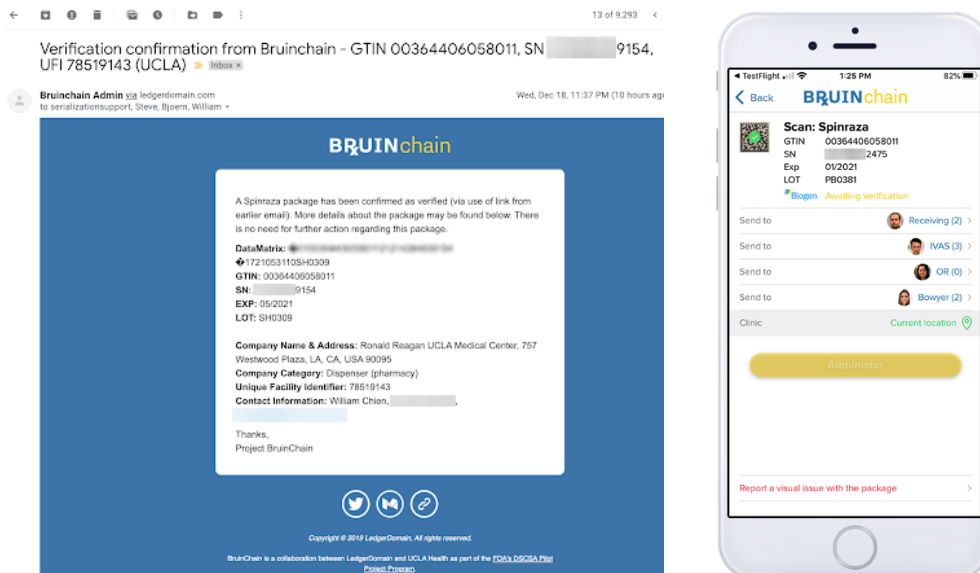
The following day, UCLA scanned a second batch of three additional incoming study drug units; again, all three generated automatic notifications and were subsequently verified as good serial numbers. As such, the live test began with six uncommitted study drug units in aggregate across the pharmacies and two study drug units committed with PHI in the clinic. These two had come in directly from a specialty distributor, Accredo, pre-dispensed (“white bagged”). All units were scanned for expiration date as well as verified by the manufacturer.

With only eight units, it is unsurprising that no duplicates were found; nonetheless the BRUINchain system does check for this, blocking retired units and requesting user feedback for units that are duplicates within the system. Duplicate scans are normative, as units are tracked with BRUINchain through their retirement or quarantine, but users are always asked to confirm the unit is indeed an existing unit, as shown in section 2.2.5.

2.4.2. LIVE PARALLEL USER-SITE TESTING WITH UCLA

During this phase, the Oraculous service was updated to provide the manufacturer with more information to aid in verification and improve record auditability. UCLA colleagues commenced the live parallel user-site testing by updating the locations of each of the drug doses. UCLA typically uses a weekly paper forecast of study drug doses as a fail-safe to ensure an adequate supply: eight doses were confirmed as being on hand and seven patients were scheduled.

Following a day of testing, the Oraculous service was further updated to tune the notifications to the manufacturer. The manufacturer now received a follow-on email confirming “Verified” in addition to those confirming “Not Verified.” As such, the manufacturer would receive a record of data sufficient to initiate a Form FDA 3911 on both suspect and non-suspect units.



The client application continued to perform as expected, as all inventories continued to match up with user commands.

Following the live test with the manufacturer verifying inventories (section 2.4.1) and through the live parallel user-site testing, the team gathered the metrics outlined below. It is important to note that no suspect or illegitimate drug was identified during the pilot, and any error reports or exclusions were performed as part of testing.

API Touches by Asset

Asset Serial Number	First Event	Last Event	Touches
XXXXXXXXX9621	Fri Dec 13 16:14:16 2019	Mon Dec 16 18:21:35 2019	57
XXXXXXXXX7449	Wed Dec 11 18:30:38 2019	Fri Dec 20 19:58:16 2019	143
XXXXXXXXX9154	Wed Dec 18 21:46:48 2019	Thu Dec 19 17:15:13 2019	64
XXXXXXXXX4202	Wed Dec 11 18:30:19 2019	Mon Dec 16 18:36:27 2019	57
XXXXXXXXX2024	Fri Dec 13 16:14:00 2019	Sat Dec 21 00:00:32 2019	99
XXXXXXXXX6442	Wed Dec 11 18:41:20 2019	Thu Dec 12 10:21:32 2019	46
XXXXXXXXX6075	Thu Dec 19 23:07:35 2019	Sat Dec 21 01:28:17 2019	65
XXXXXXXXX5195	Fri Dec 13 16:13:46 2019	Sat Dec 21 00:01:49 2019	99
XXXXXXXXX2141	Wed Dec 11 18:41:08 2019	Tue Dec 17 23:20:37 2019	59
XXXXXXXXX0150	Wed Dec 11 18:30:03 2019	Mon Dec 16 18:36:10 2019	59

Note: all times in UTC. Touches refers to API calls related to the specific asset.

Application Events and Metrics

- 10 distinct asset IDs (boxes of study drug)
- 9 distinct user IDs (including LedgerDomain personnel who did not transact)
- 428 API calls from 48 IP addresses
 - 294 inventory summary changes
 - 37 custody queries (looking up custody information on a particular asset)
 - 23 changes of custody for 10 assets
 - 28 asset verifications
 - 20 user avatar queries
 - 15 user profile updates (includes UCLA personnel reassigning location)

- 6 assets administered
- 3 queries of user by email address
- 120 notifications sent

In summary, during the busy pre-holiday week, UCLA started with six doses of the study drug in the pharmacy and two additional white-bagged doses in the clinic; at week's end, UCLA had three in pharmacy. The system tracked pharmacy doses to user input accurately throughout the week, checking each package for expiry and soliciting verification from the manufacturer.

2.4.3. FURTHER DEVELOPER SITE SCANNING TIME TRIALS

User feedback suggested that some barcodes are faster to scan than others, with the testers favoring larger barcodes with simpler (black ink on white card stock) color contrast. Time trials of bigger vs. smaller barcodes were performed to determine the importance of this factor.

The smaller study drug barcodes were approximately 7.5mm square, while the larger were approximately 10.5mm square. In study trials, the larger barcodes scanned slightly faster. With practice, 3.16 to 3.59 seconds were seen per scan for the larger barcodes, which includes: (1) pushing the scanning button, (2) aligning the package in the application reticle, (3) scanning, and (4) accepting by pushing the modal screen. The smaller barcode times were more variable, but the fastest set required 15% more time to perform the scan compared to the larger barcodes.

The manufacturer has chosen inkjet printing technology for the study drug, which results in black barcodes on white cardstock, which testers prefer. Alternative methods include laser printing, an ablation process that exposes the white carton underneath a lacquer. Often the lacquer color chosen is black or blue. These barcodes were aversive to testers, as they took longer to scan, sometimes up to 30 seconds.

3. DISCUSSION

3.1. KEY LEARNINGS

By running a live study at one of the nation's busiest pharmacies with real medications being delivered to real patients, the team gained important insights into what a larger implementation of a DSCSA verification system would look like. While not every dispenser will share that exact experience, extrapolating this performance and cost of the electronic, interoperable system mandated by the DSCSA to the dispenser community may provide some insights for policymakers.

3.1.1. PROCESSING

Barcode Reading Error Rates

A scanning success rate of 100% was observed, but initially scanning was difficult and slow. Reprogramming the cameras and re-framing the reticle improved performance. Subsequent developer-site practice dropped scanning to as fast as 3.16 seconds per scan. This validates the use of commercial off-the-shelf phones as scanning and application endpoints.

Interoperability Implementation and Implications

Throughout the course of the study, the BRUINchain application was capable of identifying expired and duplicate products. Expired products, duplicates, and failed verifications all resulted in the relevant stakeholders being alerted in real time with modal screens, mobile push notifications, and/or emails. An automated verification system was developed (the Oraculous Notification Service) to serve the role of “blockchain oracle,” allowing manufacturer study participants to verify products without requiring provisioning their membership on the BRUINchain blockchain.

User Satisfaction Ratings by Role

Study participants were surveyed following test rounds, with 6 responses.

Metric	Rating
Login success	100%
Application look and feel	93%
Notification success	100%
Barcode scanning reliability	97%

Metric	Rating
Notification format and appearance	97%
Ease of location change	92%
Overall impression	90%

Respondents reported two usability issues: slow scanning times and occasional modal screen freezes after sending notifications.

Simulated Counterfeit and Expired Lot Metrics

The team experienced a 100% success rate across scanning, expiration detection, and counterfeit detection. (As mentioned in section 2.3, the study methodology for counterfeits was to flag everything that was not the study drug and generate a modal warning.) Further on-site study with a significantly higher number of users and drugs is recommended to explore potential new edge cases.

Paperwork Reduction

According to FDA, “the burden time for [Form FDA 3911] is estimated to average 1 hour per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information.”²⁸ By

automatically sourcing all of the fields required for a Form FDA 3911, the solution explored in this study reduces reporting times to the push of a button.

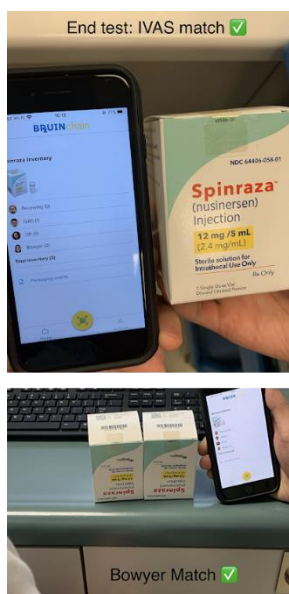
3.1.2. FINANCIAL IMPLICATIONS FOR DISPENSERS

Projected Costs to Implement

For the current study drug workflow at UCLA, a minimum of three scans were found to be required: (1) the first scan in receiving checks that the barcode is indeed a valid barcode, that the unit is not yet expired, and initiates the barcode verification process with the manufacturer; (2) after the notification is received from the manufacturer, a second scan is required to pull that unit out of quarantine, placing it into inventory and if desired, to notify the clinic; and (3) the prescriber, who is delivered a sealed box of the drug, scans again and after inspecting the vial for visual issues (such as cracks or discoloration) accepts the unit.

One could postulate over time that the number of scans required under an industry-standard interpretation of DSCSA might be lowered. For typical products that are visually inspected by the dispenser, *only two scans are required*, assuming the manufacturer verification is delayed more than a few seconds (i.e. not in real time).

According to Statista, there are 4.2 billion prescriptions dispensed each year in the US.²⁹ With a barcode scan time of 3.16 seconds, this implies 1,139 scans per hour. Based on two scans per package – one to send the barcode to the manufacturer or repackager in order to trigger the verification request, and one to check the package again after verification has been received – one might anticipate 7.4 million hours of scanning nationwide each year. According to the US Bureau of Labor Statistics, the mean average salary for the 309,550 pharmacists in the US is \$123,670 per year, or \$59.45 per hour,³⁰ while the mean average salary for the 417,860 pharmacy technicians in the US is \$34,020 per year, or \$16.35 per hour.³¹ At UCLA, the first scan was performed by a pharmacy technician and the second scan was performed by a pharmacist. Thus, assuming a roughly equal distribution of engagement with the scanning system, one can assume the value of pharmacy time as \$37.90 per hour.



This drives a best single-point estimate of the cost for barcode scanning at the dispenser level of \$280 million in labor costs. With a 30% benefit component added,³² the fully loaded labor-

related cost would be approximately \$365 million. On top of this one can also project additional requirements at the individual employee. Based on these figures, a full breakdown is shown below:

Expenditure	Unit Cost	Per	Annual Cost
Scan labor (2 scans per barcode)	\$0.087	2 Scans	\$365MM
Client hardware and training (biennial)	\$1000	Employee	\$364MM

Thus one may project that the cost of scanning, hardware, and training will amount to \$729 million, or approximately 17 cents per prescription.

Interoperability Implementation and Implications

Critically the above analysis presumes that *two scans would be required*. In a future state with a real-time blockchain-based connection, a workflow involving a single scan for the happy path would potentially be achievable. The dispenser would need to have a fast internet connection and the persistent ledger would need to reply within “internet time” (~120 milliseconds) for the entire process to be completed in a single scan. If the system performance were seconds or minutes, the receivers would have to momentarily set the box aside, and then rescan later to match the unit to its “verified” notification and move it from the quarantine bin into the regular inventory.

This represents a “two-tier warehouse” model at the receiving site, consisting of a “quarantine” tier into which drugs are scanned, and a “verified” tier that drugs are moved to upon receipt of verification. The verification tier can consist of several “sub-warehouses” representing separate stocks for programs such as 340B.

Any single-scan solution would clearly demand a highly performant, fully automated end-to-end system involving real-time access to a persistent ledger with up-to-date statuses. Human-in-the-loop systems would naturally drive high latency, and without persistence or an up-to-date ledger, a human-in-the-loop system will be necessary to drive confident verification. If it could be achieved within the required response time window, however, it would represent a \$183 million annual savings to dispensers in the United States, as well as a major bulwark against bad or fraudulent transactions.

Further benefits are recognized through the minimization of safety stock needed in the case of a potential quarantine event. *At any given time, the dispenser’s safety stock must accommodate the overall latency of the system to serve as a buffer.* The DSCSA gives each trading partner 24 hours to respond to a verification request, and the dispenser has no way of knowing how many trading partners who handled the drug prior to receipt at the dispenser. Given that tracing is

performed by chaining together 24-hour-latency messages, and that the number of trading partners is commonly thought to be up to 10, the dispenser must hold safety stock roughly proportional to the requirements of 10 days.³³

Even if the message chain can be collapsed to 24 hours, the dispenser must still hold safety stock in case of potential non-verification events. However, if the verification is done on a real-time ledger, no additional safety stock is required. With the top three wholesalers approaching \$500 billion in sales within the US, one may estimate based on a five-day week that an extra 10 days of safety stock would equate to \$20 billion in inventory.

3.2. PRACTICAL POLICY CONSIDERATIONS

3.2.1. SYSTEM COST REDUCTIONS AND SHARING

The cost and scale of the projected DSCSA deployment suggests a need to investigate other solutions that reduce total system cost. Stricter guidances for barcode sizes, color and placement represent such a potential solution, as even a 5% reduction in average scan time would save US dispensers nearly \$20 million annually.

A “bottle bill” model is worthy of consideration to drive compliance and trading partner equity. Even if a highly performant system were to reduce the cost of compliance to 10 cents per unit, this is still 10 cents taken away from patient care. Focus on tracing places the burden squarely on last-mile participants, both in terms of responsibility and cost. A blockchain system could levy 10-cent unit-level charges on those adding assets to the system and remit 10 cents per unit to those retiring barcodes. This cost-shifting³⁴ might be seen as a source not only of trading partner equity and an assignment to the least cost avoider,³⁵ but perhaps more importantly might enhance compliance and notify those adding assets with definitive assurance that their asset had been immutably retired.

Furthermore, the future adoption of radio-frequency identification (RFID) tags and readers (either standalone or in combination³⁶ with data matrix barcodes) could allow for more rapid and less expensive scanning, as pharmacists would not need to align the barcode with an optical scanner and could scan an entire “tote” with a wave of their arm.

3.2.2. DISPENSING UNDER DSCSA

Some medicines are pre-dispensed (“white bagged”) prior to their final destination through pre-paid channels; other medicines are barcoded at the case level or only on the outer package, so that by the time they are dispensed, the barcode may not be available to be scanned. This begs the question of how to best interpret “dispensing” in the DSCSA context.

3.2.3. INTEROPERABILITY AND SCOPE

The deeper question is whether policymakers advocate a solution with a single ledger which includes manufacturers and wholesalers and federates their data into a single actual or virtual persistent data store. A persistent data ledger with blockchain security protocols which covers all units traversing the United States could perhaps allow for dispensers to fulfill their obligations under DSCSA with a single scan, without trading off the security or integrity of trading partner data.

This also has major implications for the broader security of the supply chain. In the absence of a single persistent data store, dispensers and other stakeholders are left vulnerable to spoofing or man-in-the-middle attacks. Moreover, the interception of counterfeits becomes an ongoing challenge that must be identified and resolved repeatedly; whereas known counterfeits can be immediately flagged by a persistent blockchain system.

In summary, FDA's astute endorsement of standardized machine-readable product identifiers sets the stage for a global common data model for pharmaceutical supply assurance; further adroit policy decisions can take DSCSA warranties all the way to patients and their loved ones.

3.3. CONCLUSION

In conclusion, this study has introduced BRUINchain, a successful blockchain-based implementation of a system capable of meeting DSCSA standards for a dispenser operating solely on commercial off-the-shelf technology. BRUINchain is capable of real-time performance, multiple roles with differing permissions, in-app member provisioning, inventory tracking at the stockroom level, accurate barcode scanning and parsing, and verification from the manufacturer. Through a series of tests performed onsite at the UCLA pharmacy, the study has shown users' ability to use BRUINchain to efficiently scan, track, and verify drugs with minimal training.

The study has also discussed the nature of BRUINchain's persistent blockchain database, and contrasted it with comparable relational databases to highlight BRUINchain's improved security and potential to drive cost savings. Finally, the study discussed the relevant policy considerations that must be weighed to ensure American patients receive the full suite of benefits a globally accessible, DSCSA-compliant supply chain could afford them.

¹ U.S. Department of Health and Human Services Food and Drug Administration, Drug Supply Chain Security Act (DSCSA). [Internet]. U.S. Department of Health and Human Services Food and Drug Administration [updated 2019 May 22; cited 2020 January 13]. Available from: <https://www.fda.gov/drugs/drug-supply-chain-integrity/drug-supply-chain-security-act-dscsa>

² User DSCSA, the term dispenser “(A) means a retail pharmacy, hospital pharmacy, a group of chain pharmacies under common ownership and control that do not act as a wholesale distributor, or any other person authorized by law to dispense or administer prescription drugs, and the affiliated warehouses or distribution centers of such entities under common ownership and control that do not act as a wholesale distributor; and (B) does not include a person who dispenses only products to be used in animals in accordance with section 512(a)(5).” See endnote 1.

³ Standards for the Interoperable Exchange of Information for Tracing of Human, Finished, Prescription Drugs, in Paper or Electronic Format; Establishment of a Public Docket. Fed Regist. Document no. 2014-03592. [Internet]. 2014 February 20 [cited 2020 January 13]; 79(34):9745-9747. Available from: <https://www.federalregister.gov/documents/2014/02/20/2014-03592/standards-for-the-interoperable-exchange-of-information-for-tracing-of-human-finished-prescription>

⁴ U.S. Department of Health and Human Services Food and Drug Administration. DSCSA Pilot Project Program. [Internet]. U.S. Department of Health and Human Services Food and Drug Administration [updated 22 May 2019; cited 2020 January 13]. Available from: <https://www.fda.gov/drugs/drug-supply-chain-security-act-dscsa/dscsa-pilot-project-program>

⁵ UCLA Health [Internet]. Los Angeles, CA: UCLA Health. About Us: Best Healthcare, Latest Medical Technology [cited 2020 January 13]. Available from: <https://www.uclahealth.org/about-us>

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⁷ Federal Food, Drug, and Cosmetic Act 1938 (US)

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⁹ Microsoft Azure. Online transaction processing (OLTP) [Internet]. Microsoft Azure; 2019 July 26 [cited 2020 January 13]. Available from: <https://docs.microsoft.com/en-us/azure/architecture/data-guide/relational-data/online-transaction-processing>

¹⁰ Microsoft Azure. Online analytical processing (OLAP) [Internet]. Microsoft Azure; 2018 February 11 [cited 2020 January 13]. Available from: <https://docs.microsoft.com/en-us/azure/architecture/data-guide/relational-data/online-analytical-processing>

¹¹ Chowdhury M, Colman A, Kabir A, Han J, Sarda P. Blockchain Versus Database: A Critical Analysis. 2018 17th IEEE International Conference On Trust, Security And Privacy In Computing And Communications/ 12th IEEE International Conference On Big Data Science And Engineering. DOI: 10.1109/TrustCom/BigDataSE.2018.00186. Available from: https://www.researchgate.net/publication/327483781_Blockchain_Versus_Database_A_Critical_Analysis

¹² Archa, Alangot B, Achuthan K. Trace and Track: Enhanced Pharma Supply Chain Infrastructure to Prevent Fraud. *Ubiquitous Communications and Network Computing* [cited 2020 January 13]; 189-195. DOI:10.1007/978-3-319-73423-1_17

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- ¹⁵ All product names, trademarks and registered trademarks are property of their respective owners. All company, product and service names used in this paper are for identification purposes only. Use of these names, trademarks and brands does not imply endorsement. SPINRAZA is a registered trademark of Biogen Inc. Pyxis is a trademark of Becton, Dickinson and Company. UCLA, UCLA Bruins, University of California Los Angeles and all related trademarks are the property of the Regents of the University of California. Hyperledger and Hyperledger Fabric are trademarks of the Linux Foundation. The DocuSeal, Selvedge, and Oraculous software programs and the accompanying procedures, functions, and documentation described herein are sold under license agreement(s) by LedgerDomain Inc. Their use, duplication, and disclosure are subject to the restrictions stated in the license agreement(s). The QuaRxantine image is property of LedgerDomain Inc.
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- ²¹ Oracles are “services that send and verify real world occurrences and submit this information to smart contracts, triggering state changes on the blockchain.” See Voshmgir S. Token Economy: How Blockchains and Smart Contracts Revolutionize the Economy. Shermin Voshmgir; 2009.
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- ²³ Federal Food, Drug, and Cosmetic Act 1938 (US) s 582(b)(2)(A).
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