Q² Solutions®

HSBlox

WHITE PAPER

# APPLICATION OF BLOCKCHAIN IN CLINICAL RESEARCH

Utilizing Distributed Ledger Technology to ensure chain of custody, real-time status, and verifiability of data.

# DATA CHALLENGES

The success and prosperity of a pharmaceutical company can be measured by the breadth and quality of its pipeline coupled with its ability to maximize the value of each opportunity. In today's environment, with increasingly specialized and scarce opportunities to pursue, a complex web of local and international regulatory hoops to navigate, and unforgiving shareholder and market scrutiny, it is paramount to bring products to market quickly and reliably.

From a clinical trials perspective, the quest for efficiency and specialization has driven pharmaceutical companies (Pharma) to increasingly seek the expertise of contract research organizations (CROs), who carry the responsibility of meeting timelines, as well as quality assurance and data control requirements. CROs in turn look to sample laboratories, logistics partners, and specialized healthcare professionals to collect, store, and manage samples and data.

As CROs and Pharma increasingly expand outside of their domains and beyond the developed world to generate a diverse and cost-effective network of trial sites and sources of patients, the difficulty of achieving milestones and preserving acceptable data quality is magnified. A recent study of Clinical Operations leaders from global life sciences companies showed that 80% of respondents stated they regularly miss trial milestones.

At the end of the day, a complex network of local and remote systems and data sources is assembled to support a typical trial. Trial and sample data reside in disparate systems and are sourced from variety of core labs or ancillary vendors. As a result, 65% of Clinical Operations leaders report relying on outdated and manually compiled spreadsheets of data derived from multiple CTMS and EDC systems.[i]

## This data complexity leads to uncertainty for decision makers and several limitations:

1. **Cannot investigate issues in real-time**
2. **Don't know all actions being taken to address issues (visibility)**
3. **Too much data – don't know where the issues are**
4. **Don't trust the study metrics**
5. **Study metrics are out of date**

In sum, current conditions are ripe for a new technology that will provide more visibility and access to data in real-time for Pharma Sponsors, CROs and other stakeholders. In this paper we will discuss how blockchain technology can be used to overcome some of the limitations caused by disparate data systems.

# BLOCKCHAIN AND DISTRIBUTED LEDGER TECHNOLOGY

The past few years have seen a tremendous surge in dialogue about blockchain and its potential to disrupt the healthcare and life sciences ecosystems. With multiple participating stakeholders and disparate systems, sharing data, validating its provenance, and addressing privacy concerns presents many challenges. Blockchain technology is showing promise in addressing the challenges, generating auditability and traceability between stakeholders with a single source of truth that reduces errors and the need for reconciliation. In simple terms, it enables the participants who are privy to the shared facts of a transaction to know with 100% certainty that what one entity sees is what the others also see.

In this paper, we will use the term "distributed ledger" in place of "blockchain." Emily Rutland of R3 outlines this distinction by noting "Blockchain has a shared and replicated ledger comprised of information stored in "blocks" and sits below a distributed ledger and acts to verify transactions submitted by producing a new "block" to the chain. Distributed ledger is a record of consensus with cryptographic audit trail maintained and validated by nodes."[ii] So, for our purposes, a distributed ledger (Distributed Ledger Technology or "DLT") is a record of consensus between network participants with an audit trail of shared ledger entries that have been validated by the participants.

## DLT PROOF-OF-CONCEPT – SAMPLE TRACKING

This paper outlines our findings from a DLT Proof-of-Concept (POC) we conducted for human biological sample management in clinical trials. The DLT solution referenced in this paper makes use of a private permissioned ledger not a public one. The POC was done using R3's open source CORDA platform. Some of the benefits of DLT include:

- **Longitudinal immutability of records**
- **Automation of processes using smart contracts**
- **Audit & validation (visibility for audit & compliance---FDA and other regulatory bodies)**
- **Security---data in transit and at rest is encrypted; identity management is handled cryptographically**
- **Cost reduction from reduced errors and need for reconciliation since there is a single source of truth that is shared by the participants privy to the shared facts for a given transaction**
- **Real-time reporting & updates, transaction processing, and data exchange**
- **Permissioned access---only the participants involved know a transaction exists**

# APPLICATION OF DLT IN CLINICAL TRIALS

During clinical trials, human biological samples are collected at clinical investigator sites over an extended period. Flawless administration of the chain of custody is critical to sample management because correct handling impacts both the course and results of clinical trials.

Successful execution of clinical trials involves the coordination of a myriad of resources and processes. Maintaining visibility into the chain of custody can be challenging for many reasons, as can providing the level of data integrity and traceability required by regulatory authorities. At present, the chain of custody spans multiple stakeholders and disparate data systems, augmented by extensive processes at the clinical investigator sites. The result is excessive manual data entry, the need for coordination between internal and external teams, frequent opportunities for error and difficult end-of-trial reconciliation.

Sample management can involve missing or contaminated samples, incomplete data, delays in reporting results, and substandard logistics. This leads to higher costs, lack of transparency, and other problems that can be avoided with the use of better technology like DLT.

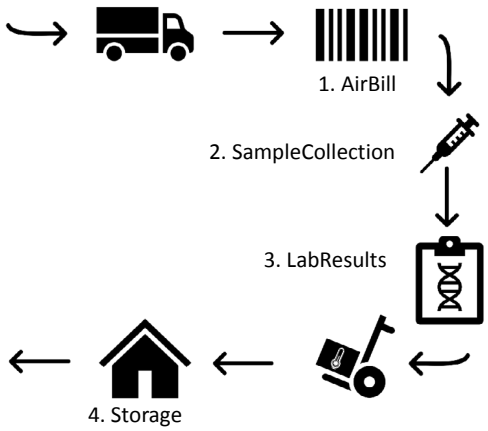
# A CASE FOR DLT

**Collectively, these factors represent a case for implementing DLT:**

- **The FDA and other regulatory bodies are tightening their scrutiny of traceability and Chain of Custody (CoC)** [iii]
- **There is no industry standard regarding the exchange of CoC information**
- **Each vendor and participant in the CoC implements what they need**
- **Assembling a full CoC record is a significant challenge, due to the various participants and disparate systems in use**
- **Trial Sponsors benefit from full end-to-end visibility**

# DLT SAMPLE TRACKING PROOF-OF-CONCEPT

With this background, Q² Solutions (**www.q2labsolutions.com**) developed a sample tracking proof-of-concept (POC) using distributed ledger technology (DLT) in partnership with HSBlox, Inc. (**www.hsblox.com**). The goal of the POC was to explore real-time tracking of biological samples in clinical trials. The POC simulated collection, transportation, test result generation, and storage of the sample. For the POC, a subset of stakeholders was represented as DLT network participating nodes: a Transportation Courier, Q² Solutions Operations, Q² Solutions Laboratory, a Storage Facility, and HSBlox Notary. A representation of the participants and associated smart contracts can be seen in Table 1 below.




| Smart Contracts | Transaction | Participating Nodes |
|---|---|---|
| 1. AirBill | 1. Trial site scans the Air Bill | Courier, Q² Operations, HSBlox Notary |
| 2. SampleCollection | 2. Q² Operations accessions a sample into its core system | Q² Operations, Q² Laboratory, HSBlox Notary |
| 3. LabResults | 3. Lab results are generated for the sample | Q² Operations, Q² Laboratory, HSBlox Notary |
| 4. Storage | 4. Sample moved to storage facility | Storage Facility, Q² Operations, HSBlox Notary |

Table 1 – POC Participants and Smart Contracts

# GOALS OF THE POC

## For the sample tracking POC, the following goals were established:

1. Ensure a streamlined and transparent process across network participants
2. Prove that real-time status updates can be tracked efficiently
3. Achieve a scalable, transparent, and cost-effective process with a DLT approach
4. Automate receipt, reporting, and reconciliation, by standardizing and integrating the process
5. Utilize a workflow-based application so that users of each entity can visualize and track details in real time
6. Utilize a node explorer application to provide visualization of the decentralized, distributed aspects of the DLT network

# WHAT WE LEARNED

Implementing a sample tracking solution with DLT can dramatically streamline the collection and sharing of information. Multiple stakeholders---each with their own systems and data repositories---represent an intelligent distributed network for gathering and disseminating clinical and operational data relevant to the trial and its outcome. Each stakeholder can share data at a granular level (see the example in **Figure 1** below), in real-time, and on a permissioned basis using smart contracts i.e. a subset of the data can be shared with one or more participants based on the configuration and logic in the Smart Contract. The Smart Contract is automatically triggered when pre-defined rules are met ---transactions written to the ledger are digitally signed and timestamped, ensuring provenance and immutability of the record at a point in time.

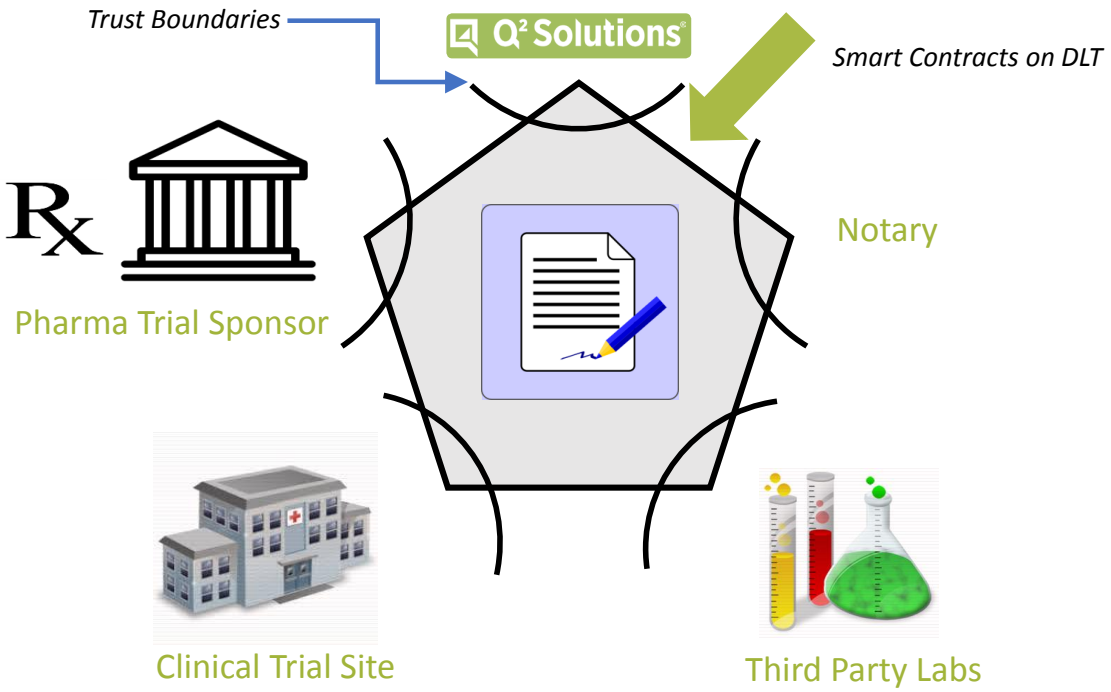



**Figure 1 – Data sharing with smart contracts**

The POC demonstrated that smart contracts can improve the efficiency and transparency of data management with respect to sample management. In the POC, the need to reconcile between entities was eliminated and trial audit processes were expedited. Transparency and traceability of facts are important to the validity of clinical trials. The benefits of this approach were seen in:

1. **Assurance of data quality**
2. **Verifiability of provenance**
3. **Elimination of reconciliation between entities**
4. **Immutable audit history**
5. **Real-time data dissemination**
6. **A single source of truth**

# DIGITAL SAMPLE MANAGER (DSM™) APPLICATION

The DSM application from HSBlox provides an interface where stakeholder entities can easily locate details of the transactions in which they participate in (**Figure 2** below). The application is deployed on each node and has an additional security layer where users, roles, and permissions care administered. Data is pulled from both ON- and OFF-ledger databases to tie the DLT-based information with the enterprise systems of the entities, providing actionable intelligence to end users.

Additionally, HSBlox Node Explorer is an administrative application for DevOps/MSO staff of the participating entities. Node Explorer helps with the granular details of the underlying data---entities see only their own information from the on-ledger data store.

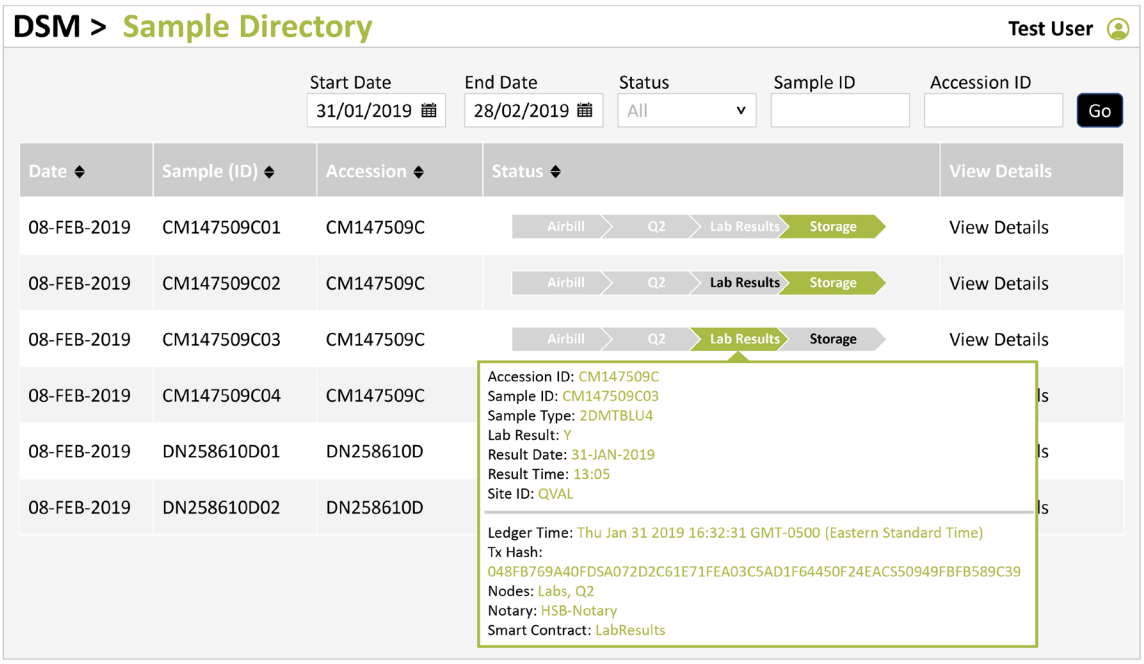



Figure 2 – Digital Sample Manager

# TECHNICAL IMPLEMENTATION DETAILS

Microsoft Azure cloud infrastructure was used for the DSM POC. The code was deployed and executed in the Microsoft Azure cloud utilizing Ds-v3 Virtual Instances with premium storage. The infrastructure was created and managed as code with HashiCorp's Terraform to provide consistency and repeatability. The schematic in Figure 3 represents a five node private permissioned distributed de-centralized network.

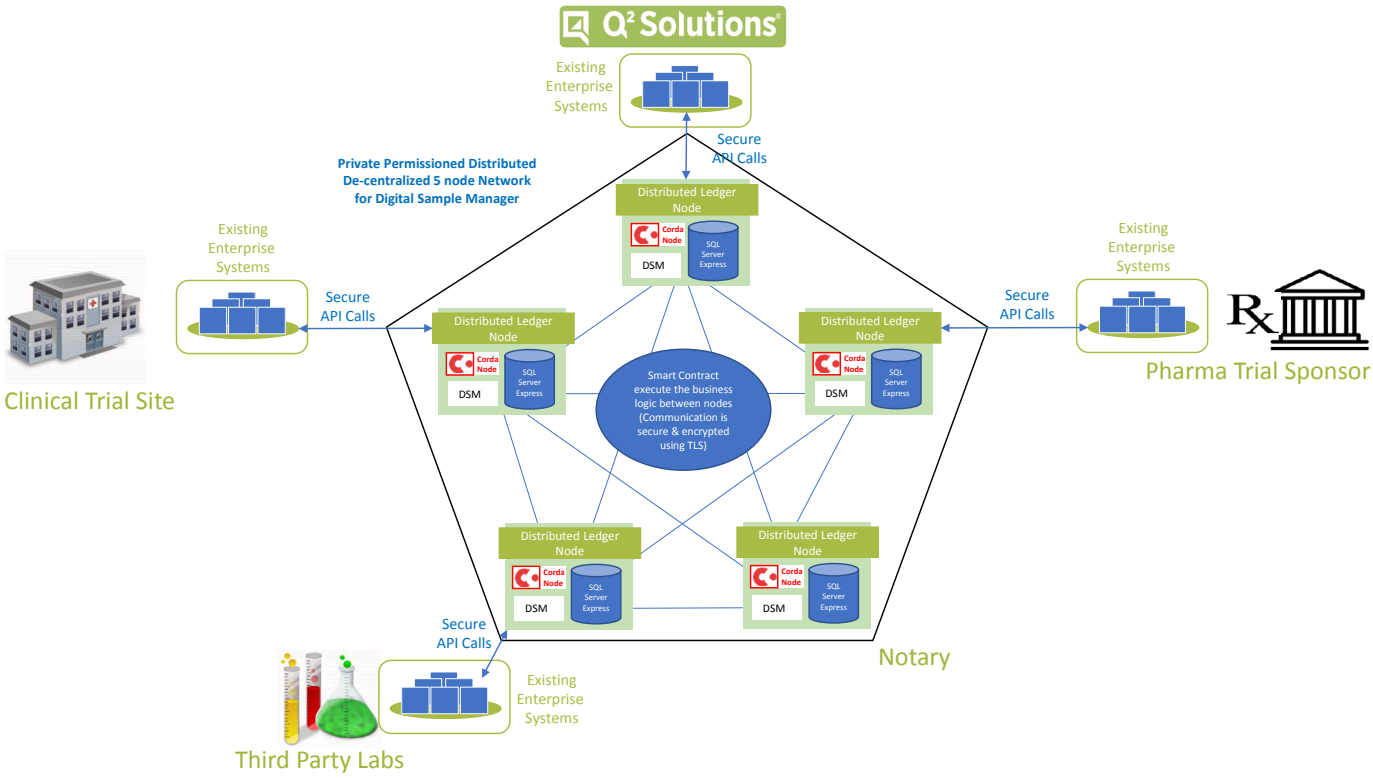



Figure 3 – Schematic depicting the 5 nodes

**The Azure Instances ran Ubuntu 16.04LTS which had R3 Corda Open Source (Version 4.0), Microsoft SQL 2017 Express, Nginx, Node.js, and Java Runtime Engine. Smart Contract code was written in Java. For the POC, On Ledger data was stored in a local SQL Express Instance. Corda exposes an API that is utilized by both the node owner's existing Enterprise Systems as well as the DSM™ application via TLS. The DSM™ application runs on Node.js. For the POC, Let's Encrypt was utilized for SSL/TLS certificates which were managed by Nginx and reverse proxied back to both Corda API and DSM™ ports.**

# THE FUTURE OF DLT IN CLINICAL TRIALS AND RESEARCH

Our POC, which focused on biological sample management, included a subset of stakeholders from the clinical trial landscape. We envision a future state where additional stakeholders are continuously added as network participants---including cross-trial data sharing [iv] and integration of the patient, where the patient can permission access to their medical records and edge data from devices. [v] Gaining access to patient medical data can provide tremendous opportunities for clinical research---creating actionable intelligence from the added data.

DLT can significantly improve patient recruitment, consent, and participation in clinical trials. According to Accenture, "Only 38 percent of patients feel knowledgeable about new products coming to market that may benefit their health and less than half of patients feel that their doctors discuss the entire spectrum of therapies." [vi]

However, patients need the incentive to donate data---and the assurance that it will remain private and secure. Expanding the pool of patients and the aggregation of their individualized data can be achieved with a DLT approach. With patients as stakeholder participants, smart contracts can govern the permissioned sharing of their medical data, as well as an immutable record of their consent. Deloitte notes, "A solution which enforces rules, privacy, and regulations in a mutually agreed upon manner, resulting in a smart contract between patient and healthcare stakeholders can be an important enabler to clinical research." [vii]

Acceleration of clinical trials and regulatory approvals can be enabled by DLT, benefiting trial sponsors, trial sites, researchers, clinicians, and patients. The identification of potential participants, their consent and enrollment and the aggregation of their data can be faster and more efficient with permissioned access approaches on DLT. [viii]

# APPENDIX - SUPPLY CHAIN OPPORTUNITIES WITH DLT

This APPENDIX provides additional examples of supply chain opportunities with DLT. Reducing complexity while improving visibility and traceability are the key challenges. The HSBlox DSM solution and DLT platform offers Pharma and Life Sciences the ability to operationalize track and trace initiatives quickly with an experienced solution provider.

A wealth of uses cases exist for track and trace initiatives in Pharma and Life Sciences. Following are some examples in the areas of drug development, supply chain, and channel distribution (**Figure 4**).

### Drug Development

- Sample Management
- Patient Consent
- Trial Data Records

### Supply Chain

- Inventory Management
- Regulatory Compliance
- Logistics Compliance

### Distribution Channels

- Trade Marketing
- Returns Authentication
- Counterfeit Prevention

Figure 4 - Example Use Cases

## Example Stakeholders, Across Multiple Use Cases

- Pharmaceutical Manufacturers
- Distributors
- Trial or Research Sponsors
- Clinical Trial Sites
- Labs
- Clinical Research Organizations
- FDA and Internal Auditors
- Shippers
- Local and Third-Party Labs
- Patients

For more granular insight, examples of transactions within the Drug Lifecycle are depicted in **Figure 5.**

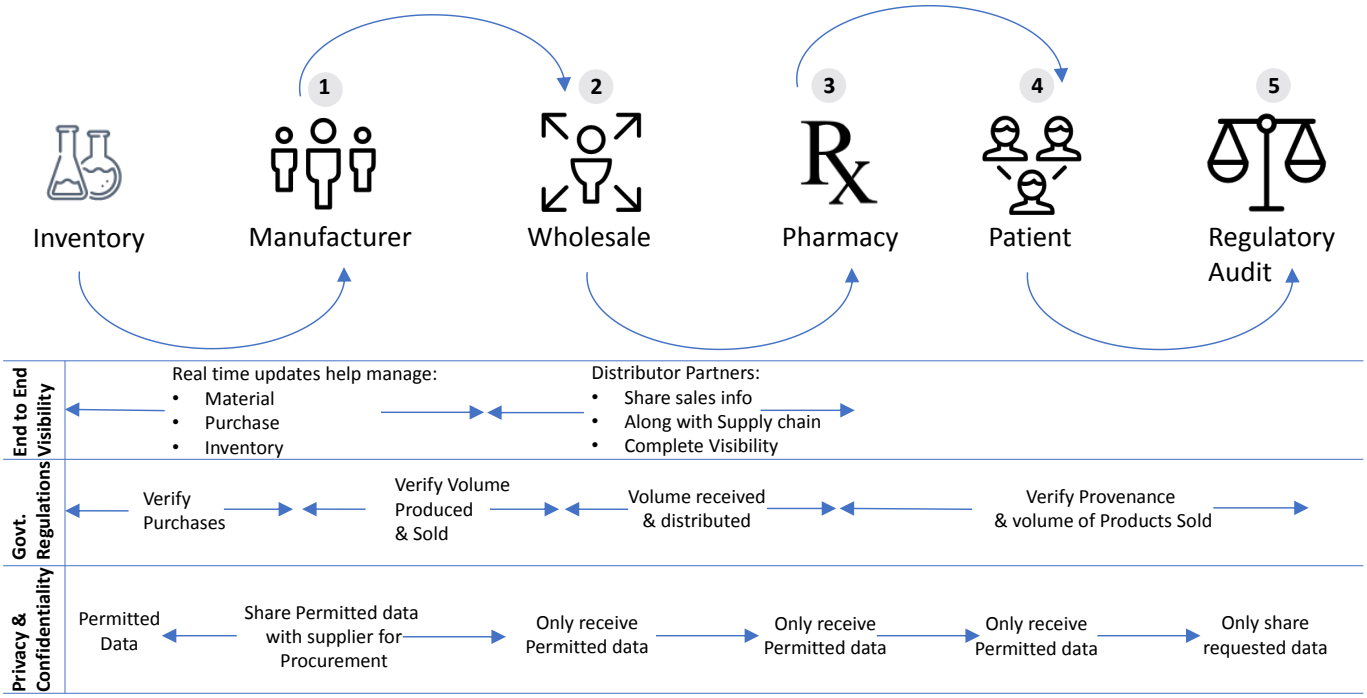



Figure 5 – Drug Lifecycle Transaction Examples

# ABOUT Q² SOLUTIONS

Q² Solutions is a leading clinical trial laboratory services organization with end-to-end laboratory services and secure, enterprise-wide biospecimen and consent management solutions. With a relentless focus on quality and innovation, Q² Solutions uses its global experience and scientific expertise to transform science and data into actionable medical insights that help customers improve human health. A joint venture of IQVIA and Quest Diagnostics, Q² Solutions combines the best of each parent organization's clinical trials laboratory services capabilities to fulfill its mission of treating each sample as if a life depends on it.

## About HSBlox

HSBlox is a leading vendor of choice for healthcare software solutions utilizing blockchain and data science. An Atlanta-based team of healthcare, fin tech, and digital supply chain management professionals, HSBlox is delivering patented solutions to the healthcare ecosystem, addressing the demand for secure, real-time information sharing and interventions. For more information, **visit www.hsblox.com.**

# GLOSSARY OF TERMS:

- **Chain of Custody** - chain-of-custody means knowing who has what, when and where. It is a chronological documentation of all parties that come in to contact with an item, and a history of all transactions.
- **Consensus Mechanism** – a set of rules that validates a transaction and records it on the ledger as an immutable record.
- **Immutability** – once a record is written to the ledger, it cannot be altered. Participants to the transaction have electronically signed the record, confirming its validity.
- **Node(s)** – nodes are the stakeholder entities participating in the DLT network.
- **Notary** - a notary is a CORDA DLT network service that provides uniqueness consensus by attesting that, for a given transaction, it has not already signed other transactions. Notarization is the point of finality.
- **Provenance** - data provenance is a historical record for any piece of data---where the data originated, tracking of changes made to the data, who made the changes, and who the data has been shared with over time. This provides assurance the information can be trusted for data validation and audit purposes.
- **Smart Contract** - A smart contract is computer code by which DLT network participants agree to share information with each other. The smart contract is automatically enforced on the network when pre-defined rules are met. Smart contracts enforce business rules, enabling automation of processes, data sharing, and transaction processing.
- **Clinical Trial Management System (CTMS)** - a software system used by biotechnology and pharmaceutical industries to manage clinical trials in clinical research. The system maintains and manages planning, performing and reporting functions, along with participant contact information, tracking deadlines and milestones.
- **Electronic Data Capture (EDC) system** - a computerized system designed for the collection of clinical data in electronic format for use mainly in human clinical trials.

[i] https://www.comprehend.com/whitepaper/clinops-benchmark-report/

[ii] http://www.finra.org/sites/default/files/2017_BC_Byte.pdf

[iii] http://www.fda.gov/downloads/ScienceResearch/FieldScience/LaboratoryManual/UCM092176.pdf

[iv] https://www.bmj.com/content/345/bmj.e7570

[v] https://www.chicagobusiness.com/health-care/allscripts-partners-microsoft-match-patients-clinical-trials

[vi] https://www.accenture.com/t20180409T144103Z__w__/us-en/_acnmedia/PDF-71/Accenture_Blockchain_Innovations_Life_Sciences.pdf

[vii] https://www2.deloitte.com/us/en/pages/public-sector/articles/blockchain-opportunities-for-health-care.html

[viii] https://www.bcg.com/en-us/publications/2018/prescription-for-blockchain-healthcare.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