A Survey on Application of Blockchain Technology in Drug Supply Chain Management

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***Abstract*—Drug counterfeiting and trafficking are common all over the world. The main reason for this is that the traditional drug supply chain model is opaque, and the database is controlled by the direct interest person, so there is a chance that the actual controller tampers with or falsifies the data for personal gain. The blockchain, as a distributed ledger, can achieve process transparency, data sharing, and autonomous management in the pharmaceutical supply chain through its unique cryptographic algorithms, smart contracts, and consensus mechanisms. However, it introduces a number of new issues, such as scalability, system interoperability, and regulatory policies. This paper discusses the benefits of blockchain technology in enabling the drug supply chain, as well as some academic research and mature industry solutions in this area. We also go over some of the issues that need to be addressed and potential response strategies for using blockchain technology in pharmaceutical supply chain scenarios. Finally, in order to address issues with current drug supply chain regulation, we propose a new model that incorporates the "governing blockchain by blockchain" architecture in order to achieve safe and efficient automated supply chain management.**

Keywords—blockchain regulation, drug supply chain, governing blockchain by blockchain, counterfeit drug governance

I. INTRODUCTION

The number of people who die from malaria is about 700,000 per year, while as many as 200,000 die from counterfeit drugs [1]. The FBI and the International Anti-Counterfeit Coalition(IACC) report that counterfeit drugs are one of the largest criminal businesses of the 21st century, with new counterfeit drug manufacturers entering the market every day [2][3]. The World Health Organization(WHO) defines counterfeit medicine as "a product that has been deliberately falsified in its manufacture and/or in its identity and/or origin, so as to make it appear to be a genuine product". Counterfeit medicines may contain insufficient or incorrect ingredients or false information (e.g., incorrect labeling information and incorrect packaging) [4]. According to the WHO, one in ten medicines in developing countries is either below acceptable standards or completely counterfeit [5]. The Asia-Pacific, Africa and Latin America regions are the most affected by counterfeit medicines, where nearly 30% of the medicines are counterfeit and where nearly 1.5 million people die from them each year [6]. Developed countries are no exception, with Europe also reporting nearly double the number of counterfeit drug cases compared to the previous year [7]. In addition, an increasing number of people are purchasing drugs through online pharmacies and other unauthorized distribution channels, which has expanded the sales channels of fake drugs and made them more difficult to trace [8]. The problem of drug counterfeiting exists mainly because the process of the drug supply chain is not transparent. As a result, mistrust has emerged between drug consumers and manufacturers. In a WHO survey, it has been passively accepted that 10% of the drugs in the world are counterfeit [9]. For the prevention of drug counterfeiting, Erwin Blackstone et al. made three recommendations: 1. strengthen supply chain management, 2. increase control over secondary drug markets, 3. use new technologies to track and trace counterfeit drugs [10]. These recommendations have given rise to the solution of applying blockchain technology to the drug supply chain, which is a solution to the root cause of drug counterfeiting.

Blockchain technology can provide a distributed and decentralized data ledger for pharmaceutical supply chain systems, where relevant data can be stored during the pharmaceutical supply chain process. Transparent visibility, authenticity and secure storage of supply chain data can be achieved through blockchain, and blockchain can provide a platform for data sharing, thereby reducing communication costs and enhancing trust. According to McKinsey & Company survey, the cost of supply chain activities accounts for 25% of the cost of pharmaceuticals, and to the extent that suppliers, manufacturers, regulators, and back-end healthcare providers can improve the efficiency of collaboration, the cost of pharmaceuticals will be reduced [11]. Risk factors in the supply chain include information infrastructure downtime, lack of information transparency between logistics and markets, lack of compatibility of IT platforms between supply chain partners, and cybersecurity [12]. Applying blockchain to the pharmaceutical supply chain can mitigate the impact of these risk factors.

The main contributions of the paper are as follows:

- Summarizing the problems with traditional centralized supply chain solutions and discussing the benefits of applying blockchain to the pharmaceutical supply chain.
- Analyzing existing blockchain-based drug supply solutions in academia and industry and summarizing their current problems.
- Proposing a "governing blockchain by blockchain" architecture in the pharmaceutical supply chain field, so as to achieve efficient, safe pharmaceutical supply chain supervision.

The remainder of this paper is as follows. In Section 2, we introduce the drug lifecycle, the traditional supply chain process and its problems, in addition provide an overview of blockchain technology and the role of blockchain in the lifecycle. In Section III, we do a review of blockchain-based drug supply chain systems for an analytical summary. In Section 4, we discuss the problems and challenges facing the application of blockchain technology in pharmaceutical supply chain and future research directions and propose a "governing blockchain by blockchain" structure in pharmaceutical supply chain scenarios. In Section 5, we summarize the whole paper.

II. Background

This section first briefly introduces the drug lifecycle and traditional supply chain processes and blockchain technology, analyzes the shortcomings of existing centralized solutions, and then discusses what benefits each process in the drug lifecycle can gain from blockchain.

A. Problems with The Traditional Pharmaceutical Model

The life cycle of a drug is shown in Fig. 1. It consists of six main stages: research, manufacture, distribution, retail, use and disposal. Each stage of the life cycle needs to be well-regulated and controlled. In fact, this is currently difficult to achieve. Stakeholders in the drug supply chain include raw material suppliers, manufacturers, warehouses, distributors, pharmacies, and final consumers. The process is shown in Fig. 2. At present, there are two modes of drug traceability in China, which are self-built traceability systems by pharmaceutical enterprises and traceability services provided by using third-party platforms.

The following problems exist in traditional models:

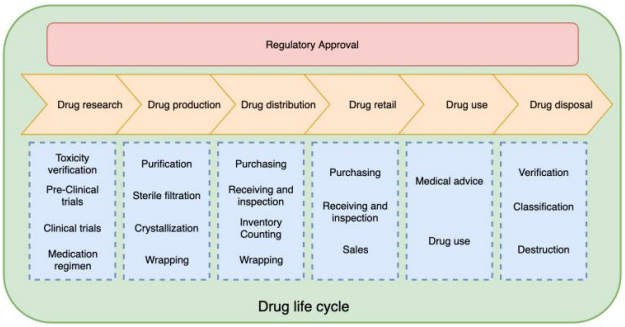

Fig. 1. Drug life cycle.

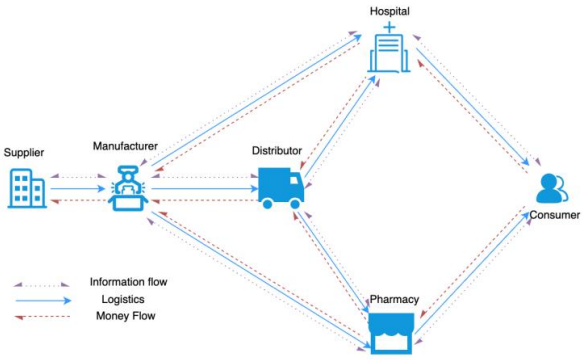

Fig. 2. Pharmaceutical supply chain process.

- Authenticity of drug data: The drug database is controlled by pharmaceutical companies, so there is a possibility of data tampering or falsification. For example, the modification of key data such as the manufacture, source and expiration. This data is crucial to consumers and involves the safety of medication use.
- Traceability data integrity: Due to the complex structure of the drug supply chain, more layers and that the whole life cycle is very long, it is difficult to record the data of the whole life cycle process. Therefore, in part of the gray unrecorded process, there will be the possibility of fake drugs mixed in.
- Sensitive data privacy: Pharmaceutical companies using third-party traceability platforms need to upload drug data to the database. The third-party platform holds all the drug information entered into the traceability system. For pharmaceutical companies, sensitive data may be classified, analyzed and conducted gray transactions.
- System reliability: In the traditional centralized database, once the server is down or other accidents, the traceability platform will not be able to provide services, even the data does not exist or can not be recovered.
- Difficult to regulate: At present, drug supervision is mainly based on random inspection, with consumer complaints and reports as auxiliary supervision. This can prevent drug safety accidents and play a regulatory

role to a certain extent, but such a regulatory approach is far from sufficient.

The above problems are mainly due to the fact that centralized databases have limited security and data opacity. In the new generation of blockchain-enabled drug supply chain, each data holder needs to upload data to the blockchain. Ultimately, transparency is achieved, and timestamp and Hash mechanisms ensure that the data cannot be tampered with.

B. Blockchain Technology

Blockchain is a concept introduced by Satoshi Nakamoto in 2008 as a peer-to-peer network [13]. In fact, before Satoshi Nakamoto formally proposed blockchain, blockchain-like concepts and the underlying technologies had already been proposed [14-17]. In 2013, Vitalik designed Ether in his white paper [18], which added smart contracts on the basis of blockchain. The Linux Foundation launched an open-source blockchain project, Hyperledger, in 2015. Hyperledger differs from permissionless chains such as Ether and Bitcoin in that it builds a permissioned chain, in which nodes need to be authorized to join the system [19]. The evolution of blockchain is shown in Fig. 3.

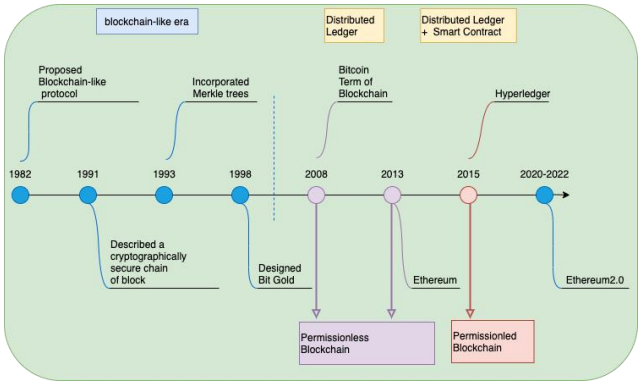

Fig. 3. Blockchain development history.

The blockchain network acts as a peer-to-peer network and is a chained storage structure where each full node has a full copy of the ledger for maintenance. There is a special kind of node in the blockchain, the miner node, which is generated through consensus algorithms such as POW, POS. The miner node packages the transactions in the blockchain network into blocks and broadcasts them to all nodes, while other nodes add the newly generated blockchain to their copy. The blockchain is decentralized by such a consensus mechanism. Instead of a centralized institution maintaining a master ledger, each node maintains its ledger, so that the true state of the ledger can be guaranteed against forgery as long as no more than half of the nodes have malicious nodes. A single block consists of a block header and a block body. The real verified transaction data is stored in the block body, and a unique Merkle root is generated through the hash process of Merkle data. Data stored in the block header includes the hash value of the previous block, timestamp, difficulty, random number nonce, etc. The block structure is shown in Fig. 4. Due to the characteristics of the hash function, if the block content is slightly modified, its hash value will change dramatically, which is impossible to tamper with due to the chain structure of the blockchain. Asymmetric cryptography is also used in the blockchain to implement data encryption and data signature to ensure security.

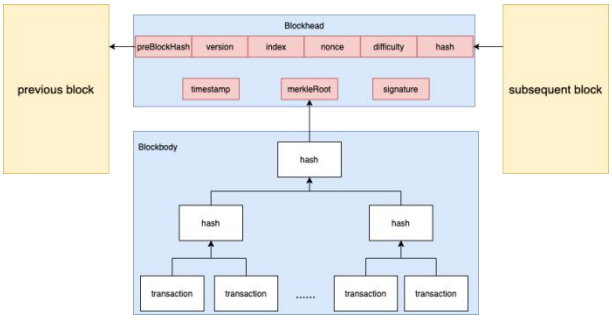

Fig. 4. Block structure.

C. The Role of Blockchain Technology in The Drug Lifecycle

It is a very complex and long process from initial drug development to final drug disposal, which also involves various entities, people, facilities, raw materials and so on [20]. In the traditional process, there is a lack of accurate and valid data due to opacity and the problem of data silos. For drugs, the sooner they are developed and put into use, the more people gain. The sooner problematic drugs are identified, the sooner they can be recalled, and the less impact and damage they cause. Among them, trust issues are the main reason for slowing down the decision-making among organizations, and blockchain can achieve data accuracy, privacy, transparency, tamper-evident and traceability, thus maximizing the trust among stakeholders and accelerating the drug development and recall process. The role of blockchain will be discussed below in terms of each process of the drug lifecycle.

- R&D Stage: In the traditional model, research activities are isolated among labs, institutions and industries. In contrast, blockchain technology intervenes to enable information sharing through its distributed, tamper-evident and transparent ledger, and to guarantee ownership issues to enhance trust as well as reduce time, economic and personnel costs.
- Production Stage: The existing manufacturing model lacks universality. Since various raw material suppliers are usually spread all over the world, the lack of common legal standards and the inability to guarantee the shipping conditions during transportation leads to high supply costs. Blockchain, on the other hand, enables seamless oversight, thus ensuring that raw materials, products, equipment, storage and transportation are reliably controlled, and it provides a globally accessible platform for borderless data sharing.
- Distribution Stage: The current distributors are also spread all over the world, and there are common problems with transportation and condition control. Under the traditional model, product recall is also complicated, inefficient and costly due to the opaque information, in which there may also be counterfeit drugs mixed into the process. But Blockchain can provide an untamperable ledger record of all information about distributors and information about

storage and shipping conditions, thus allowing for quick and reliable flagging and recall of problematic drugs.

- Use Stage: Patients can have little trust in doctors' prescriptions due to the asymmetry of doctor-patient information. At the same time, the existing model, the lack of information interchange between different institutions also leads to extremely high medical costs. With the application of blockchain technology, the sharing of patient data can be realized. Through Internet-of-Things(IoT) and other technologies, doctors can be the first to know the adverse reactions of drugs, so that they can take measures. At the same time, the information of adverse reactions on the chain can help patients or doctors to better measure the side effects of the drug.
- Disposal Stage: In the current model, the disposal of waste drug ingredients and the flow of drugs are opaque. Blockchain technology, however, can help governments track harmful drugs and hold those involved accountable, while patients can be guided to safely dispose of waste drugs.

III. An Overview of Blockchain Applications in Pharmaceutical Supply Chain Scenarios

With the arrival of blockchain 3.0 era, people have realized that blockchain is not tied to cryptocurrency and gradually started to combine it with various fields such as education [21][22], banking [23], government [25], healthcare [26][27], logistics [28], agriculture [29], power grid [31], energy [32], Internet of things [33][34] and supply chain [35], blockchain has become the protagonist of the Internet of Value era.

The pharmaceutical supply chain is a more complex process compared to other general supply chain scenarios, and the regulation or traceability of data on it is also more important because once a certain drug has a problem, it may cause a huge health impact on the user or even directly cause the death of the user. Existing technologies such as RFID [36], Date-Matrix [37], and NFC [38] have started to be applied in the supply chain scenario, but they still cannot meet the demand of establishing a transparent supply chain. And the application of blockchain technology can make the supply chain process more transparent and secure and ensure that the process data cannot be tampered with. Fig. 5 represents a basic blockchain-based pharmaceutical supply chain architecture. The application of blockchain in pharmaceutical supply chain will be discussed by academia and industry respectively as follows.

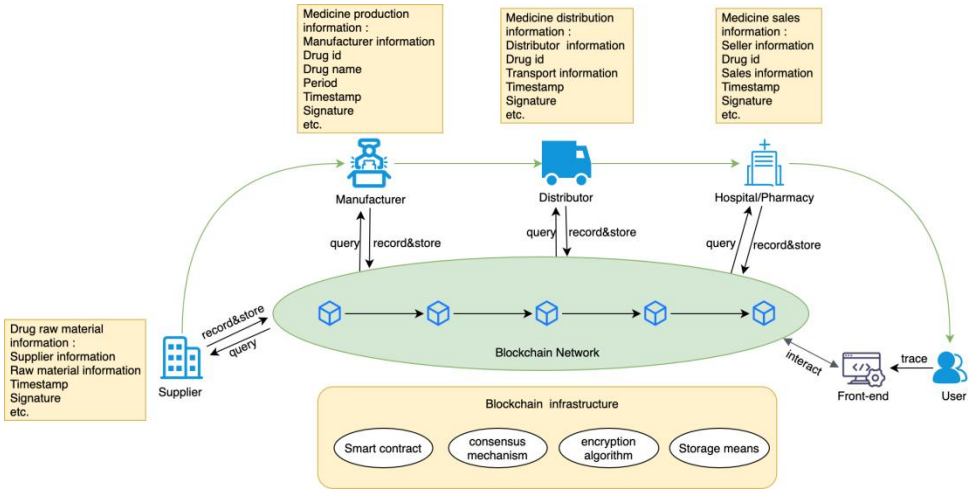

Fig. 5. Blockchain-based pharmaceutical supply chain framework.

A. Blockchain-based Drug Supply Chain Research in Academia

Gcoin-based regulatory model for drug supply chain[39] J.H. Tseng applies the Gcoin blockchain to the drug supply chain to create transparent drug business data for drug data flow. He also converts traditional testing and review models to a regulatory network model. With the Gcoin blockchain system, all regulators can track drugs in the supply chain without having to enter factories, warehouses and pharmacies, which can significantly reduce regulatory costs. The solution uses the Gcoin blockchain system to improve the efficiency of information exchange and combines the open government and decentralized autonomous organization (DAO) regulatory models to ensure a secure and transparent pharmaceutical supply chain ecosystem. Due to Gcoin's excellent regulatory design, and the ability to global governance model, it is very suitable for the application in the field of pharmaceutical supply chain, while being able to apply the Gcoin blockchain prevention double flower mechanism to moderate the problem of counterfeit drugs. In terms of supply chain data sharing, system participating nodes can use the blockchain platform to establish trust relationships based on economic and mathematical approaches without knowing each other, thus reducing communication costs in the supply chain. Overall the solution is still relatively informative.

On-chain and off-chain collaborative supply chain[40] This solution proposes a blockchain-based drug supply chain to address the existing drug supply chain regulatory issues. It uses mixed on-chain and off-chain storage, and the detailed

information of drugs can be stored off-chain to reduce the burden of blockchain storage as well as to enhance the traceability and transparency of drug supply. Also, due to this two-layer mechanism, data privacy can be effectively ensured. Because all large file data is stored under the chain, the amount of data on the chain is also more controllable, and there will not be a situation where the average user cannot afford the amount of data for blockchain applications as time goes by.

Drug Recall Chain[41] Divyansh Agrawa et al. have researched a blockchain-based management solution that combines forward and reverse chains to solve the problem of drug recalls. The solution supports secure and transparent transactions, reduces time and economic costs in the drug recall process, and increases transport reliability. In addition, they present two mathematical models that allow manufacturers to calculate the overall cost of the recall process, the time spent, and the reliability of different route transportation modes. However, for more complex and common cross-border transactions, countries differ in both policies drug recalls and on transportation costs, so the solution is not practical in the more common cross-border scenarios, and its data model for calculating costs cannot be used in cross-border scenarios.

Pharmacosurveillance Blockchain System[42] The system prototype is actually a DApp supported by a DFS backend that supports a private chain network. It has five starting nodes (FDA, manufacturer, distributor, retailer, and consumer portal), with the FDA overseeing data validation and the supply chain process initiated by the manufacturer and recursively validated for each transaction. Consumers can scan barcodes on receipts through the consumer portal to view the flow of drugs. In addition, the DApp is able to detect anomalies, unauthorized data embedding and drug losses by comparing DFS content with bookkeeping records.

PharmaCrypto [43] PharmaCrypt is based on Ether and was created using the AWS platform to record and timestamp product transfers in the pharmaceutical supply chain. As drugs move through the supply chain, each shipment transaction is recorded and time-stamped by scanning a barcode. Users obtain drug information by scanning the barcode of the drug package to trace and verify the drug to prevent the infiltration of counterfeit drugs. Nevertheless, the solution seems to be only for some small and medium-sized applications and cannot be generalized for large pharmaceutical companies. Because the annual business volume of large companies is staggering, and all the data is stored on the chain, the invalid data on the chain cannot be deleted. Over time, the data on the chain may reach a point where it cannot be carried. Also, due to the characteristics of the blockchain, the final data migration will become very difficult.

BRUINchain [44] The project was part of the FDA DSCSA pilot project program and was tested in a series of real-world scenarios at the UCLA Health Center. BRUINchain is able to flag drugs that have passed their expiration date and verify them with the manufacturer, allowing users to scan barcodes on drug packaging to isolate suspicious and illegal products at the last mile of the drug supply chain (pharmacist to patient, the most complex area of the drug supply chain).

The hyperledger-based DSCSA model [45] The model implements a blockchain-based prototype capable of meeting the new regulatory requirements defined by the US FDA in the DSCSA. The prototype uses the reference model1 proposed by the DSCSA Supply Chain Center and is implemented in the Hyperledger Composer platform, which can build models for various entities and access control rules in the drug supply chain to reduce drug counterfeiting.

Smart Hospital Supply Chain [46] Jamil creates a smart healthcare ecosystem with a pharmaceutical supply chain based on Hyperledger Fabric for secure pharmaceutical supply chain record storage. Under this system, prescribing information can be shared and effectively controlled between different departments of the hospital, thus enabling efficient sharing of medical information. In addition, the system uses smart contracts to allow authorized users to access medication flow records and patient medical records for a limited time. The solution is a data-sharing platform within the hospital, recording not only the flow of drugs within the hospital, but also all kinds of medical information within the hospital. Medical information is more sensitive than drug flow information, and the solution only uses smart contracts to protect privacy, which is clearly not enough. By contrast, perhaps the approach could be extended beyond the hospital scenario to use this scheme in a full medical scenario. Of course this would also require a changed privacy protection policy.

Vaccine production chain [47] To address the drawbacks of centralized and opaque management of the traditional vaccine supply chain, Shaoliang proposes a two-layer blockchain-based approach to regulate vaccine production. The method is mainly based on three mechanisms: 1. two-layer blockchain structure, 2. consensus mechanism for multi-node collaboration, 3. cutting mechanism based on timestamp and information interaction. In actual application, users can check the whole process of vaccine production by simply scanning the QR code of the vaccine package, then the information cannot be displayed, which means the vaccine is fake and can be refused and reported to relevant institutions. Overall the program enables transparent regulation of the vaccine production process and discourages vaccine counterfeiting. When invalid blocks are cut, the blocks need to be reordered due to the unique hash chain structure of the blockchain. Thus each block hash changes, which not only violates the tamper-evident property of blockchain, but also requires ho-hum cost. All the above solutions are blockchain-based drug supply chain schemes, which can overcome the problems existing in the traditional model. The summary and comparison of them are shown in Table I.

B. Blockchain-based Drug Traceability Research in Industry

In addition to academia with research on blockchain + pharmaceutical supply chain, industrial technology companies have also launched their proven solutions for this track.

ADLT [48] iSolve LCC is currently working with several pharmaceutical companies to promote its ADLT (Advanced Digital Ledger Technology) blockchain solution to better enable the integrity of the drug supply chain. The platform provides an interoperable solution to facilitate secure data

transfer and create the data sources required for business or regulatory reasons, among others. ADLT creates distributed, tamper-evident and auditable records that can be inspected by regulators at any time, thereby building sufficient trust and transparency between organizations.

TABLE I. BLOCKCHAIN-BASED PHARMACEUTICAL SUPPLY CHAIN SOLUTION SUMMARY

Projects	Data Storage	Blockchain Platform	Consensus	Access Control	Management level	Features
Tseng J H[39]	On-chain	Gcoin	POW	×	Batch	Represent the nodes in Gcoin as different roles in the supply chain.
Al Noman M[40]	On-chain and off-chain	Ethereum	POS	×	Item	Lighten the burden of blockchain storage.
Agrawal D[41]	On-chain practice off-chain hybrid storage	Hyperledger Composer	PBFT	√	Batch	Two mathematical models are proposed for producers to calculate the overall cost, time spent and reliability of different transportation modes by route.
Chien W[44]	On-chain practice off-chain hybrid storage	Hyperledger fabric	PBFT	√	Item	Meet DSCSA standards and use COTS technology
Jamil F[46]	Couch DB	Hyperledger fabric	PBFT	√	Prescription	Efficient sharing of medical information by sharing and controlling prescribing information between different departments of the hospital.
Sylim P[42]	DFS	Hyperledger /Ethereum	DPOS /PBFT	×	Batch	Detect anomalies by comparing DFS content with book records.
Sinclair D[45]	On-chain	Hyperledger Composer	PBFT	√	Item	Meet the new regulatory requirements defined in the DSCSA
Peng S[47]	Double layers storage	Hyperledger fabric	PBFT	√	Batch	Existence of useless blockchain cropping mechanism to improve blockchain storage space usage efficiency
Saxena N[43]	On-chain	AWS	POS	×	Item	Interviews with professionals in the pharmaceutical industry as well as the blockchain industry, with references to opinions

MediLedger [49] The MediLedger network, launched by Chronicled, enables trust and automation between companies. The MediLedger network combines a secure peer-to-peer messaging network with a decentralized blockchain network to become the ultimate bridge between trading partners. Product validation on MediLedger supports product identification of U.S. prescription drugs with sub-second verification of data against the original manufacturer's data and supports full control of the data by the data owner.

FarmaTrust [50] FarmaTrust provides enterprise-grade blockchain solutions to use digitization to solve the challenges facing medical products. The solution provides an end-to-end, transparent and tamper-evident record of the entire drug supply chain to protect patients from counterfeit and substandard drugs and improve patient trust. The solution also provides digital analytics based on artificial intelligence for manufacturers to make predictions so that customers know what to make, when to make it, how much to make and where to sell it, thus helping manufacturers to make accurate decisions to improve productivity and reduce production costs. In addition, the solution fully complies with the regulatory requirements of the FMD/DSCSA.

Modum [51] It aims to digitize the supply chain of sensitive commodities with the help of modern technology. Focusing on system interoperability and governance of information exchange, Modum proposes an open interoperable data standards solution for seamless trusted data exchange and borderless interoperability. In real-world projects, Modum can address data collection in the pharmaceutical supply chain and automate and digitize supply chain processes with new technologies. In addition, it can use the data collected to perform advanced analytics and predictive functions through AI tools to help customers with decision-making.

VeChain ToolChain™ [52] This is a blockchain trusted data service platform independently developed by VeChain Technology, which aims to help enterprises realize data value-added and business speed-up through blockchain technology, and accelerate the pace of digital transformation of enterprises. They propose a transparent supply chain solution and a cold chain and smart healthcare solution, based on IoT technology and blockchain technology, capable of collecting key data from each participant in each supply chain link, such as procurement, production, distribution and circulation, and storing them on the blockchain. It supports maintaining product management accuracy for each product and recording the information and flow process of each item to enhance user trust. In the practical application scenario, it can realize transparent supply chain, upstream and downstream data collaboration, break information silos, real-time data monitoring and special drug transportation management, and finally establish a smart medical system and reduce information asymmetry between doctors and patients.

Waltonchain [53] Waltonchain is an underlying business ecology public chain that uniquely uses RFID technology to combine blockchain technology with IoT technology to ensure that the data is real from the source. In addition, Waltonchain has a unique cross-chain ecology that allows for cross-chain data sharing and effective and fast indexing. On Waltonchain, merchants can establish various sub-chains according to their needs, and monitor the whole process of production, logistics, warehousing and retailing of all products. As a typical business

eco-chain, the main feature of Walton Chain is to ensure that all data (including data of property rights ownership and data of commodity flow, etc.) is true and reliable. The traceability fidelity system realized by blockchain technology and related RFID hardware system includes RFID tags, RFID smart readers, sub-chains, cross-chain nodes, and data application checking system platform. The system can open up the data flow of production, logistics, warehousing, sales and other links to ensure that the data is true, and each commodity is traceable. It can simplify the process, reduce the cost of enterprises, and also ensure the interests of consumers. Consumers can easily check the authenticity and quality of the goods purchased.

All of these solutions are mature blockchain-based solutions launched by various types of technologies, some of which are already in practical application, while some are only conceptual prototypes, and the analysis of these solutions is compared in Table II. In addition, various pharmaceutical giants have started their blockchain layout [49][54-57], which shows that blockchain will become the core technology of medical digitalization in the future.

TABLE II. SUMMARY OF SUPPLY CHAIN-BASED PHARMACEUTICAL SUPPLY CHAIN SOLUTIONS FOR INDUSTRY

Projects	Data Storage	Blockchain Platform	Consensus	Access Control	Management level	Features
ADLT[48]	On-chain	Hyperledger /Ethereum	PBFT /POW	×	-	It integrates IoMT, machine learning, and big data to improve patient outcomes and help guide research and development.
MediLedger [49]	On-chain	MediLedger	POA	√	-	The data on the chain and the original manufacturer data can be verified at subsecond level.
FarmaTrust [50]	On-chain	Tomochain	POA	√	Item	It has strong expansibility, can aggregate different legacy system data, and combine AI technology to provide decision support for manufacturers.
Modum [51]	On-chain	Ehereum	POW /POS	√	On demand	It has seamless and credible data exchange, borderless interoperability, and combines artificial intelligence technology to provide analysis and prediction services.
VeChain [51]	Off-chain and On-chain	VeChain ToolChain™	POA	√	Item	It uses IoT technology to collect key data to ensure authenticity.
Waltonchain [52]	Child and parent chains, cross-chain storage	Waltonchain	WPoC	√	Item	It has a unique cross-chain ecology, which can realize cross-chain data sharing and effective fast indexing, and use self-developed RFID chips to realize automatic data chaining.

IV. DISCUSSION OF BLOCKCHAIN-BASED SOLUTIONS IN DRUG SUPPLY CHAIN SCENARIOS

A. Problems and Challenges

1) Interoperability: For most existing drug traceability solutions, there is no unified and standardized solution for integration, making it difficult to manage in a unified manner. For blockchains created by different stakeholders, they actually form data silos that are more complex and difficult to interact with than traditional models.

2) Scalability: Blockchain features are permanent and immutable, which prevents malicious falsification or tampering of data. However, it is these features that are often much more costly to expand business or change data when systems are updated. In addition, smart contracts, a very important feature of blockchain, cannot be changed when they are deployed to the chain.

3) The trade-off between privacy and transparency: According to a survey by the World Health Organization, there is a public demand for transparency and visibility of the pharmaceutical supply chain [58]. Then there is also some sensitive data in the pharmaceutical supply chain that pharmaceutical companies do not want to expose to consumers or competitors. Nonetheless, on the other hand, having full transparency for collaborators within the same organization can greatly improve efficiency and trust. So specific policies need to be tailored to achieve this difficult requirement. However, it is often difficult to weigh the privacy needs of different nodes, which can vary. Moreover, if critical information is leaked, it may result in unfair competition and lead to market imbalance.

4) Input data authenticity: In the blockchain-based supply chain system, although the data on the chain can guarantee untamperability, the node terminal data is still uploaded manually. That is, there is still the possibility of data forgery and tampering in this last mile.

5) Blockchain security: Due to some design flaws in the blockchain itself (e.g., architecture, consensus, or smart contract vulnerabilities), there have been numerous past incidents of attacks on blockchain systems, such as THE DAO project [59]. At present, blockchain technology is still in continuous development. Although scholars are actively improving the blockchain architecture to make it a more perfect technology, there are still many problems that cannot be solved.

6) Lack of perfect laws and regulation: Blockchain, as an emerging technology, involves legal boundaries that are difficult to define. For example, when a new transaction is

executed in the network, it is difficult for these agencies to clearly define the jurisdiction and the correct legal obligations of the relevant stakeholders. In addition, many laws and regulations in the traditional regulation of pharmaceuticals are inherently imperfect, and the role of regulators becomes even more complex when applying blockchain to drug traceability.

B. *Future Outlook*

As for the security of the blockchain itself, with more and more technological innovations and the generation of various cryptographic algorithms, the security of the blockchain is bound to be optimized in the generation of updates, while various types of attacks are also being upgraded, and such issues will always need to be studied. In terms of data privacy, extremely sensitive data can be put into a trusted execution environment(TEE) for processing [60][61]. As for the extensibility of blockchain, the editable blockchain [62], which is also being researched by scholars, can solve this problem well. Through a special hash function, the trimming of blocks can be realized without compromising some existing blockchain features, and applying this editable blockchain to the supply chain system can greatly optimize storage efficiency and give enterprises the space to expand their business or modify their business.

Blockchain technology is obviously unable to do efficient data processing, the large amount of data stored within the blockchain chain is a greater asset in today's era where data is a resource. Artificial intelligence(AI), another popular technology, has excellent data processing capability and can train models through data to help manufacturers make decisions, help patients recommend drugs, etc. Therefore, combining AI technology with blockchain technology to strengthen data processing capability is also an important direction for future development. Meanwhile, on the issue of the authenticity of input data mentioned above, The IoT can connect and exchange data with other devices or systems over the Internet through a network of physical objects embedded with sensors, software, and other technologies [63], so that data at the node terminals can be automatically uploaded through IoT devices to achieve full automation of the supply chain and improve supply chain efficiency, reduce costs, ensure the authenticity of input data. The integration of blockchain and these technologies has become a research hotspot. However, due to the openness of blockchain itself, the introduced AI model and numerous resource-limited IoT devices will be more vulnerable to attack, so the security scenario within the system needs to be considered more complex. In addition, various IoT devices will generate a huge amount of data, which is far from enough to support the existing open-source blockchain. Future research on blockchain security and performance will be a major focus.

In addition, as these new technology policies are currently in a state of improvement, it is necessary to build a complete and comprehensive set of legal controls in the future.

C. *Governing Blockchain by Blockchain Architecture*

The existing drug supply chain programs are all aimed at drug traceability alone, and most participants are private organizations or consumers, lacking official intervention. Moreover, there are some loopholes in such a scheme. Since its production supervision is still in the traditional mode, pharmaceutical companies may falsify production records for personal interests, which eventually leads to the supply chain of drugs that are traceable and of regular origin but are of inferior quality. Academician Chen Chun proposed that the research of "governing blockchain by blockchain" supervision system is an important development trend of blockchain supervision technology [64]. "Governing blockchain by blockchain" is to use blockchain technologies such as consensus mechanisms and smart contracts to perform efficient digital supervision of the supervised blockchain. By applying this architecture to the pharmaceutical supply chain, the interoperability between different supply chains can be achieved, and an efficient and secure regulatory framework can be formed, as shown in Fig. 6:

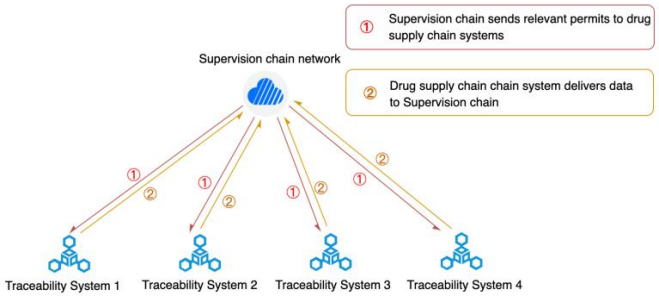

Fig. 6. Governing blockchain by blockchain architecture.

Multiple authorities involved in the regulation of pharmaceuticals (such as the Drug Administration, the General Administration of Markets, and Notaries) form a chain of custody. Various pharmaceutical supply chain solutions in the market (either traditional supply chains or blockchain-based supply chains) are embedded in this regulatory framework, thus enabling some scalability. Review nodes are deployed on both the supply chain and the supervision chain, and the supervision chain interacts with the traceability chain through a cross-chain mechanism, which also enables intelligent regulation by smart contracting existing drug regulations.

V. Conclusion

In this paper, we discuss the application of blockchain in pharmaceutical supply chain scenarios, provide an overview of traditional supply chain processes and pharmaceutical processes, and then summarize current pharmaceutical lifecycle problems and the role blockchain can play. We finally concluded that there are six major challenges facing the application of blockchain technology in drug supply chain scenarios by analyzing and comparing some of the studies on blockchain in drug supply chain scenarios: interoperability between different systems, scalability of blockchain itself, trade-off between privacy and transparency, authenticity of input data, security of blockchain itself, and imperfect laws and regulations. To address these new blockchain-related issues, more research and incorporation of editable blockchain technology, as well as improved cryptography, is required. Although the editable blockchain is a more contentious technology, it is necessary for practical scenarios where business expansion and updates are required. Furthermore, due

to interoperability and scalability issues between different systems, regulatory authorities are unable to achieve efficient and safe regulation. This paper proposes a drug supply chain "governing blockchain by blockchain" architecture in which multiple departments involved in drug regulation form a chain of custody to regulate different blockchain-based supply chain systems, which is also scalable for traditional supply chain systems. This architecture allows for a safe and efficient regulatory strategy. In the future, we will enhance the framework to address current interoperability and extensibility issues, as well as establish a comprehensive regulatory framework for the drug supply chain, allowing for the regulation of the entire drug research, production, distribution, and transportation process.

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