Tina Plevnik[1]

BLOCKCHAIN AND ARCHIVING IN CLINICAL TRIALS

Abstract

Purpose: *As blockchain is presented as a potential tool for archiving purposes, the aim of the research was to investigate blockchain technology as a possible solution for archiving of clinical trial records, considering that many clinical researchers and sponsors have problems with documentation.*

Method/approach: *The approach taken in this research builds on the literature review and the content analysis method for the selected literature focusing on blockchain technology for archiving in clinical trials.*

Results: *Clinical trial documentation must remain complete, legible, authentic, and available for review during the required archiving period. The properties of blockchain represent a possible solution in all phases of a clinical trial, from their inception to trial completion and in the archival period. Current trends indicate the use of blockchain throughout the entire period of clinical research, including data archival and storage.*

Conclusion/findings: *Currently, the best solution for archiving clinical trial e-records would be that only hashes of clinical trial e-records are stored on the blockchain to confirm the authenticity and immutability of the original e-records. Further research should be conducted to ensure long-term accessibility of blockchain and compliance with GDPR, EMA and other regulatory agencies. Appropriate measures related to the challenges and limitations of blockchain should be addressed.*

Keywords: *blockchain, archiving, clinical trials*

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1 INTRODUCTION

Clinical trials are part of the process of bringing a new medicinal product to the market (Akhondzadeh, 2016). Archiving of the created documentation is an important part of the clinical trial process, being also a legal and regulatory requirement which must be executed with the same attention to detail as any other part of the clinical trial. It can also be a very expensive and labour-intensive activity (Dinnett et al., 2011).

The purpose of the research was to investigate blockchain technology as a possible solution for archiving of the records generated in clinical trials, considering that many clinical researchers and sponsors of clinical trials have problems with documentation, including data storage and document management systems (Rogers et al., 2020), which is also evident from the most common inspection and audit findings during inspections of good clinical practice (Annual Report, 2022).

As blockchain is presented as a potential tool for archiving purposes, which is not only secure, but also meets archival standards of authenticity, reliability, and trustworthiness (Woodall and Ringel, 2020), the aim of the research was to investigate blockchain for applications in clinical trials, advantages of blockchain solutions, possible challenges, and use cases of blockchain in clinical trials.

2 LITERATURE OR THEORETICAL BACKGROUND OVERVIEW

2.1 CLINICAL TRIALS

Clinical trials are clinical studies on humans that determine or verify clinical, pharmacological or other pharmacodynamic effects, determine possible side effects and study the absorption, distribution, metabolism and excretion of the medicinal product under trial (Regulation, 2014). A clinical trial is a process that consists of several steps i.e., protocol design, recruitment, follow-up, data collection, analysis, final results and archiving, as the final stage of the clinical trial. Archiving is the secure storage of essential documents in clinical research (Dinnett et al., 2011). The Trial Master File (TMF) is the repository of all essential documents related to the management and conduct of clinical trials, from their inception to the end of the archival period. The legislation does not differentiate between paper and electronic TMF (eTMF) (Guideline, 2018).

2.2 BLOCKCHAIN

Blockchain consists of decentralized ledgers located on a system of peer-to-peer (P2P) computers where all changes must be approved by various authorized nodes. It is called a distributed ledger system because every participant in the network has a copy of all transactions (Pence, 2021). The implementation of blockchain technology provides many advantages (see Figure 1) such as auditability, decentralization, anonymity, and transparency (Omar et al., 2021).

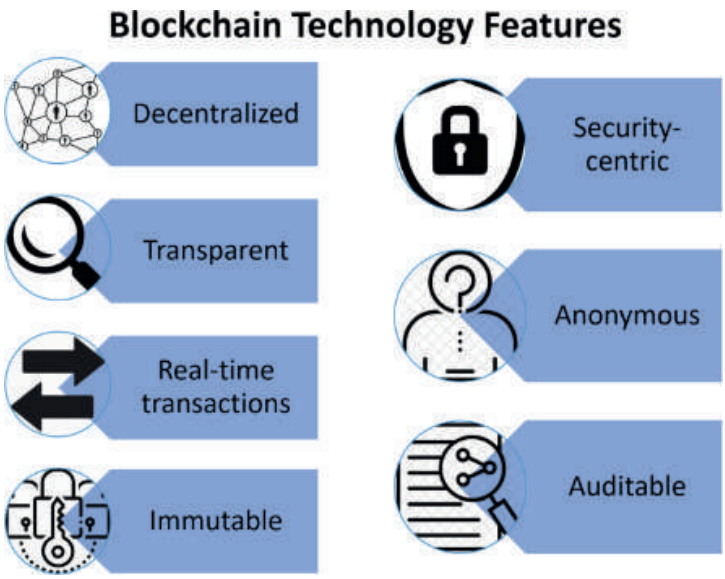

Figure 1: Blockchain Technology Features (Omar et al., 2021)

Researchers have proposed a way to modify the operation of Bitcoin, especially its mining function, to achieve distributed storage of archival data (Miller et al., 2014). By checking or hash validation, the authenticity of e-records can be confirmed as well as whether any changes or corrections have been made (Bhatia et al., 2020). Various pilot projects are introducing blockchain technology into the processes of ensuring reliable long-term e-storage. To protect the integrity of e-records in the e-health project, the government of Estonia has introduced a mirror blockchain system for e-record storage which uses the Guardtime system. The pilot Swedish land registration system uses a blockchain system for e-recordkeeping, where e-records are no longer just mirrored on-chain but are actively created on-chain in the form of smart contracts (Lemieux, 2017). Many current and proposed applications of blockchain technology are also tied to solving e-record-keeping challenges in property rights transfers (Lemieux, 2016). ARCHANGEL proposes using distributed ledger technology to cryptographically guarantee the provenance, immutability and so the integrity of archived documents (Collomosse et al., 2018). Mediterranean Hospital in Cyprus has adopted the E-HCert application, that provides an archival solution based on the VeChain Thor blockchain for laboratory test results and vaccination certificates (E-HCert, 2020).

3 RESEARCH DESIGN

The approach taken in this research builds on the available literature focusing on blockchain technology as a possible solution for archiving in clinical trials.

We conducted a literature review from April to May 2023, using selected combinations of keywords and reviewing the summaries of the relevant literature. To explore the topic under investigation we additionally used the content analysis method for the selected literature.

The paper addresses the following research questions:

- RQ1: What are the requirements for archiving of clinical trial records?
- RQ2: What are the applications of blockchain technology in clinical trials?
- RQ3: Which blockchain types can be used in clinical trials?

- RQ4: What are the challenges for the usage of blockchain technology in clinical trials?
- RQ5: Which are the use cases of blockchain in clinical trials?

4 RESULTS

4.1 ARCHIVING REQUEREMENTS FOR CLINICAL TRIALS

TMF should be immediately available and directly accessible to auditors and inspectors, which can review and verify that the sponsor and investigators/institutions have conducted the trial in accordance with applicable regulatory requirements and principles and Good Clinical Practice standards. With the new regulation, applicable from 31 January 2022, the archiving times for the TMF have been extended to at least 25 years after the end of the clinical trial or for the trial documentation relating to the full traceability of the ATIMP (Advanced Therapy Investigational Medicinal Product) to 30 years after the expiry date of the product or longer if required by the clinical trial authorisation (Regulation, 2014).

Sponsors of clinical trials should take appropriate actions to ensure that the TMF remains available for inspection for the required archiving time. The media used to archive TMF shall be such that the content remains complete, legible and maintains authenticity throughout the archiving period. Any alteration to the content of the TMF should be traceable (Regulation, 2014; Guideline, 2018). The bit level integrity of the archived data should be verified periodically using checksums. The guidance of the use of such checksums is provided in ISO 16363 (Stiles et.al., 2014).

4.2 APPLICATIONS OF BLOCKCHAIN IN CLINICAL TRIALS

There are several applications of blockchain technology in clinical trials. The use of blockchain can reduce the time of the enrolment of the patient for a clinical trial (Zhuang et al., 2019), improve the traceability of the consents from the patients (Benchoufi et al., 2018) and transparency (Nugent et al., 2016), maintain the confidentiality of the patient's data (Manish et al., 2021), ensure persistent monitoring and data integrity (Omar et al., 2021). The integration of blockchain technology could also be used for big data analytics (Zheng et al., 2017) and clinical data management from initiation to the submission and archiving of the study (Gazali et al., 2017).

4.3 BLOCKCHAIN TYPES FOR CLINICAL TRIALS

Blockchain technologies can be mainly divided into three types: Public blockchain, Private blockchain and Consortium blockchains (Iuon-Chang & Tzu-Chun, 2017).

Public blockchains are of permissionless type e.g., Bitcoin, Ethereum and Litecoin (Baalamurugan et al., 2022). Security and transparency are the key advantage of this type of blockchain. Some of the limitations of public blockchains are extremely slow transaction processing time, scalability, and energy consumption (Omar et al., 2021). Private blockchains are permissioned blockchains (Baalamurugan et al., 2022). Data privacy and security compliance can easily be achieved, because clinal trial data is stored on authorized nodes (Kosba et al., 2016) and it is possible to use computationally inexpensive protocols to verify transactions (Omar et al., 2021). Platforms that use the private blockchain concept include Hyperledger, Hashgraph, and Corda (Baalamurugan et al., 2022). The consortium is known as a hybrid or semi-private blockchain and has almost the same advantages as private blockchains. However, they operate within different groups rather than a single entity. One of the key problems with the consortium blockchain is that its centralized structure makes it vulnerable to malicious players (Omar et al., 2021).

4.4 CHALENGES FOR THE USAGE OF BLOCKCHAIN TECHNOLOGY IN CLINICAL TRIALS

Due to the limitation of the block size and required duration to create a new block (Zheng et al., 2018) scalability is a challenge, especially in clinical trials, as they involve a large number of participants and will make a large number of transactions per second (Manish et al., 2021). There is no guarantee of transactional anonymity of blockchain-based networks because each public key's balances and transactions are available to all network users (Watanabe, 2016). Privacy leakage is critical in the medical industry because protecting sensitive patient data is crucial (Omar et al., 2021). While blockchain frameworks increase the storage capacity, they also present many challenges in terms of large volumes, variety, and speed of e-records, also recognized as big data (Omar et al., 2021). Not only is this data expensive to store, but data access operations can also fail if/when the cost exceeds the data size limit set by the Blockchain network (Soltanisehat et al., 2023). Many clinical trial companies still rely on paperwork for some procedures. Immediate adoption of blockchain-based clinical trials would not be easy, since changing the behaviour and habit roles of individuals is extremely difficult for any industry (Omar et al., 2021). The immutable nature of blockchain technology is a double-edged sword. The data attached to the chain cannot be changed, even if there is a valid reason. In complex data systems, updates and data changes are inevitable and no one can be sure that the original data is uploaded to the blockchain correctly (Hang et al., 2022). Selfish mining poses a major security risk for clinical trial applications (Manish et al., 2021), since the blockchain is susceptible to attacks by colluding selfish miners. Nodes with more than 51% computing power could reverse the blockchain and the performed transaction. Based on selfish mining, many other attacks have been proposed to show that blockchain is not so secure (Zheng et al., 2018).

4.5 USE CASES OF BLOCKCHAIN IN CLINICAL TRIALS

This section outlines the recent trends of blockchain applications in clinical trials.

Clinical Trials Intelligence is a distributed technology platform, targeted to address the critical pain points of clinical trials, e.g., data analytics, patient recruitment, vendor management, risk monitoring and clinical data visualization. Clinical Trials Intelligence uses Ethereum-based smart contracts to facilitate access control, reimbursement payments and clinical data hash storage (Clintex Whitepaper, 2020.)

TriNetX is a global health research network that connects the world of medicinal product discovery and development from pharmaceutical companies to the study site and investigator to patient. TriNetX optimizes protocol design and feasibility, site selection, patient recruitment, and enables discovery by generating real-world evidence (TriNetX, 2023).

Innoplexus provides advanced artificial intelligence (AI) and blockchain solutions that support all stages of medicinal product development from pipeline to market. This constantly updated data repository is serving pharmaceutical companies, the biotech industry, and contract research organizations (Innoplexus, n.d.).

Data collection and study management platform Triall's eClinical solutions are designed to support any therapeutic area, study design and study phase, from study initiation to completion and beyond. Triall's product Triall eTMF provides a single, secure environment for managing trial-related documents and ensuring inspection readiness throughout the clinical trial lifecycle (Triall, 2023).

Embleema helps healthcare professionals construct clinical trials, including patient recruiting and study design, and also supports long-term storage of scientific data, data analytics, and methods to interpret it (Embleema, 2022).

Biopharma Ledger is a Blockchain platform that provides data management and clinical solutions throughout the entire period of clinical research, including data archival and storage, to improve biopharma processes and data management (ACL Digital, 2023).

TCS ADD™ enables digital ecosystems, simplifies data complexity, and drives innovation in clinical trials to bring medicines to market faster and it also offers a metadata repository that automates study construction, enables robust governance, and is quickly transformed and generated for submission datasets (TATA, 2023).

5 DISCUSSION

Documentation generated in a clinical trial must remain complete, legible, authentic, and available for review during the required archiving period. Any changes to the content must be traceable. The properties of blockchain represent a possible solution in all phases of a clinical trial, from their inception to trial completion and in the archival period. The use of blockchain can reduce the time for patient recruitment, improve the traceability of the consents from the patients, maintain the confidentiality of the patient's data, ensure data integrity, and can also be used for big data analytics and clinical data management from initiation to archiving. A private blockchain is more appropriate for clinical trials as data privacy and security compliance can easily be achieved, because clinal trial data is stored on authorized nodes and it's also less vulnerable to malicious players.

Besides to the archiving of clinical trial-phase-compilable metadata on the Blockchain, different clinical trial steps can also be chained together so that each step depends on its predecessor, using smart contracts, that can enforce the level of transparency, traceability, and control over clinical trial sequences (Benchoufi & Ravaud, 2017). Regulations and application submission requirements can be seen as a set of business rules that can be managed on a blockchain. The regulatory audits and validation of the recorded trial data are slow, expensive, and labour-intensive. Introduction of the blockchain can reduce this burden, as organizations can quickly prove the validity of data due to the immutability of collected e-records and the fact that the authorities' specifications have been incorporated and executed by the implemented smart contracts (Glover & Hermans, 2017).

The use of blockchain also brings some challenges such as scalability, privacy leakage, storage of big data and high costs, the immutability of the data, problems with the transition to blockchain technology, and selfish mining. Zheng et al. (2018) proposed some solutions for the scalability problem, privacy leakage and the selfish mining problem. Decentralized storage mechanisms are potential solutions to be explored and implemented by blockchain-based companies, since currently storing data on a blockchain is expensive and limited (Omar et al., 2021). The InterPlanetary File System (IPFS) is an example of this decentralized storage technology (Benet, 2014). Each file stored on the IPFS network is assigned a unique cryptographic hash, making each file's history immutable and traceable. In this system, the downloading speed is higher since the files are distributed over the network. As a result, IPFS links stored on the blockchain directly refer to information stored on the IPFS network without storing the actual data on the blockchain (Benet, 2014). Another example of this decentralized storage technology is FileCoin (FileCoin, n. d.).

Current trends indicate the use of blockchain throughout the entire period of clinical research, including data archive and storage (e.g., BioPharma Ledger and Triall) or address the critical points of clinical trials and clinical data hash storage (e.g., Clinical trials intelligence and Embleema). But if only hashes of the e-records are stored on the blockchain, the requirements for preserving the originals (or digitized copies) do not change significantly (Lemieux, 2017) and the e-records still have to be archived in an appropriate system for long-term e-storage. It is also not certain that in the future blockchain technology

e-records will be accessible or usable outside of their original system or platform (Bhatia et al., 2020) for example in 25 or 30 years, as required for the eTMF in clinical trials.

6 CONCLUSIONS

The best solution for archiving clinical trial e-records would be, that the original e-records are archived outside of the blockchain (e.g., in a trusted e-repository) and only hashes of these e-records are stored on the blockchain to confirm the authenticity and immutability of the original. Decentralized storage technology such as IPFS and FileCoin can also be explored. Further research should be conducted to ensure the long-term accessibility of blockchain and the compliance with GDPR, EMA and other regulatory agencies. Appropriate measures related to the challenges and limitations of blockchain should be addressed.

REFERENCES

ACL Digital. 2023. Available at https://www.acldigital.com/offerings/blockchain/biopharma-ledger-platform (accessed 16.4.2023).

Akhondzadeh, S. (2016). The importance of clinical trials in drug development. *Avicenna journal of medical biotechnology*, *8*(4), 151–151. Available at https://www.ajmb.org/ PDF/en/ FullText/ 249.pdf (accessed 16.4.2023).

Annual Report of the Good Clinical Practice Inspectors' Working Group. (2020). *European Medicines Agency*. Available at https://www.ema.europa.eu/en/documents/report/ annual-report-good-clinical-practice-inspectors-working-group-2020_en.pdf (accessed 12.4.2023).

Baalamurugan, K. M., Kumar, S. R., Kumar, A., Kumar, V., & Padmanaban, S. (2022). *Blockchain Security in Cloud Computing*. Springer International Publishing. Available at https://link.springer.com/book/10.1007/978-3-030-70501-5 (accessed 16.5.2023).

Benchoufi, M., & Ravaud, P. (2017). Blockchain technology for improving clinical research quality. *Trials*, *18*(1), 335. Available at https://doi.org/10.1186/s13063-017-2035-z (accessed 19.5.2023).

Benchoufi, M., Porcher, R., & Ravaud, P. (2018). Blockchain protocols in clinical trials: Transparency and traceability of consent. *F1000Research*, *6*, 66. Available at https://f1000research.com/articles/6-66/v5 (accessed 19.5.2023).

Benet, J. (2014). IPFS-Content Addressed, Versioned, P2P File System. Available at https://arxiv.org/abs/1407.3561 (accessed 16.5.2023).

Bhatia, S., Douglas, E. K., & Most, M. (2020). Blockchain and records management: Disruptive force or new approach? *Records Management Journal*, *30*(3), 277–286. Available at https://doi.org/10.1108/RMJ-08-2019-0040 (accessed 12.4.2023).

Clintex Whitepaper. (2020). Available at https://clintex.io/pdf/Clintex_CTi_Whitepaper.pdf (accessed 16.5.2023).

Collomosse, J., Bui, T., Brown, A., Sheridan, J., Green, A., Bell, M., Fawcett, J., Higgins, J., & Thereaux, O. (2018). ARCHANGEL: Trusted Archives of Digital Public Documents. *Proceedings of the ACM Symposium on Document Engineering 2018*, 1–4. Available at https://doi.org/10.1145/3209280.3229120 (accessed 12.4.2023).

Dinnett, E. M., Gaw, A., Ronald, E. S. & Tolmie E. P. (2011). Archiving Approach in the UK. *Applied Clinical Trials*, *20*(6), 46–50. Available at https://www. appliedclinicaltrialsonline.com/view/archiving-approach-uk (accessed 16.4.2023).

E-HCert. (2020). Available at https://e-hcert.com/ (accessed 19.5.2023).

Embleema. (2022). Available at https://www.embleema.com/ (accessed 19.5.2023).

Filecoin. (n.d.). Available at https://dataonboarding.filecoin.io/#case-studies (accessed 16.4.2023).

Gazali, Kaur, S., & Singh, I. (2017). Artificial intelligence based clinical data management systems: A review. *Informatics in Medicine Unlocked*, *9*, 219–229. Available at https://www.sciencedirect.com/science/article/pii/S2352914817301247?via%3Dihub (accessed 16.5.2023).

Glover, D. G., & Hermans, J. (2017). Improving the traceability of the clinical trial supply chain. Applied Clinical Trials, *26*(12). Available at https://www. appliedclinicaltrialsonline. com/view/improving-traceability-clinical-trial-supply-chain (accessed 16.4.2023).

Hang, L., Chen, C., Zhang, L., & Yang, J. (2022). Blockchain for applications of clinical trials: Taxonomy, challenges, and future directions. *IET Communications*, *16*(20), 2371–2393. Available at https://doi.org/10.1049/cmu2.12488 (accessed 16.5.2023).

Innoplexus. (n. d.). Available at https://www.innoplexus.com/(accessed 16.5.2023).

Iuon-Chang, L., & Tzu-Chun L. (2017). A Survey of Blockchain Security Issues and Challenges. *International Journal of Network Security*, *19*(5). Available at http://ijns.jalaxy. com.tw/contents/ijns-v19-n5/ijns-2017-v19-n5-p653-659.pdf (accessed 25.5.2023).

Guideline on the content, management and archiving of the clinical trial master file (paper and/or electronic). (2018). *European Medicines Agency.* Available at https://www. ema.europa.eu/en/documents/scientific-guideline/guideline-content-management-archiving-clinical-trial-master-file-paper/electronic_en.pdf (accessed 12.4.2023).

Kosba, A., Miller, A., Shi, E., Wen, Z., & Papamanthou, C. (2016). Hawk: The Blockchain Model of Cryptography and Privacy-Preserving Smart Contracts. *2016 IEEE Symposium on Security and Privacy (SP)*, 839–858. Available at https://doi.org/ 10.1109/SP.2016.55 (accessed 12.4.2023).

Lemieux, V. (2016). Trusting Records: is Blockchain technology the answer*? Records Management Journal 26* (2), 110–139. Available at https://www.researchgate.net/ publication/ 284437902_Trusting_Records_Is_ Blockchain_Technology_the_Answer (accessed 12.4.2023).

Lemieux, V. (2017). A typology of blockchain recordkeeping solutions and some reflections on their implications for the future of archival preservation. *IEEE International Conference on Big Data (Big Data)*, 2271–2278. Available at https://doi.org/10.1109/BigData.2017. 8258180 (accessed 12.4.2023).

Manish, Katiyar, D., & Singhal, S. (2021). Blockchain technology in management of clinical trials: A review of its applications, regulatory concerns and challenges. *Materials Today: Proceedings*, *47*, 198–206. Available at https://doi.org/10.1016/j.matpr.2021.04.095 (accessed 16.5.2023).

Miller, A., Juels, A., Shi, E., Parno, B., & Katz, J. (2014). Permacoin: Repurposing Bitcoin Work for Data Preservation. *2014 IEEE Symposium on Security and Privacy*, 475–490. Available at https://doi.org/10.1109/SP.2014.37 (accessed 16.5.2023).

Nugent, T., Upton, D., & Cimpoesu, M. (2016). Improving data transparency in clinical trials using blockchain smart contracts. *F1000Research*, *5*, 2541. Available at https:// f1000research.com/articles/5-2541/v1 (accessed 19.5.2023).

Omar, I. A., Jayaraman, R., Salah, K., Yaqoob, I., & Ellahham, S. (2021). Applications of Blockchain Technology in Clinical Trials: Review and Open Challenges. *Arabian Journal for Science and Engineering*, *46*(4), 3001–3015. Available at https://doi.org/10.1007/s13369-020-04989-3 (accessed 16.4.2023).

Pence, H. (2021). Blockchain and the Pharmaceutical Industry. *Chimica Oggi*, *38*. Available at https://www.teknoscienze.com/tks_article/blockchain-and-the-pharmaceutical-industry/ (accessed 19.5.2023).

Rogers, C. A., Ahearn, J. D., & Bartlett, M. G. (2020). Data Integrity in the Pharmaceutical Industry: Analysis of Inspections and Warning Letters Issued by the Bioresearch Monitoring Program Between Fiscal Years 2007–2018. *Therapeutic Innovation & Regulatory Science*, *54*(5), 1123–1133. Available at https://doi.org/10.1007/s43441-020-00129-z (accessed 19.5.2023).

Stiles, T. (2014). *A guide to archiving of electronic records* (1st edition). Scientific Archivists Group Limited. Available at https://the-hsraa.org/wp-content/uploads/2017/12/AGuidetoArchivingElectronicRecordsv1.pdf (accessed 16.4.2023).

Soltanisehat, L., Alizadeh, R., Hao, H., & Choo, K.-K. R. (2023). Technical, Temporal, and Spatial Research Challenges and Opportunities in Blockchain-Based Healthcare: A Systematic Literature Review. *IEEE Transactions on Engineering Management*, *70*(1), 353–368. Available at https://ieeexplore.ieee.org/document/9184928 (accessed 10.5.2023).

Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC. (2014). *OJ L*, 158. Available at https://eur-lex.europa.eu/legal-content/EN/TXT/ PDF/ ?uri= CELEX:02014R0536-20221205&from=EN (accessed 16.4.2023).

TATA. (2023). Available at https://www.tcs.com/what-we-do/products-platforms/tcs-add (accessed 16.5.2023).

Triall. (2023). Available at https://www.triall.io/ (accessed 16.5.2023).

Trinetx. (2023). Available at https://trinetx.com/ (accessed 16.5.2023).

Watanabe, H., Fujimura, S., Nakadaira, A., Miyazaki, Y., Akutsu, A., & Kishigami, J. (2016). Blockchain contract: Securing a blockchain applied to smart contracts. 2016 IEEE International Conference on Consumer Electronics (ICCE), 467–468. Available at https://ieeexplore.ieee. org/document/7430693 (accessed 19.5.2023).

Woodall, A., & Ringel, S. (2020). Blockchain archival discourse: Trust and the imaginaries of digital preservation. *New Media & Society*, *22*(12), 2200–2217. Available at https://doi. org/10.1177/1461444819888756 (accessed 12.4.2023).

Zheng, Z., Xie, S., Dai, H., Chen, X., & Wang, H. (2017). An Overview of Blockchain Technology: Architecture, Consensus, and Future Trends. *2017 IEEE International Congress on Big Data (BigData Congress)*, 557–564. Available at https://ieeexplore.ieee.org/document/8029379 (accessed 19.5.2023).

Zheng, Z., Xie, S., Dai, H. N., Chen, X., & Wang, H. (2018). Blockchain challenges and opportunities: A survey. *International Journal of Web and Grid Services*, *14*(4). Available at https://www.inderscienceonline.com/doi/abs/10.1504/IJWGS. 2018.095647 (accessed 19.5.2023).

Zhuang, Y., Sheets, L. R., Shae, Z., Chen, Y.-W., Tsai, J. J. P., & Shyu, C.-R. (2019). Applying Blockchain Technology to Enhance Clinical Trial Recruitment. *AMIA ... Annual Symposium Proceedings. AMIA Symposium*, *2019*, 1276–1285. Available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7153067/ (accessed 16.5.2023).

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