Turkish Online Journal of Qualitative Inquiry (TOJQI)
Volume 12, Issue 8, July 2021: 2113-2124

# Strategic Advantage of Block Chain in the Clinical Trials

Dr.Lakshmi Vishnu Murthy Tunuguntla[a] , Dr Naga Venkatesh Devaguptapu[b]
Prakash Chandra Tunuguntla[c]

[a] Professor, Goa Institute of Management Goa.
[b] Professor, Goa Institute of Management Goa,
[c]CEO, VRbiztec, Hyderabad

**Abstract**

The purpose of this paper is to first understand the current state of the clinical trials process, painpoints associated with it and suggest methods to integrate the process with block chain technology for eliminating/minimizing painpoints. The existing process has been analysed and major pain points observed were recruitment and retaining of participants, execution of contracts between the players, traceability & security of the data relating to the participants. Subsequently a "to-be" process with different stakeholder interaction and block chain intervention has been designed to overcome the painpoints identified in current state.The "to-be" process also addresses data that is to be exchanged among the stakeholders,and sequence of interaction among the stakeholdersAnother salient feature of this paper is the structuring of the smart contracts among the sponsors, researchers and the participants in a transparent way.

**Key Words:** Blockchain, clinical trials process, block chain implementation

## 1. Introduction

Clinical trials are a subset of clinical research. Clinical research mainly involves the creation of new drugs for improvement of the healthcare process. The focus areas of clinical research are diagnosis, cause, prevention, and cure. Usually it takes years and for some viruses, it took almost a decade. COVID 19 has helped the need/importance of fast tracking the clinical research for drug discovery. The conventional process has issues ranging from participant recruitment, retention, traceability, security of data, which call for technology solution/integration into the process. Block Chain technology, which is based on cryptology and decentralized architecture has the potential to address the issues. Researchers have been studying the application of block technology across the entire life cycle of clinical trials and its potential to help in improving the process effectiveness and efficiency.

## 2. Literature survey

In clinical trials, (Schindler et al, 2020) conducted research on multiple phases where the subjects are recruited for drug testing. There seem to be lot of issues in traditional approach leading to delay, gestation periods, recruitment and retention of participants. The study on "Clinical Trial Master File Migration" by Rupani (2020) has focused on the need to speed up the clinical trial process, meeting the objective of cost effectiveness and at the same time ensuring data integrity.Stamatellis et al

(2020) studied the impact of block chaintechnologieson clinical trials across the process steps. Davis and Pai (2020) in their research have explained the need to deal with challenges posed by pandemic like COVID, to the clinical trials of medical products. Buhrmann,Riper andOssebaard (2020) studied relationship & impact between Health Technologies Assessment (HTA) and pharmaceutical healthcare. The advent of new technology like IOT and the respective IOT devices, possibility and impact of IoT devices & remote patient monitoring systems, its impact on data integrity/data transfer were analysed by Griggs et al (2018)and found that block chain technology can provide effective solutions.

So while the new technologies are being explored, Albanese et al (2020) study focused on need to have a Block-chain Framework to ensure DataQuality for Clinical Trials, that involves multiple organization as there are lot of delays, in exchange of information and integrity of information.In the wake of the new technologies, Choudhury et al (2018) explained that IoT devices & remote patient monitoring systems rise in popularity and rise in transactions**,** there could be challenges to maintaindata integrity and transfer of data. In order to cater to the protected health information (PHI) developed by these devices, this research suggested using block chain based smart contracts to aid secured analysis and management of medical sensors. Benchoufi, R. and Benchoufi P (2017)have analysed the integrative and facilitative role that block chain technology to address the challenges faced in clinical trials viz., Reproducibility, data sharing, personal data privacy concerns and patient enrolment.

Amanda et al (2020) suggested, a framework that could handle & monitor data in multi-site CTs was suggested by few researchers Though there has been research and discussion, around leveraging block chain with clinical trials, the extent of implementation is yet to take place.Glover and Hermans (2017) described aframework called "BlockTrial" that was designed and developed, which helps users to carry out trials-relating to smart contracts on Ethereum network .Benchoufi, and Porcher (2018) in their study, described how the smart contracts help researchers to access the data, enable them to query for data stored on off-chains .Chaudhari et al (2020) in their study implemented ablockchain-based solution that supports patients/stakeholders to deal with their consent communication in a way with features of transparency, immutability, traceability and security. Choudhury et al (2018)created a framework, which can handle the dynamic nature of consent management. Brooks et al(2011)suggested a block chain technology-based framework, which can ensure Institutional Review Board (IRB) regulations (i.e., participant recruitment, consent management, data sharing ((secondary), risk monitoring, and additionally generate auto assessments for periodical and regular review) on data collection. In essence, existing literature indicates that researchers have studied, several blockchain platforms for CTs to assessthe system preparedness and issues involved. But few studies carried out by have customized the approach for creating consensus algorithms and plausible architectures, which can take care of the needs of CTs. Many other studies have stressed the issues in CTs (Brooks et al, 2011). The issues include ensuring of patient privacy, their enrolment, obtaining approval to meet regulatory needs, upholding integrity of data, and making it available for verification/validation. Blockchain technology could play pivotal role in handling of CTdata, can nurture innovation& process improvements.

## 3. Research gap

From the Literature survey we found that majority of the research is trying to address the problems in clinical trials using block chain without having an appreciation for the current state of clinical trials encompassing four phases and the pain points within each phase. The pain points in each phase are not addressed appropriately. Another key gap that was observed was the criteria for applying the block chain technology and how each pain point is addressed by block chain. The earlier research did not focus on the key data that flows across various phases among the participants of the process. The key smart contracts applicable in each phase have not been identified appropriately.

It is in this context;this paper offers a blockchain-based solution to mitigate the pain points associated with CTs. Specifically, it provides a framework that covers process elements such as data management, protocol compliance, data integrity, and transparency-related issues in CTs and smart contracts.

## 4. Current state of Clinical trials– Process flow

### 4.1 Phase 1

The phase 1 clinical trials are the first step after the pre-clinical trials. In this phase, trails are carried to by administering the new drug to humans, on an experimental basis, for the first time, to analyse its impact on humans. The Phase 1 clinical trial tests the drug in a small group of people (usually 15-100 participants). Researchers design Phase 1 clinical trials to understand a) What the experimental drug's serious adverse effects are? b) To find a dose that can be given and c) How the experimental drug is absorbed and processed in the body.

### 4.2 Phase 2

The phase 2 clinical trials are carried out to learn on how well the experimental drug is working in people who have a disease or condition. There are usually 100-500 participants. Researchers design Phase 2 clinical trials to a) Learn if the experimental drug may work in people who have a certain disease or condition and b) Continue to learn about the required dosage of the experimental drug works

### 4.3 Phase 3

The phase 3 clinical trials are carried out, if the results of Phase 1 and Phase 2 clinical trials are positive. The experimental drug is administered to a larger number of participants with identified disease or condition. There are usually 1000-5000 participants. Researchers design Phase 3 clinical trials to a) Analyse/confirm the adverse medical effects and the results seen in earlier phases and b) To learn how well the experimental drug works compared to another drug or compared to a placebo.

### 4.4 Phase 4

In this phase, trials are undertaken, after approval of the experimental drug, by regulatory authorities. They are spread over several years, due to involvement of large number of participants. Researchers design Phase 4 clinical trials to a) Learn how a new drug works when people are taking it as part of their everyday livesand b) Identify and evaluate the long-term effects of a new drug over a lengthy period for a greater number of patients. During the field survey, the researchers spoke to some

pharmaceutical organizations, studied/identified the process and it is described as a process flow. The interviewing technique was used to elicit data and understand the pain points. The pain points are described below.

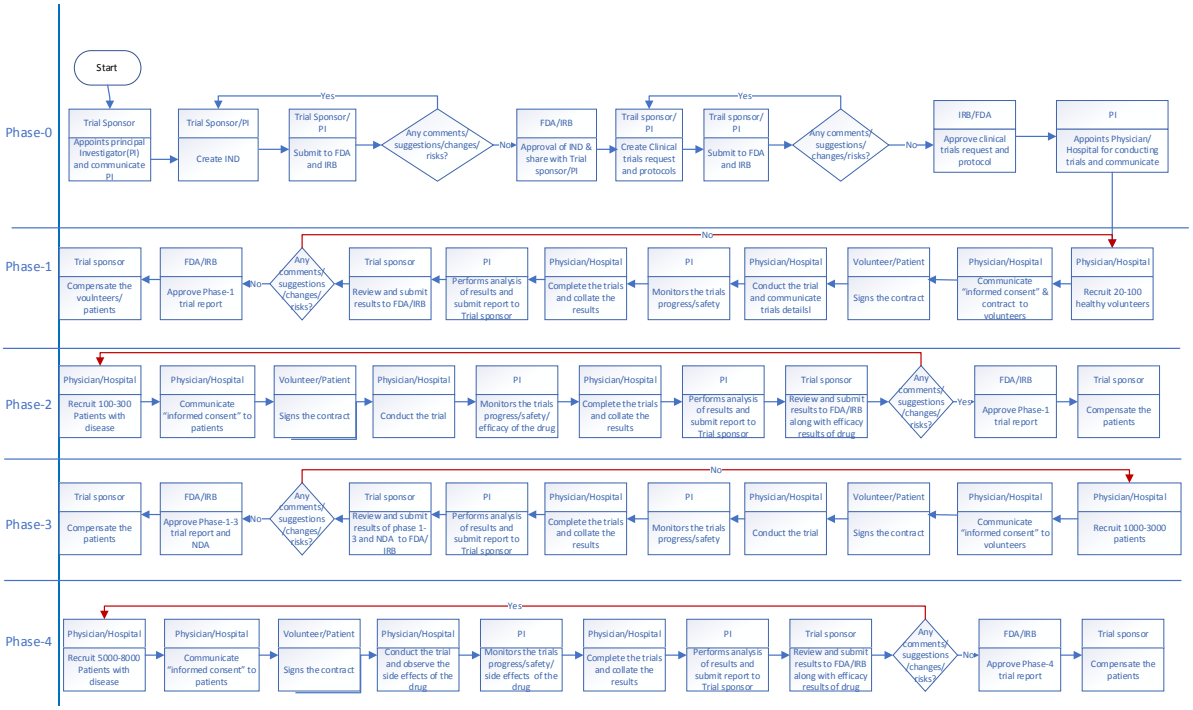


**Figure 1** Current state of clinical trials

### 5. Major Painpoints in the process across all phases

From the Secondary research we could identify major pain points in the current Clinical trial process across different phases.

- Consent & Contract Management of Patients

- Providing right consent forms as per the protocols, storing and tracking the consent forms is another concern
- Difficulty in tracking the Data with respect to the changes in patients/volunteers
  - Lack of Standard protocols among regulatory bodies for sharing of data
  - Non-availability of data on common platform leading to delays in the process
  - Documents Verification & Approval
- As there is large amount of data to be verified for approval by regulators, it takes a lot of time as the data is not available on a common platform . Source Data verification takes 20-30 % of the clinical trial budget and time. Data aggregation also takes a lot of time.
- Issues with Serious Adverse Events (SAE) may result in issues with insurance and settling the claims takes lot of time as there is no centralised system

- Privacy issues of volunteers as data can be seen by unauthorised people
- Data Management/Document Sharing

- Lot of time is spent on reviews as there are multiple stakeholders and multiple versions of the document.

- Lack of traceability once the number of drug users increase

All the identified pain points add on to the time and costs of the clinical trials which can be reduced with the automation of manual processes, by using disruptive technologies like Blockchain.

## 6. Justification for Block chain technology implementation in clinical trials process

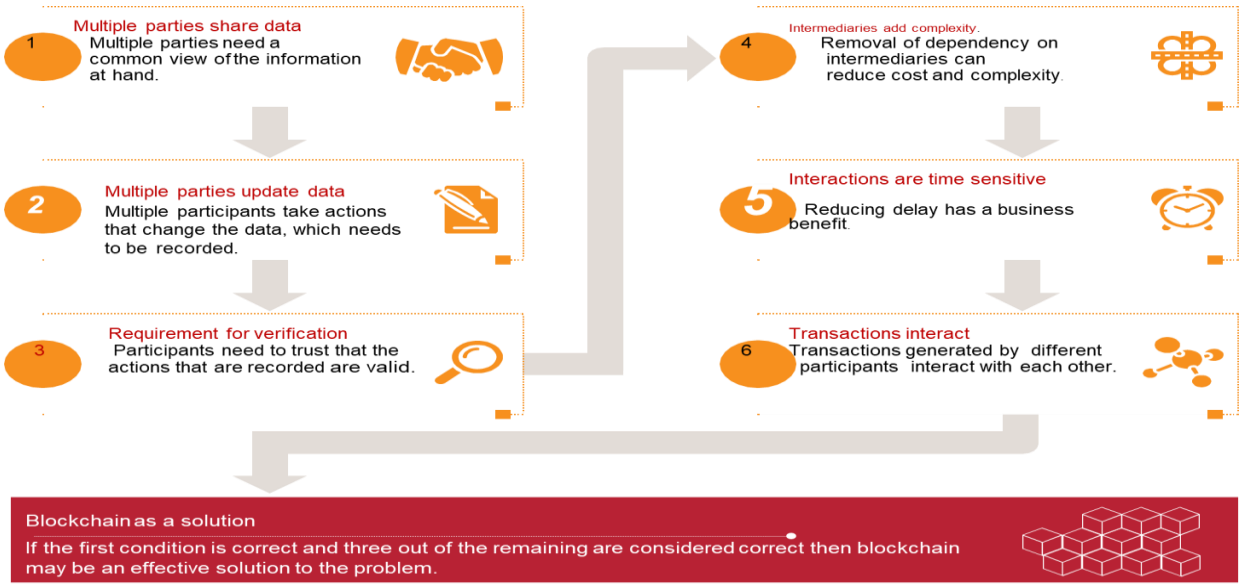


**Figure 2** Criteria for Blockchain implementation

From the above diagram, condition 1,2,3,4 and 5 are considered as requirements for clinical trials. So Block chain technology is a most appropriate solution for addressing the pain points in clinical trials

## 7. Addressing the pain points using the block chain and architecture

**Table 1**Pain points addressed using blockchain

| **Pain points** | **How block chain addresses the pain point** |
|---|---|
| Consent & Contract Management of Patients<br>• Inability to Provide right consent forms as per the protocols,<br>• Storing and tracking the consent forms<br>• Difficulty in tracking the Data with respect to the changes in patients/volunteers | System provides right consent forms as the patient log in to the system.<br>The data of each consent form is stored in Block chain and cannot be manipulated.<br>When the volunteer is changed a new block is created and can be accessed by the respective stakeholder, based on the access rights |
| Lack of Standard protocols among regulatory bodies for sharing of data | Creation of standard protocols through standard user interface with required information.<br>Sharing of data among all stakeholder institutions to a common platform, by a |

| | |
|---|---|
| | permissioned ledger using IBM Hyperledger |
| Non-availability of data on common platform leading to delays | All the data is available on block chain and can be accessed without approaching the respective stakeholders based on appropriate access authorizations |
| Documents Verification & Approval<br>• As there is large amount of data to be verified for approval by regulators, it takes a lot of time as the data is not available on a common platform . Source Data verification takes 20-30 % of the clinical trial budget and time. Data aggregation also takes a lot of time.<br>• Issues with Serious Adverse Events (SAE) may result in issues with insurance and settling the claims takes lot of time as there is no centralised system | Since the data is available as it is uploaded, the regulators will have all the details that are required. The verification process is greatly simplified and reduces the presence of wrong versions of different documents.<br>The trials report at the end of each trial is on the block chain that also has the information of the SAEs. This info is captured and cross tabbed with the patient records. This is a validated document by the hospital. Then for each of the SAE, there could be designated compensation from the insurance company and the payments can be managed through the "smart contract" mechanism available in block chain |
| Privacy issues of volunteers as data can be seen by unauthorised people | Since the data is seen only by authorized entities, the privacy of data is protected |
| Data Management/Document Sharing<br>• Lot of time is spent on reviews as there are multiple stakeholders and multiple versions of the document.<br>• Lack of traceability once the number of drug users increase | Since the entire data is available on Block chain platform, the required data can be accessed by a specific stakeholder based on his right of access.<br>The data can be traced on block chain platform through querying process. Blockchain will lead to open access data sharing model which can be viewed by appropriate stakeholders |

All the pain points of the phases of the existing clinical trial process have been analysed and mapped, along with the prerequisites for Blockchain implementation.

## 8. Blockchain Architecture for CT trials

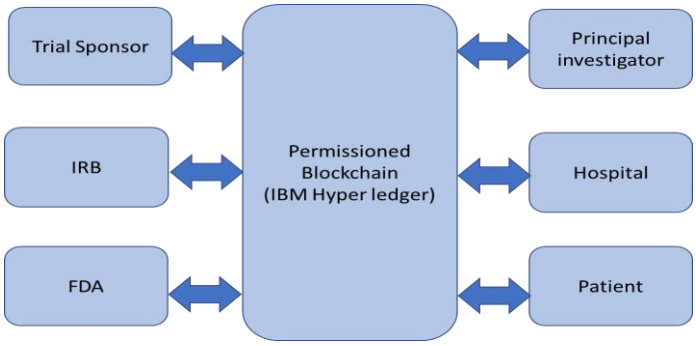


**Figure 3** Architecture of the Blockchain

The above figure presents a system overview of the CT process. The recommended system architecture places the IBM hyper ledger block chain at the centre of the model, where stakeholders can actively interact with it. By doing so, it aims to decentralize data management in CT, by potentially eliminating the role of entities like Contract Research Organization (CRO). The CT processes carried out in conventional way, get monitored/overseen by the CRO. This process is explained in multiple steps as shown in Figure 4.

## 9. To be process using Block chain implementation

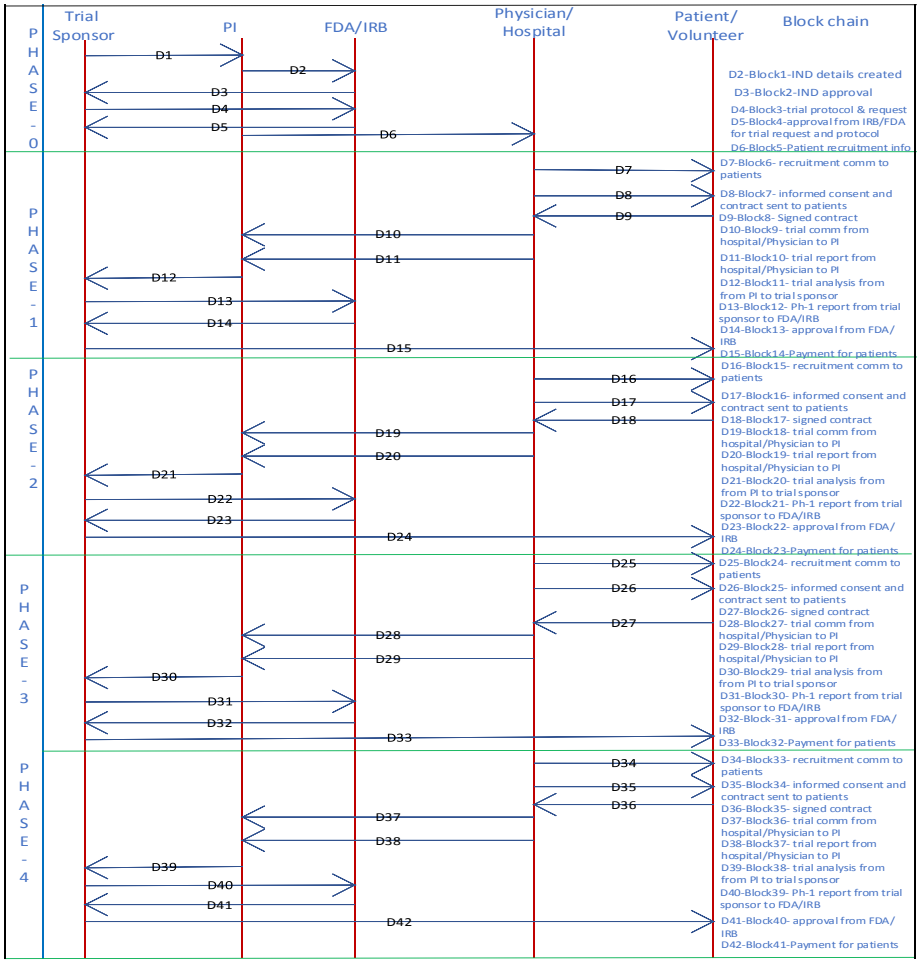


**Figure 4** Clinical Trials process using Block chain

**Table 2** Data exchange among stakeholders

| **Arrow number** | **Data beingexchanged among entities in stakeholders of the process** |
|---|---|
| D1 | Details of PI and details of communication to PI |
| D2 | Details of IND submitted to IRB/FDA |
| D3 | Approval from FDA/IRB |
| D4 | Trial protocol and request – data to IRB/FDA |
| D5 | Approval from FDA/IRB for trial protocol and trial request |
| D6 | Appointment details of Physician/hospital and communication to Hospital |
| D7 | Recruitment communication to patients/volunteers |
| D8 | Informed consent/contract communication to patients/volunteers |
| D9 | Signed Contract sent to the hospital |
| D10 | Trial communication from physician/hospital to PI |
| D11 | physician/hospital completes the trial and share data with PI |
| D12 | Trial data analysis from PI to sponsor |
| D13 | Trials result submission to IRB/FDA for Phase-1 |
| D14 | IRB/FDA approval for Phase-1 trial report |
| D15 | Payment details to volunteers/patients for Phase-1 trials |
| D16 | Recruitment communication to patients/volunteers |
| D17 | Informed consent/contract communication to patients/volunteers |
| D18 | Signed Contract sent to the hospital |
| D19 | Trial communication from physician/hospital to PI |
| D20 | physician/hospital completes the trial and share data with PI |
| D21 | Trial data analysis from PI to sponsor |
| D22 | Trials result submission to IRB/FDA for Phase-1 |
| D23 | IRB/FDA approval for Phase-1 trial report |
| D24 | Payment details to volunteers/patients for Phase-2 trials |
| D25 | Recruitment communication to patients/volunteers |
| D26 | Informed consent/contract communication to patients/volunteers |
| D27 | Signed Contract sent to the hospital |
| D28 | Trial communication from physician/hospital to PI |
| D29 | physician/hospital completes the trial and share data with PI |
| D30 | Trial data analysis from PI to sponsor |
| D31 | Trials result submission to IRB/FDA for Phase 1-3 and NDA |
| D32 | IRB/FDA approval for Phase-3 trial report |
| D33 | Payment details to volunteers/patients for Phase-3 trials |
| D34 | Recruitment communication to patients/volunteers |
| D35 | Informed consent/contract communication to patients/volunteers |
| D36 | Signed Contract sent to the hospital |
| D37 | Trial communication from physician/hospital to PI |
| D38 | physician/hospital completes the trial and share data with PI |

| | |
|---|---|
| D39 | Trial data analysis from PI to sponsor |
| D40 | Trials result submission to IRB/FDA for Phase-4 along with efficacy results |
| D41 | IRB/FDA approval for Phase-4 trial report |
| D42 | Payment details to volunteers/patients for Phase-4 trials |

In figure 4, the stakeholders in the target system are divided into six groups. The clinical trial initiation and management are carried out by the trial sponsor, Principal investigator; whereas, the regulatory authority and ethics committee are handled by the Food and Drug Administration (FDA) and IRB. The other stakeholders involved in the clinical site are principal investigator (PI), hospital, and patient. In our system design, the trial sponsor initiates the CT process by appointing a Principal investigator and then together they design IND. Then this goes through the approval process by FDA/IRB. Subsequently the protocols, request for trials also prepared and they go through the approval process by FDA/IRB. These events are governed by the creation of Hashed files for the respective submissions and smart contracts for some of the events as defined in the smart contracts section.The hospital is responsible to contact with patients, explain the informed consent, get the contracts signed by the patients, monitor and track the patient's progress during different phases of the clinical trials. These steps create the hashed files on the block chain system, and are stored. Subsequently, some of the events in this process is governed by smart contracts, as defined in the smart contract system. Assmart contracts track and monitor the transactions, based on the occurrence of specific events, during the execution of the CT process, the concerned stakeholders are notified through the alerts. Another salient aspect is to protect the identity of patients easily, as each patient would have an encrypted address mapped to their identity, and the details can be viewed through appropriate access authorizations. It is always better for the hospital to access the data, as it would be able to understand the progress of the patient during the trials, and provide feedback to the patient thus avoiding the mis-interpretation of the results.

As shown in Figure 4, the framework enables the storage of collection of hashed files, that could be retrieved anytime when incorporated within the blockchain. Files stored on the block chain network are given a unique cryptographic hash which is later used to track the corresponding file. This makes block chain an ideal place to store data as files, with features of traceability, immutability and time stamping. Examples of documents that could be stored include viz., Investigational New Drug (IND) application, protocol, Standard Operating Procedure (SOP), Case Report Forms (CRFs), PI's resume, obtaining consent from patients. The Block chain can be used to capture the medical history, monitor the trial process to detect Serious Adverse Event (SAE). The other data which gets stored includes outcome of the lab tests, financial/safety reports, conclusion report for the study. Block chain allows the users to make necessary changes during the entire CT life cycle. For example, if changes need to be made for document that is already uploaded, a user can reupload the modified version of the document on the block chain,by creating a new hash value for storage on the blockchain. In this way, a legitimate change or any protocol amendment can be accommodated after uploading the document to the blockchain.

**10. MajorSmart contracts in the clinical trials - block chain system**

## 10.1 Smart Contracts

### Request for CT Initiation in Phase-1

Input = Trial ID,Start Date, IND, End Date, Patients Count, Protocol, SOP

Event: Approval of the IND, Clinical trial request, protocol by IRB and FDA

If the Approval by FDA = "Yes" and approval by IRB = "YES"

Then, create the approval form and mail to Trial sponsor with IND, Clinical trial request, protocol, start date, end date, trail ID

Else, create a rejection request with the details of IND, Clinical trial request, protocol

### Patient Enrolment

Event :signing of informed consent

Input = Patient ID, consent, medical history (previously updated)

If CT Initiation is Accepted and consent signed = "Yes"

Then generate contract with the above inputs and the compensation details for the patients incase of an SAE confirmed by the hospital/physician, bank account details of the patient and share the contract with the patient and the PI

Else the contract is not generated

### Patient allocation to Trial

Event : Patient allocation to trial

Input = Patient ID, contract, medical history (previously updated)

If Contract signed by patient = Yes"

Then create the patients for trial-1 phase and send communication to the trial sponsor/PI and the patient

Else do not allocate the patient to Phase-1 trials

### Payment to the patients

Event : completion of trials for a phase

If the trial completed = "Yes",

Then trigger payment process

Transfer the amount to patient 1, 2,…n as per the contract to the respective bank account from the account of the clinical trials

Else, do not trigger the payment process

**Compensation from Insurance companies incase of SAEs**

Event : established SAEs for a single or group of patients in a specific phase

If the SAE established for patient = “yes” in the trial report from Hospital,

Then trigger payment process

Transfer the amount to patient 1, 2,…n as per the contract to the respective bank account from the account of the Insurnace company mentioned in the contract

Else,Do not trigger payment process

**New Drug Application approval in phase-3**

Input = Trial phase, start date, end date, trail ID

Event: Approval of NDA by IRB and FDA

If the Approval by FDA = “Yes” and approval by IRB = “YES”

Then, create the approval form and mail to Trial sponsor with Trial phase, start date, end date, trail ID

Else, create a rejection request with the details of trail phase, start date and End date and trial ID

**10.2 Smart Contract Architecture**

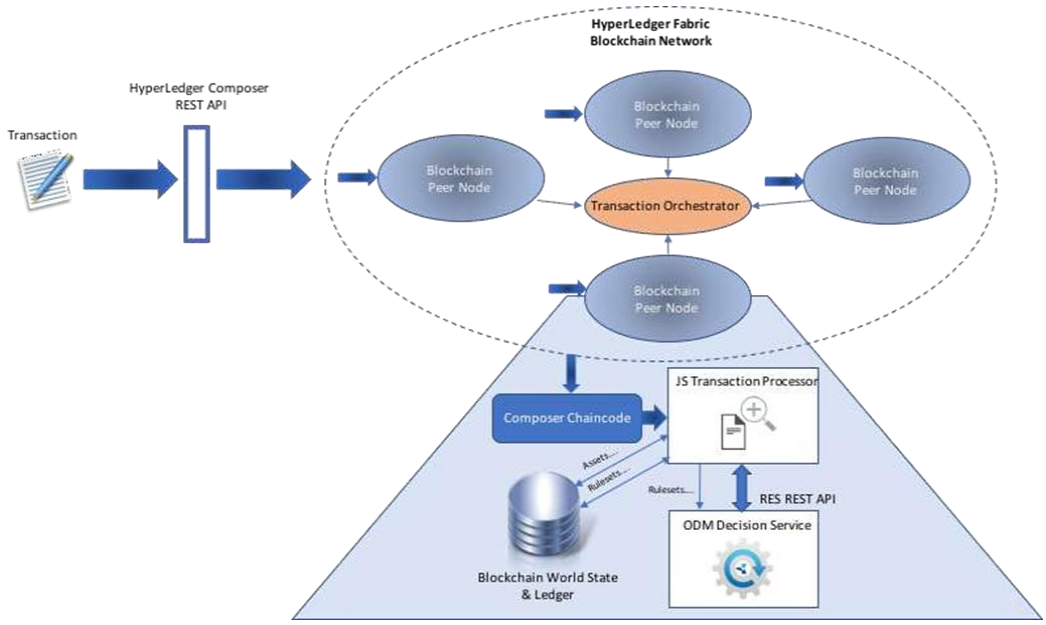


**Figure 5** Smart contracts architecture

## 11. Conclusion

Blockchain has the potential to transform the strategy, structure and processes related to clinical trials. It can change the clinical information assortment, information sharing and tasks. Clinical Trials carried out using blockchain innovation can facilitate seamless information move, assure information access across between stakeholders, reduce information asymmetry, and rearrange the clinical preliminary review and provide accurate results. By examining the current process, it's basically obvious that the phases of clinical trials tend to have glitches due information anomaly, adjustment, information protection, information misfortune. The research findings indicate that the pain points currently impacting clinical trials, can be addressed by utilization of Blockchain. As the information path advances the blocks would be created. These blocks will have time stamp which shields it from any tampering of information security lapses. The restricted access offers protection of security and confidentiality. The information duplication which occurs during reinforcement gets eliminated through block chain. With the block chain, presentation of smart contract is feasible at various stages like auditing the solicitation of trail by IRB, beginning screening of member information by specialists/legal group. Block chain would help in overcoming the challenges faced in the current state

## References

1. Amanda , B. J., Nuttall, J., Bull, A., Worswick, L., Mullee, M., Peveler, R., Griffiths, G. (2020). Using digital tools in the recruitment and retention in randomised controlled trials: survey of UK Clinical Trial Units and a qualitative study. *Trials*, 1-11.
2. Benchoufi, M., Porcher, R., & Phillippe. (2018). Blockchain protocols in clinical trials: Transparency and traceability of consent. *F1000Research*, 1-66.
3. Benchoufi, M., Ravaud, & Philippe. (2017). Blockchain technology for improving clinical research quality. *Trials*, 1-5.
4. Brooks, R. R., Wang, C. K., Yu, L., & Oakley, J. (2011). Scrybe: A Blockchain Ledger for Clinical Trials. *SCrybe*, 1-5.
5. Chaudhari, N., Ravi, R., Gogtay, J. N., & Thatte, M. U. (2020). Recruitment and retention of the participants in clinical trials: Challenges and solutions. *Perspectives in Clinical Research*, 64-69.
6. Choudhury, O., Sarker, H., Rudolph, N., Foreman, M., Fay , N., Dhuliawala, M., . . . Das, A. K. (2018). Enforcing Human Subject Regulations using Blockchain and Smart Contracts. *Block Chain in Healthcare Today*, 1-14.
7. Davis, S., & Pai, S. (2020). Challenges and opportunities for sponsors in conducting clinical trials during a pandemic. *Perspectives in Clinical Research*, 115-120.
8. Glover, D., & Hermans, J. (2017). Improving the Traceability of the Clinical Trial Supply Chain. *Clinical Technlogy*, 36-38.
9. Griggs, N. K., Ossipova, O., Kohlios, P. C., & Baccarini, N. A. (2018). Healthcare Blockchain System Using Smart Contracts for Secure Automated Remote Patient Monitoring. *Journal of Medical Systems*, 42-49.
10. Rupani, M. Z. (2020). Clinical trial master file migration: A preordained step for a centralized electronic trial master file. *Perspective sin Clinical Research*, 139-141.
11. Schindler, T. M., Grieger, F., Zak, A., Rorig, R., Konka, K. C., Ellsworth, A., . . . Crandall, C. (2020). Patient preferences when searching for clinical trials and adherence of study records to ClinicalTrials.gov guidance in key registry data fields. *PLOS ONE*, 1-15.
12. Stamatellis, C., Papadopoulas, P., Pitropakis, N., Katsikas, S., & Buchnan, W. J. (2020). A Privacy-Preserving Healthcare Framework Using - Hyperledger Fabric. *Sensors*, 1-14.
13. V, C., Buhrmann, L., Riper, H., & Ossebaard, C. H. (2020). Health technology assessment frameworks for eHealth: A systematic review. *International Journal of Technology Assessment in Health Care*, 204-215.