Team 😊 order with the daybreak - since July 2019

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https://github.com/hyperledger-labs/patient-consent
Challenges in Healthcare: Compliance

For the all industries and services

Higher Regulations for Medtech Providers

New Regulations

= Longer time2market and Development costs
Pain points for Medtech and Pharma: Focus Clinical Trials

- Governance - Compliance
- Data & Process Security
- Portability
- Data Privacy
- Competitive Market entry
- Data & Process Traceability
- Process Scalability
- Data Interoperability
- Process Integration

Deniz
Clinical Trials: A complex and distributed process with great amount of data flow

<table>
<thead>
<tr>
<th>Laboratory Phase</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>Phase 4 (On the market)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Why?</td>
<td>• Find the safe dose&lt;br&gt;• Test on the mice&lt;br&gt;• Impacts</td>
<td>• Healthy individuals&lt;br&gt;• Find the safe dose on humans&lt;br&gt;• Way to take the drug&lt;br&gt;• Monitor the impacts (side effects)</td>
<td>• Find the safe dose on humans&lt;br&gt;• Effects on certain diseases&lt;br&gt;• Monitor the impacts (side effects)</td>
<td>• Which dose is the most effective in Phase 2&lt;br&gt;• Compare the new drug or use with the standard treatment?&lt;br&gt;• Monitor the impacts (side effects)</td>
</tr>
<tr>
<td>Number of patient total</td>
<td>One site: 10 patients</td>
<td>&lt; 800</td>
<td>1000 – several 10000</td>
<td>1000 – several 10000</td>
</tr>
<tr>
<td>Number of sites</td>
<td>1 site for rare disease - Min 2 to keep two different views – (up to 10 sites)</td>
<td>Up to 80 sites</td>
<td>Up to 100 sites</td>
<td>Up to 100 sites</td>
</tr>
<tr>
<td>Duration (years)</td>
<td>Up 2 – 3 years (only in US)</td>
<td>2 - 5</td>
<td>2 - 5</td>
<td>1 - 3</td>
</tr>
<tr>
<td>Protocol changes?</td>
<td>No big changes</td>
<td>1 - 2 times</td>
<td>3 – 6 times</td>
<td>2 – 5 times</td>
</tr>
<tr>
<td>Requests (times)</td>
<td>Approval at the beginning *(site) + protocol changes * (site)</td>
<td>Approval at the beginning *(site) + protocol changes * (site)</td>
<td>Approval at the beginning *(site) + protocol changes * (site)</td>
<td>Approval in the beginning *(site) + protocol changes * (site)</td>
</tr>
<tr>
<td>Approvals (times)</td>
<td>Initial consent (20 – 80) + (protocol changes * patient number)</td>
<td>Initial consent (800 – 5000) + (protocol changes * patient number)</td>
<td>Initial consent (1000 – 10000) + (protocol changes * patient number)</td>
<td>Initial consent (1000 – 10000) + (protocol changes * patient number)</td>
</tr>
</tbody>
</table>
Clinical Trials: We want to accelerate the flow
Question: Integration with the legacy systems?

• Clinical Trials Workflow?
• Which process we need the most?
• Which protocols and API-Standards we can define?
• Which CTMS`s can be integrated? Veeva, Medidata, Informa, Oracle?

The solution?
## Solution is Enterprise Blockchain.

### Why we need Enterprise Blockchain in Clinical Trials?

We provide with our Use Case

1. **High process validation efficiency for regulators**
2. **Low cost process and defined governance**
3. **Provide GDPR Compliance, security and data protection**
4. **Consolidate and integrate the distributed landscape ecosystem**
5. **Close the open-end processes between stakeholders - ledgers**

### Results:

1. **Better Compliance with Trial Governance** with the blockchain
2. **Security** through cryptography
3. **Build trust and automation** with smart contracts
4. **Transparency** with transactions
5. **Traceability** with blocks
6. **Immutability** with blocks
7. **Integration of stakeholders** with the distributed ledger architecture

Higher value to sponsors, investigators and patients centric trials to accelerate the clinical trial process
Two examples:

1. Increased efficiency of regulatory approval in Clinical Trials:

Compliance and quicker regulatory approval →
USD$ 17 million revenue per extra day saved while on patent monopoly.

Twenty-four billion dollars from 1,393 days of patent extension and pediatric extension on Lipitor. This is the additional revenue which Pfizer received from sales between May 30, 2006 (when its primary patent on Lipitor would have expired) and March 24, 2010 (when its patent term and pediatric extensions expired.


1. Clinical Trials in oncology:

- Trial duration of between
- 15 to min. 10 years,
- in which one day at CRO costs 15000 USD min,
- and patient data from 5000 to 25000 USD

15 years * 220 days * 15000 USD/day and 5000 USD * 10000 patient data (min) = 49.5 millions + 50 Millions = 100 millions USD for only one trial

8 in this trial we need to calculate few other positions), and you need multiple trials for one drug

Most importantly, the time2market before the other competitors.

- With our Use Case you can save min. 25% of the efforts and the time for the clinical trials. If you improve:
- Compliance and scalability of the clinical sites
- Leverage for the virtual trials
- Integration with patient data

Our value proposition is:

✓ We use the **existing technology** for the **existing challenges** to develop **non-existing patient centric solutions**, that uses Blockchain, Artificial Intelligence, IoT, and most important with the **domain knowledge**

✓ Patients will get a better visibility on the available clinical trials and will be able to manage their consent in a very simple way but most importantly in a secure and immutable way (blockchain).

✓ The benefit for the Pharma Companies, Medtech`s is a considerable reduction of time and costs compared to the standard process. Additionally, our service allows the users to optimize their patient selection criteria to ensure that the desired number of patients will be available to potentially enroll in their clinical trial.

✓ The benefit for the patients is a better visibility of the available clinical trials which they might be able to join based on the patient selection criteria.

✓ We need collaborations with the expert user`s, industry to excel our solution, starting with E-Consent in Clinical Trial, and build the next blocks, Patient Recruitment and Clinical Monitoring
Use Case realizations with two frameworks, Hyperledger Fabric and Sawtooth, and benchmark with the defined criteria

- We assume that our investigator is a hospital with the patient initial consent and we have no other sites

- Trial Protocol: will be implemented as smart contract

- Protocol amendment and criteria definition: Initial protocol is included in consent management. The protocol may change during clinical trials based on adverse events and patient compliance. The patient will have to consent to the changed protocol.

- Consent Validation: After the consent we have the include and exclude criteria check
Use Case Scope: Econsent Scope Fix per 20191124

Principal Investigator

Run Pre-Screening Check
- List the potential candidates
- List the healthy individuals (only for the Phase 1)

Inform & ask consent each of the candidates
- Informed Consent Document

Give or reject consent

Patient
- Patient Data kept in the DB

List the patients with the consent

Protocol amendment?
- Approval of the regulatory body

EDC

Recruit needed patient
- Check need for patient recruitment

Collect and update the Patient Data
- Exclude the patient
- Include the patient

Sponsor

Trial Protocol
- Baseline Requirements

Protocol Exclusion Criteria
- Blood -> vendor center
- Any Medical value

Third bodies

Clinical Monitoring - Hired vendors:
- AiCure - Testify the drug intake with the monitoring of drug swallowing video with mobile
- Tablet - voice recorder
- Recording the patient activity
- Monitoring the sleep
Use Case Scope: Econsent Scope Mid of 2020

Patient

List the potential candidates
Inform & ask consent each of the candidates
Give or reject consent

Recruit needed patient
Check need for patient recruitment

Collect and update the Patient Data
Exclude the patient
Include the patient

Trial Protocol

EDC

Sponsor

Principal Investigator

Trial Protocol

List the patients with the consent

List the healthy individuals (only for the Phase 1)

Informed Consent Document

Web instance specific for the patient for reading

Protocol amendment?

Approval of the regulatory body

Trial Protocol Baseline Requirements

Exclude the patient
Check the eligibility
Collect and update the Patient Data

EDC

Sponsor

Principal Investigator

Clinical Monitoring - Hired vendor
- AlCure: Testify the drug intake with the monitoring of drug swallowing video with mobile
- Tablet – voice recorder
- Recording the patient activity
- Monitoring the sleep

Third bodies

Inclusion Exclusion Criteria
Blood -> vendor center any Medical value

Ihor
Target audiences;

**Pharma;**

**EU Member states:**
Sanofi, Novonordisk, BoehringerIngelheim

**CH:**
Roche, Novartis

**India:**
Torrent
http://www.torrentpharma.com/
Glenmark Pharma,
https://www.glenmarkpharma.com/
Jubilент Biosys
https://www.jubilantbiosys.com

**UK:**
GSK, AstraZeneca, Biogen

**Investigators;**
**CH:** 5 Big Canton and regional Hospitals

**CRO`s**
**EU:** Icon, IQVIA, PPD, PRA Health Sciences, MedPace

**Patient Data Provider**
**CH:** Clinerion
**US:** AmazonWebServices

Patient recruiters
What are benefits for the Hyperledger Community

- Baseline and a viable POC for the next projects: like further Clinical Trial Integrations with Patient Recruitment and Monitoring

- Convergence of Hyperledger Components, Identity Management and API`s, Standardization of API`s and clinical trials components

- Comparison of two Hyperledger frameworks, Fabric and Sawtooth with one specific use case, pro`s and con`s, Benchmarking and Use Case Assessment

- Assessment and customization of use cases to the suitability of the solutions and possible improvement proposals

- Great motivation for the open source community for a portfolio of different ecosystem
Solution: Big Picture for Clinical Trial

- **Data Ingress E-Health Records**
- **Data Ingress CRO Data**
- **Data Ingress IOT Data**

Clinical Trial Process Workflow

- **BlockChain Network**
- **Web App**
- **Data API**
- **Configuration API**
Legend:

- **CA**

Hyperledger Fabric Patient Consent Network

- Data Channel (trial events & transactions)
- Consent Channel
- Patient Channel

Legacy System Interfaces

Clinical Trial Data and Process Flow

- IOT Data Gateway
- IOT Source
- Mobile Client
- Fabric SDK / Smart Contracts
- Patient Consent Web App(s)

Peers Nodes for Participating Orgs

- John
- Kent
Vision: Hyperledger Sawtooth Architecture

Client
- IoT
- Web
- Mobile
- Admin CLI

Sawtooth Node

Backend
- REST-API

Blockchain
- Consent/Identity/Authorization Management Component
- Data Management Component
- Consensus engine
- Settings

APIs:
- Create client
- Grant Access
- Revoke Access

Sawtooth Node
- Validator
Demo with Hyperledger Sawtooth

Demo
Q & A
Annex: Ongoing work

- Automation of data communication from patient channel to trial channel
- Confirm - Fabric Technical Approach for persisting baseline Patient data within an active clinical trial.

**Issue Board**

- **Issue 1**
  - HF Clinical questions
  - Prepare use case step 1 from Patient Consent Flow
  - Implement scenario for step 1
  - Adopt the app to be GDPR compliant

**Open tasks**

- JIRA - Linux Foundation
  - Trigger points for consent
    - Task 2: Identify entities, actions, roles, permissions
    - Task 3:

**On going**

- Confirm - Must patient data for patients who DO NOT qualify for a clinical trial be retained and "linked" with the trial?
- Confirm - When a trial progresses Phases (Ex: Phase 1 -> Phase 2) are explicit consents required from patients to continue in the next Phase?
- Confirm - USFDA requirement that all trial events be visible to an Oversight role - all channels, actors, data.
Annex: – Benchmark Fabric 2 Sawtooth

- Use case realizations with two frameworks, Hyperledger Fabric and Sawtooth, and benchmark with the following criteria
  - Consensus algorithm
  - Applications nature
  - API’s and security
  - Transaction speed
  - Block interval
  - Block size
  - Communication protocol
  - Energy consumption per transaction
  - ?????
  - Applicability for use case – Functionality smart contracts, transactions, ledgers, consent,