Abstract. Quality of processes and products is based on traceability and review of both components, material processing and product flow throughout the manufacturing and supply chain. Blockchain technology enables cross-border audit trail and traceability while reducing costs. Donors are the providers of biological raw material (starting material). They can share their health records when donating by using an IPS document or a FHIR Questionnaire-response resource. It allows health personnel to retrieve and verify relevant clinical information when donating. Additionally, health personnel can generate an anonymized and de-identified digital twin of the donor for research purposes, and it can be updated over time. The starting material can include a reference to a digital twin of an unknown supplier, which improves the data quality and enhances research possibilities. Adverse reactions and events can be also recorded on blockchain to improve safety, transparency, traceability, medical research and product quality.

Keywords. traceability, biological, products

1. Introduction

Advanced Therapy Medicinal Products (ATMPs) are medicines for human use that are based on genes, tissues or cells. The ATMPs consist of three basic categories of products: 1) gene therapy medicinal products (GTMPs); 2) somatic cell therapies [1]; and 3) tissue engineering products, as well as any combination of the above. In addition, safety regulations apply to donor sperm and ova intended for use in assisted human reproduction (AHR) by a recipient who is not the spouse, common-law partner or sexual partner of the donor. This includes the use of donor sperm in assisted human reproduction techniques (e.g., in vitro fertilization). Safety regulations also apply to ova that has been obtained from a donor and that is intended for the donor's use (i.e. via in vitro fertilization) as a surrogate mother, and to donor sperm that is distributed by an establishment or health professional to a recipient for their personal use [2].
Chain of Identity (COI) is the association of a unique donor’s identifier to their raw material and the resulting medical product of biological origin, from collection to manufacturing and aftercare monitoring. On the other hand, Chain of Custody (COC) is the traceability of actions (locations, employee, timestamp) from the collection of the raw material from a donor to the administration of the biological product to a patient. A key aspect of regulatory compliance is an audit trace, which includes a person as a key part of the Chain of Identity (COI) and Chain of Custody (COC). Traceability can prove that products meet certain standards or comply with industry regulations.

The EMA’s Guidelines for Good Clinical Practice specific to Advanced Therapy Medicinal Products [3] states in the section 7: “The traceability system should be bidirectional (from donor to subject and from subject to donor) and data should be kept for 30 years after the expiry date of the product, unless a longer time period is required in the clinical trial authorisation”. Applying blockchain technology for audit trail, data immutability and traceability in both COI, COC and Clinical Trial Application (CTA) is a key element to provide transparency for each record in AHR, CTA and ATMP (history of actions, events, participants, components, etc.).

Private smart-contracts deployed in an Hyperledger Fabric network can ensure the safety and privacy of patients, donors and participants in clinical trials while also reducing timelines, aid researchers and clinicians in recording clinical data in real time as soon as it becomes available. It enables cross-border audit trail while reducing costs, as the need for traditional audits, file reviews, lost document investigations, and litigation would decrease due to the existence of blockchain’s immutable data. Additionally, de-identified data can be stored on blockchain to improve quality of data for research and to enhance accuracy, collaboration, while preserving privacy and regulatory compliance [4].

2. Method

The Procedure for the Global Unified Registration and Universal Identification of Donors enables each donor to have its own unique and universal identifier for cross-border identification [5]. Likewise, health personnel are enabled to record donation encounters and procedures on the blockchain, linked to the global UUID of the donor (for example: type of donation, timestamp and result). Consequently, health personnel attending donors are able to check for compliance with donation regulation within the given territory, such as number of donations, time lapse between them, excluded donation status, amongst others. As a result bad practice is minimized, including over the limit donation, and donation from excluded donors, thanks to enforced traceability[6].

At the same time, each document created in AHR, CTA and ATMP can have a randomly generated and collision-free Unique Universal Identifier (UUID v4). An UUID v4 can also be associated with every raw material (COI) and step performed (COC) in any donation, cell therapy and clinical trial application (CTA), to audit and trace collection, manufacturing and supply chain of biological products for medicinal purposes [7]. It improves the resilience of any Information System (IS), because the client applications can continue creating, registering and processing (e.g.: printing) data locally, with or without network connection, which will be synchronized with the IS when the network connection is ready. Once the data is synchronized with the IS, it can
do additional actions such as associating sequential codes to the UUID (ISBT-128 code, GTIN, etc.), registering the data on a blockchain network, etc.

Donors or their legal guardians can share health records when donating by using the donor’s global UUID. For example, it can be done by an IPS document provided by the donor to the facility or by a response to a FHIR Questionnaire provided by the facility to the donor. It allows health personnel to retrieve and verify relevant clinical information such as history of donations in different facilities in one or more territories, history of diseases, current medications and conditions, etc. [4] Additionally, the data of the donor (supplier) can be anonymized and de-identified for research purposes by the health personnel, for example by a check-box in a FHIR Questionnaire [8], so the starting material can include a reference to a de-identified digital twin of an unknown supplier, which improves data quality and enables enhances research possibilities.

3. Discussion

A FHIR Questionnaire-response and a FHIR Bundle Document (such as an IPS) containing donor’s relevant medical data can be received in the software application of the health personnel in a donation facility both online and offline (e.g.: by using bluetooth). The confidential app of the health personnel attending the donor can generate the data of both extraction procedure, raw material extracted from the donor (supplier of the starting material) and an anonymized and de-identified digital twin of the donor, for example, following a data de-identification and minimization process similar to SMART Health Cards (SHC) [9], but deleting personal data in the FHIR Patient resource (in order to keep only the country of residence, year and sex of birth) and changing the resource identifiers to others.

When a network connection is available, the software application of the health personnel sends both collection data (which can include the donor’s global UUID), starting material data and digital twin data, to an Application Programming Interface (API), which sends some data to one or more public or private smart-contracts deployed in one or more channels of an Hyperledger Fabric blockchain network (e.g.: biological channel and research channel for a territory).

4. Conclusion

A digital twin with anonymous and de-identified donor data can be generated at a donation facility through a software application by a healthcare professional and recorded on a blockchain network along with collection and source material data. The digital twin identifier (UUID v4) is linked by the professional application to distinct identifiers of starting materials (UUID v4) extracted from the same donor. The collection facility is the only one who can link the universal donor identifier with the digital twin generated. A donor can then send updated versions of the medical records to the facility by using the donor’s global UUID. The facility can retrieve the donor's private digital twin identifier from its information system and update the digital twin on the blockchain, improving research efficiency and capabilities. In case of ova and sperm donors, data on the digital twins of the biological parents of an individual born through assisted reproduction can be accessed.
In this way, specific data from the collection process can be known on the one hand, but also data such as year of birth, sex at birth, country and some relevant medical codes related to the supplier of the anonymous starting material on the other hand, such as blood pressure, previously administered medications, as well as others that are considered relevant by the health personnel who perform the extraction of the biological material, anonymously and securely, in order to carry out research studies, statistical analyzes and to study relationships between the quality of products of biological origin, the extraction conditions and the characteristics of the starting material suppliers. Additionally, health professionals can register on the blockchain network adverse effects detected in a recipient of biological material or product, as well as the recipient's digital twin, linked to the biological product, to improve transparency, traceability, medical research and product quality. In case of an event that affects the quality of a biological material or product occurs or is detected, it can also be recorded in the blockchain network. In this way, both an owner and a recipient of a biological material or product can find out if it is suitable for use or if the recipient requires a medical review as a result of a registered event, improving safety.

References