Detection of Delay Points in the Batch Release of Products in a Pharmaceutical Company

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Abstract

The Company is a multinational enterprise that produces and sells pharmaceutical products in several European and external markets. In Portugal, the Company only oversees the distribution process, hiring a Pre-Wholesaler, with agreed conditions and standards, to receive, store, and verify the transport conditions of products. Upon registering each arrival into the information system, the Pre-Wholesaler sends samples to the quality control department of the Company. Products that meet standards are released to a Wholesaler (which then distributes them to the retail). This process is called Batch Release. Over the years, the process has become more complex due to increasingly stringent European and national pharmaceutical regulation and to the service level the Company wants to offer its clients. Company officers say that what once took one day, now takes nine. Any reduction in the process duration is likely to carry a significant reduction in costs tied up as inventory. The process was first described in Systems Modelling Language (SysML) to detect delay points in the system. Then, this model was used as a reference to specify the foundation of a Blockchain technology application, which makes it possible to know the reasoning behind the delays and cope with them.

Keywords: Pharmaceutical Industry, Supply Chain, Batch Release, Delay, SysML, Blockchain

Introduction

Background

Quality is of the utmost importance in the Pharmaceutical Industry due to heavy national and European regulation. Meaning, failure to comply with quality regulation has a substantial consequence for the company. For this reason, the pharmaceutical industry's supply chain is long and complex, with several quality verification steps, starting during production, up until after the product's arrival at the retailer. These checks are required in order to prevent the release of faulty products to the market. Figure 1 shows a simplified diagram of the Pharmaceutical Industry's supply chain. The Batch Release is an important step in this supply chain where, after arriving at the pre-wholesaler's warehouse, the products are verified for quality and cleared for distribution to wholesalers.

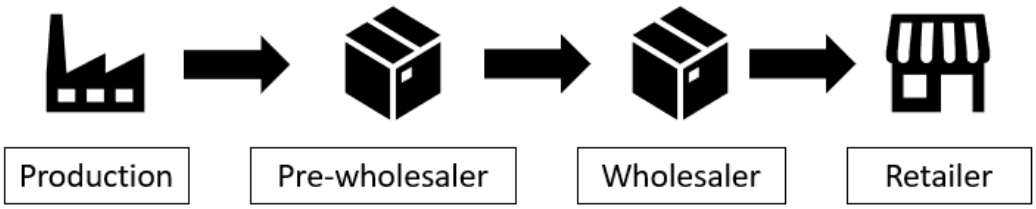

Figure 1 - A simple illustration of the Pharmaceutical Industry's supply chain

Problem Definition

The Company's supply chain has associated costs, one of which is the inventory cost from holding products in stock. The total inventory cost is proportionate to the time the stock stays on hold in the

warehouse, meaning the longer the products stay stored, the higher the cost. The Batch Release stage currently has a duration of nine days, while it took one in the past, and the inventory on hold has increased in proportion. Sized to 5M€ waiting to be released, it is a concern for the Company.

Project Objectives

The main goal of this project is to detect the delays in the Company's batch release process and providing a way to find the reasoning for these delays, in order to cope with them afterwards.

This project uses the Model-Based Systems Engineering (MBSE) methodology to identify the problem causing these symptoms, the delays. MBSE is the formal application of modeling to support system design, analysis, optimization, verification and validation. It begins in the conceptual phase, and may continue throughout development and into subsequent system life cycle phases such as operations [1]. This application of MBSE uses Systems Modelling Language (SysML) as the modeling language to formally describe and analyze the system. SysML is a general-purpose modelling language for complex engineering systems [2]. It uses a graphical notation to support the analysis, design and verification of systems, including facilities, procedures and personnel [3].

The first phase of this project was the development of a reference structure for the Batch Release Process. This phase had the purpose of identifying how much time is spent in each stage of the process and what are the delay points within the system.

The second phase used the reference structure to develop the foundation of a Blockchain technology procedure, as a means to cope with the issues found. The Blockchain results will help evaluate the performance of each step (e.g. the Pre-Wholesaler verification) and the need for redundant steps.

State of the Art

MBSE

Model Based Systems Engineering (MBSE) is a methodology that applies systems modelling to support analysis [4], design [5] [6] [7] [8] [9], specification [10] [11] and validation [4] [12] of a system being developed [13] [14]. MBSE uses Systems Modelling Language (SysML) as a tool in order to create a cohesive model of the system from specification, improving design quality and communications among the development team [7] [12] [13].

SysML is a visual modeling language that was adapted from the Unified Modelling Language (UML) to enhance the traditional top-down systems engineering process [13] [14] [15]. Although the UML is pretty extensive, SysML added some needed elements for systems engineers while removing others, focused on information systems modelling, to diminish the complexity of the tool [14].

The SysML uses a simple diagram approach to describe systems, where basic structure components, called Blocks, are used to represent the elements of the system [2] [13] [14] [15]. In Figure 2, the structural view represents how the different elements that define the structure of the system, the

Blocks, are combined. The behavioral view describes the activities, states and users in which the blocks from the structural model are involved with [14] [15].

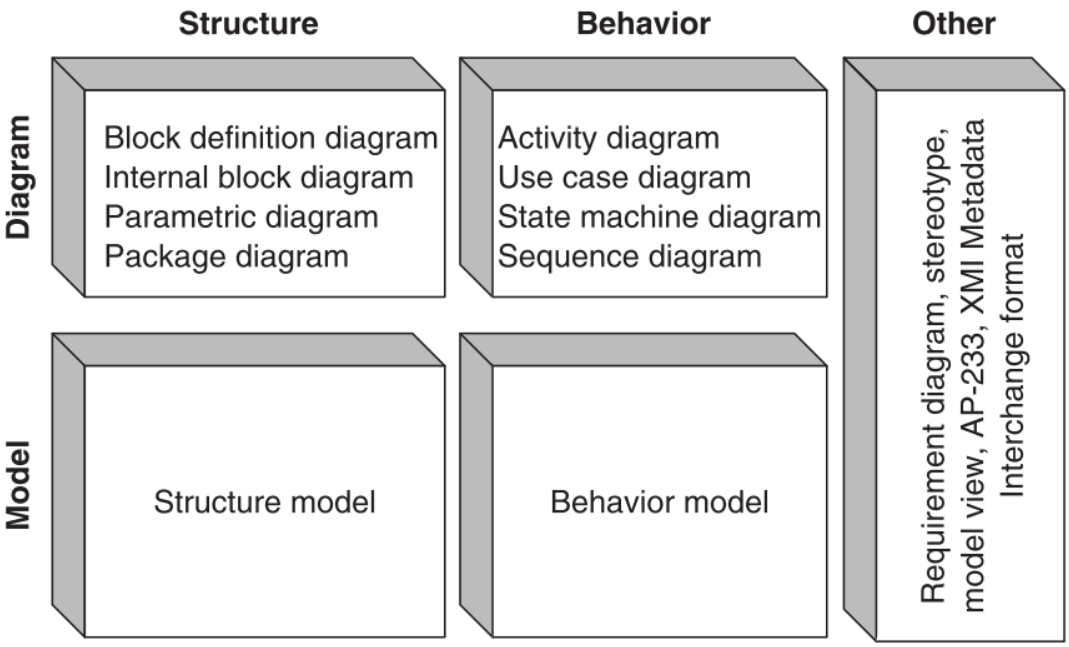

Figure 2 - SysML model types and associated diagrams [14]

Blockchain

Blockchain technology is a peer-to-peer network of information technology that keeps a record of digital transactions in a distributed ledger, accessible by any participants in the system [16]. A peer-to-peer is a type of network, where its maintenance tasks and responsibilities are shared between several devices, called peers [17]. This is opposed to the traditional databases, which are sited in centralized servers and controlled by a single mediator like a bank or the government. Being decentralized and cryptographic, blockchain technology builds trust between peers, therefore bringing major security benefits [18]. Hacker attacks that usually target the large mediators, such as banks, are unfeasible and virtually impossible, as the blockchain registers all alterations that would occur with the hacking attempt.

Blockchain solutions are built on grounds of four key futures:

- **Decentralized Validation** - All relevant peers in the network need to validate each transaction, otherwise it will not go through. For example, the transaction for a warehouse door opening for an incoming delivery truck will only occur if both the truck driver and the warehouse doorman participants approve it.
- **Redundancy** - The Blockchain is decentralized, meaning its replicated on all peers of the network. This results in the Blockchain being unaffected even if some of its storage hardware is lost.
- **Immutable Storage** - All blocks are linked, so tampering with one block requires changing all successive blocks. All registered data also has a digital fingerprint with timestamp. So, even if

tampering is successful, the change stands out as obvious, as the new fingerprint does not correspond to the old one.

- **Encryption** - Due to transaction validation being made with digital signatures, which are based on pairs of cryptographic public and private keys, only the participants in the network can register data in the Blockchain. These properties make Blockchain very desirable to monitor large amounts of information.

The tool used to create a Blockchain business architecture for the Company is the IBM Blockchain Platform, which is an enterprise-ready development platform powered by the Hyperledger Composer open source engine [19]. Hyperledger Composer provides a Playground environment where the user can create and test their Blockchain business networks.

The Blockchain business architecture contains 3 elements:

- **Assets** represent the goods, services or property in the business. These can include anything from cars, animals, documents or workers. Assets can have many properties, requiring only a unique identifier. Some of these properties can be related to other assets in the network.
- **Participants** represent the business members who can own assets or submit transactions. Like assets, participants just require a unique identifier and may have many other properties.
- **Transactions** represent the interactions between participants and assets. An example is a sale. A participant sells an asset to another participant, therefore changing its ownership.

A business architecture is stored in an archive (*.bna*) composed of four types of files:

- **Model** file (*.cto*), usually created by the business analyst, describes the business environment by defining the structure and relationship between the three model elements: assets, participants and transactions.
- **Script** files (*.js*), usually created in JavaScript by developers implementing the system requirements provided by the business analyst.
- **Access Control** files (*.acl*) define the access rights of each participant in the business architecture, meaning each entity can only alter the data it has access to.
- **Query** File (*.qry*), states the details of the business architecture (e.g. name, version, etc.).

A business architecture built in the Playground cannot interact with other software, but its .bna archive can be extracted and imported to IBM Blockchain Platform which can later be linked with external systems.

Methodology

The methodology used in this project has two stages:

- The first stage was building a SysML model (.rpy) to illustrate the batch release process system with the information and data provided by the Company;
- In the second stage, these diagrams were then used as a frame architecture for a Blockchain technology application.

Figure 3 illustrates this methodology. The Company information and data were converted into a SysML model (.rpy), which was later adapted to a Blockchain model file (.cto).

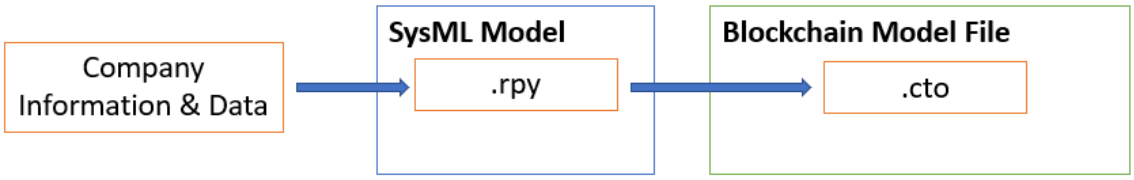

Figure 3 - The two-stage methodology used in this project.

Project Diagram Sequence

The SysML model began with the building of a block definition diagram of the main structural elements of the system (**1**). This was followed by the creation of a use case diagram (uc) defining the main actors involved with the process and what actions they perform to interact with the system (**2**).

Two activity diagrams (act) were created from the uc's, one for the central batch release process and another for the local batch release process, which describe the sequence of activities in each of these processes (**3**). From the act's, a state machine diagram (stm) was built for each of the core blocks in the system, the Batch and the Duty of Care (DoC). These diagrams describe the lifecycle of the blocks, showing what states they go through and what are the triggering conditions for changing states (**4**).

Afterwards, a block definition diagram with variables was created (**5**). Variables offer a way to evaluate the performance of the system with provided data. Finally, using the variables and elements from the other diagrams, a sequence diagram (sd) for each of the core blocks of the system was created. These sd's allow checking the sequence of actions of the process, and how these actions affect the system and in what way they affect it (**6**).

This stage of the methodology is shown in Figure 4.

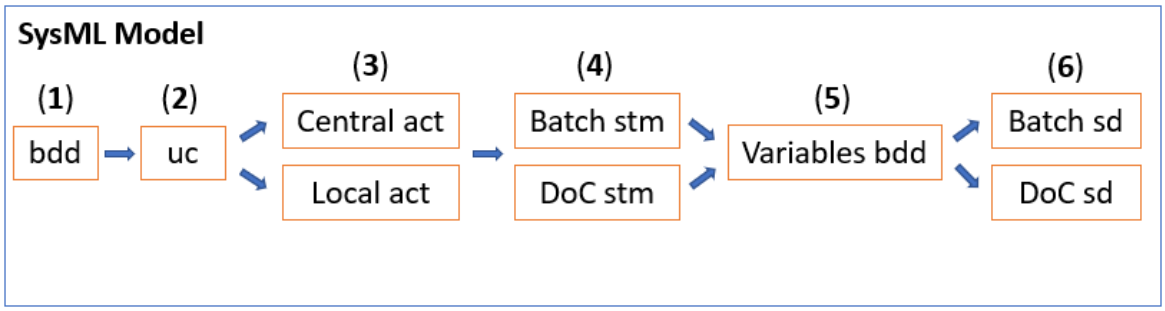

Figure 4 - The diagrams used in the project and the sequence they were created.

Blockchain Transition

Pairing elements from both software models showed several resemblances. This made the transition from one model to the other very smooth and transparent.

The actors in SysML correspond to the main entities who interact with and influence the system through their actions [13] [14] [15]. This is very similar to the role of the participants in IBM Blockchain Platform, who are the business members that own assets in the system and can submit transactions that alter the system [19].

The core blocks in SysML are the main structural elements of the system, and where the process is built around of. These undergo several states during its lifecycle (detailed in the stm's) which change depending on the triggered event that happens during a process [13] [14] [15]. The assets in IBM Blockchain Platform are the goods or possessions being transacted from one participant to another within the system [19].

Events are the triggers for a block state change in a SysML model [13] [14] [15]. Transactions are the procedures, in IBM Blockchain Platform, that make an asset change ownership when certain criteria are met [19].

With its elements being very similar, the conversion of the SysML model to a Blockchain Model File was made, with the main actors becoming the participants, the core blocks becoming the assets and the events becoming the transactions. This conversion was made using the Hyperledger Composer Playground provided by the IBM Blockchain Platform [19]. Figure 5 illustrates this transition.

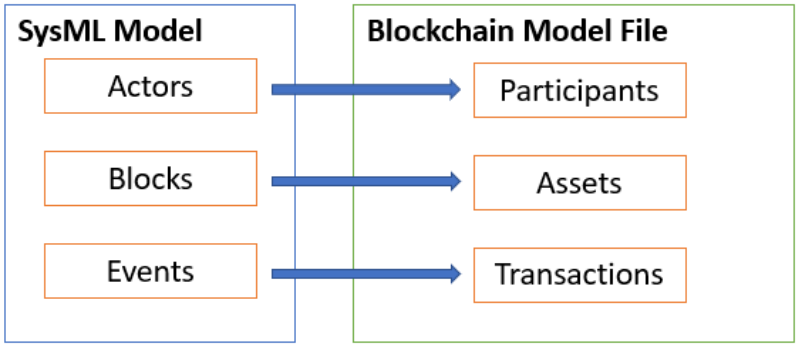

Figure 5 - How the SysML and Blockchain model file elements were connected to each other

Results & Discussion

Model Background

To find what makes a Batch Release and to help clarify what are the problem symptoms the Company is currently dealing with, there were eight meetings with the Company and one visit to the Pre-Wholesaler's installations. These meetings resulted in several remarks about the Company's Batch Release Process:

- The Batch Release Process is a complex stage in the Company's supply chain, and there is no reference model which details the process steps and entities involved;
- There are two types of Batch Release: a central release which takes nine days and a local one which takes five days;
- The Pre-Wholesaler has one day, established by contract, since the arrival of the truck carrying the shipments to register the batches in one of the Company's software;
- During the Batch Release there are two types of quality verification, one related to the quality of the product itself, and the other associated with the documentation about the product. Both the product and its documentation are always in constant update and need to comply with the

Company's quality requirements and government regulations, which are different depending of the importing country;

- The value of the batches waiting to be released is approximately 5M €, meaning this is a big concern for the Company;
- There are several software platforms being used by the Company in different steps of the Batch Release process, from which three of them the time logs can be obtained.

SysML Model

Having in consideration the background remarks, a SysML model composed of nine diagrams was created, resulting in some observations about the Company batch release process being made:

- The Pre-Wholesaler's warehouse is taking three days to perform the batch verification, not meeting the agreement to complete this task in one day;
- The central batch release process takes three days more than the local one, due to the need of a DoC review performed by the QPEU;
- There is only information about the number of rejected batches and not how many faults were found and by whom, meaning there's no way to check the actual need for each step, because each actor's actual effectiveness is unknown.

Blockchain Model

Using the SysML model as the base architecture, a Blockchain business model file (.cto) was built in Hyperledger Composer Playground and tested by creating a sample population, resulting in multiple observations:

- ### Participants
  - The participants are the entities within the Company's actors which submit transactions in the batch release process Blockchain business network;
  - These were modeled after the main actors of the batch release process SysML model;
  - These are the only entities with access to the Blockchain business network records and can submit transactions, although, if required, this can be altered.
- ### Assets
  - The assets were modeled after the Batch and DoC, the core blocks defined in the SysML model and the elements on which the batch release process is centered;
  - The attributes BatchState and DoCState were modeled after the states represented the respective state machine diagrams;
  - If required by the Company, more attributes can be added to the assets. The transactions change the state of each of the assets, the Batch and DoC, and were modeled after the triggers represented in the respective state machine diagrams;
- ### Transactions
  - These can only be submitted by valid participants in the batch release process Blockchain business network;

- In order for transactions to work properly, a Script file (.js) with all the requirements must be created,
- The period of each stage of the batch release process can be accurately measured by checking the interval between timestamps of the corresponding transactions.

➢ Testing

- Testing shows that the model file asset and participant creation work as planned, because the sample population was successfully created as intended;
- There is no way of verifying the transaction submission as this would require the Script file (.js) to be implemented.

Discussion & Future Work

The SysML model showed the several delays points of batch release process, including some unexpected by the Company, like the delay in the Pre-wholesaler. To improve the accuracy of this model, more details about the process are required, like the number of deviations found. Data like this will allow the drawing of a graph showing the behavior over time for each of the Variable blocks. These graphs help provide a better evaluation of the current situation of the Company. This is done with the creation of performance KPI's using the Variables data as inputs. For example, using the variables *Deviations Found* and *Deviations Found by QPEU* as inputs, a KPI for the effectiveness of the QPEU can be created, which provides the percentage of defective batches found by this actor. These KPI's allow the Company to act according to the behavior observed, to improve the system performance.

To provide accurate data for input to the Variables, the Blockchain model file could be implemented alongside the current Company software. This would require the other complementary Blockchain business architecture files in order for it to work properly. The Script file (.js), which contains the system requirements that allow the model file to work, and the Access Control file (.acl) which dictates the access permission to the system, preventing unauthorized personnel to alter or access the information contained within the files. When implemented, the complete Blockchain application provides the Company with precise real-time data obtained from the other software currently in use.

The Blockchain model file testing shows promising results, as each of the elements of the population was created the way it was pretended, in conformity with the SysML model of the batch release process. If for any valid reason, new information or parameters are required to add to the model, this is possible by erasing the former component, altering the model file, and creating the new component with the updated information. The Blockchain will record all these changes however, including the erasing or creation of a new asset or altering the model file.

Conclusion

Developing the Blockchain business architecture foundation for the Company's batch release process is the first step for coping with the delay points within the system. This architecture could only be built by having deep understanding of how the process works, which was accomplished with the creation of a SysML model of the system. This model was build using the information and data provided by the Company, during the several meetings held.

The SysML model showed multiple delay points detected in the system, including some unexpected by the Company (such as a delay in the Pre-Wholesaler's Warehouse), and how long these delays were. The model also worked as the framework for creating the Model file (.cto) of the Blockchain business architecture. Due to the several common elements shared between the two software, the creation of the Model file in Hyperledger Composer Playground was very smooth.

To complete the implementation of the Blockchain business architecture, two other files are required, the Script (.js) and the Access Control file (.acl). The first describes what are the system requirements for the model file, while the latter states what entities can access or alter the data within the system.

The implementation of a Blockchain platform allows the Company to evaluate its current situation. Using the information obtained from the platform (e.g. the time each process stage takes), the Company can create performance KPI's (e.g. the time the warehouse takes to perform its tasks) that allow it to take action according to the performance observed (e.g. replacing the Pre-Wholesaler). It will also allow the Company to verify if redundant steps (e.g. DoC review by the QPEU) are required in the batch release process.

Acting on the source of the delays found in the system will result in reducing the total duration of the batch release process and, consequently, diminish the Company's inventory costs currently estimated at 5M€. If this value is proportional to the duration of the batch release process, making it go from nine to five days (40% reduction) corresponds to over 2M€ savings for the potential value of this project.

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