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Holistic Model-Based Perspective on MedTech-Pharma Interfaces for New Combination Product Development

Yaroslav Menshenin[1], Jude Cancellieri[2], Guillaume Bonnefond[3], Romain Pinquié[1], Pierre Chevrier[1]

[1] Univ. Grenoble Alpes, CNRS, Grenoble INP, G-SCOP, France
[2] BD Medical - Pharmaceutical Systems, Becton Dickinson and Company, Franklin Lakes, NJ, USA
[3] BD Medical - Pharmaceutical Systems, Becton Dickinson and Company, Le Pont-de-Claix, France

Abstract: In today's product development landscape, MedTech combination products are becoming increasingly complex, integrating both software and hardware components. Combination products such as on-body injectors and autoinjectors are designed to assist end-users in administering drugs into the patient's body, enabling controlled drug delivery with a time delay. These products typically consist of two regulated components: the drug, developed by pharmaceutical industry, and the drug delivery system, developed by the MedTech industry. From the MedTech developer's perspective, the innovation process begins under uncertainty due to a lack of, or very limited, information about the drug's parameters. As a result, the MedTech industry must carry out early-stage design activities based on design assumptions. This paper aims to develop a holistic framework for defining MedTech-Pharma interfaces. Such a framework would accelerate innovation across engineering design teams and support faster time-to-market for MedTech product development in collaboration with the pharmaceutical industry.

Keywords: MedTech-Pharma, combination product, systems engineering, MBSE, new product development

1 Introduction

The average global life expectancy in the mid-twentieth century was 49 years old (Dattani et al., 2023). This number has increased significantly over the past few decades. By 2050, more than 2 billion people over the age of 60 are projected to be living on the planet by 2050, which is a drastic increase from 1 billion in 2020 (World Health Organization, 2022). Despite substantial gains in life expectancy over the last century, many challenges remain, as the progression of various diseases is closely linked to aging. Additionally, another crucial factor that must be considered is quality of life.

There is also growing interest in chronic disease management, which may become central to the future of healthcare. Chronic conditions often affect individuals over extended periods, not only during old age. This context creates sustained demand for pharmaceutical products. Pharma's investment in such treatments reflects the industry's strategic shift toward long-term disease management and prevention, while also underscoring the need for MedTech to develop devices that effectively deliver these drugs.

These trends in population ageing and chronic disease management call for significant innovation across the entire healthcare sector, including medical technologies and pharmaceutical developments. This spans from building modern healthcare infrastructure (Reichardt et al., 2012) to developing new drugs (Evans, 2011) and designing advanced medical technologies (Guerineau, 2024) with diverse applications aimed at improving quality of life and preventing global pandemics (Medina et al., 2013). The recent pandemic has revealed hidden potential in accelerating regulatory approvals within this traditionally conservative, "safety-first" principle (FDA, 2021).

This paper primarily focuses on the challenges associated with the design and development of new drug delivery systems (DDS), which serve as the device constituent parts of combination products. The goal is to place such product development within a holistic perspective that integrates the needs of both the MedTech and pharmaceutical industries. One key challenge is that MedTech developers should initiate innovation and early-stage design under uncertainty, often due to a limited or unavailable drug parameters information from pharmaceutical partners. Consequently, the main objective of this work is to address the interfaces between MedTech and Pharma by applying systems engineering approach, supported by the model-based systems engineering (MBSE) paradigm.

This paper argues that systems engineering should play a central role in healthcare research and practice due to its fundamental principles of holism and cross-functional nature, both of which are intrinsic to the discipline. A holistic view is especially important when addressing the challenges posed by chronic conditions, as these have long-term consequences that extend across social, economic, political, and technological dimensions of society. For example, in Germany, the old-age dependency ratio (defined as the number of people of working age, 15-64 years, divided by the number of people of retirement age, over 65 years) increased from 16 retirees per 100 working-age individuals in the mid- twentieth century to 29 at the beginning of the twenty-first century (Christensen et al., 2009). This figure is projected to double by 2050 (Christensen et al., 2009). This would have direct implications for the labor market, social welfare system, and the economy.

This paper emphasizes the use of a Design Structure Matrix (DSM)-based approach (Steward, 1981; Eppinger and Browning, 2012) to analyze the interfaces between the MedTech and pharmaceutical industries. The focus on DSM is relevant, as it is one of the most widely used methods in systems engineering. Its broad applicability across various industries makes it particularly relevant to examine how DSM has been adapted for use in the healthcare sector and what types of problems it has helped address.

This paper is structured as follows: Section 1 presents a global overview and key trends in the healthcare sector from both MedTech and pharmaceutical perspectives. Section 2 provides a literature review on systems engineering, with a particular focus on the application of the DSM to healthcare challenges. Sub-section 2.1 discusses systems engineering and MBSE, while Sub-section 2.2 explores the use of DSM in the healthcare context. Section 3 outlines the research method employed in this study. Section 4 introduces the MedTech-Pharma combination product case study. Sub-section 4.1 provides an overview of the MedTech combination product, and Sub-section 4.2 addresses the complexity of MedTech-Pharma communication during the new product development process. Section 5 presents and discusses the results, and Section 6 concludes the paper by outlining the limitations of the current study and directions for future research.

2 Systems Engineering and DSM in Healthcare Sector

The purpose of this section's literature review is to highlight the state-of-the-art in systems engineering and MBSE within the healthcare and MedTech (Sub-section 2.1) sectors, as well as the application of the Design Structure Matrix (DSM) in healthcare (Sub-section 2.2). The literature review covers the heritage of systems engineering, including MBSE, and explores extensions of DSM-based methods such as the Domain Mapping Matrix (DMM) and Multi-Domain Matrix (MDM) approaches.

2.1 Systems Engineering and MBSE in Healthcare

The absence of a systems approach in the healthcare sector has been recognized in previous research (Komashie and Clarkson, 2016). One contributing factor to the limited application of systems engineering in healthcare is the lack of a unified maps of the healthcare system that clearly positions its various sub-sectors within the broader landscape of health. Even the term 'healthcare system' itself lacks a consistent and universally accepted definition among researchers. In this work, the term ‘health and care system’ is defined as “a collection of people and entities that work together to achieve a defined health or care objective” (Komashie and Clarkson, 2016). The terms “healthcare system” and “health and care system” are used interchangeably throughout the manuscript.

Nevertheless, traces of systems engineering activities can be found in different sub-sectors of healthcare. For instance, in the application of the modeling requirements in hospital information system environment through the system of systems approach (Lahboube et al., 2014). The unified modeling language (UML)-based approach to model the healthcare functions for the Electronic Medical Record (EMR) and Electronic Health Record (EHR) is presented in (Chang et al., 2011). Special place for systems engineering in healthcare is dedicated to the medical device development. Traditional approach was focused on linear device development, however, “...due to the many challenges and complexities associated with medical device design and development, a smooth development path rarely occurs”, which calls for a more iterative design process (Shluzas et al., 2009; Pietzsch et al., 2009; Glazkova et al., 2022). Such a transition requires a careful exploration of where the iterative process brings advantage, as the agile-stage-gate practice for manufacturers has shown its utility when the distinction between where the designers are in the product development process is clearly made (Cooper and Fürst, 2020). This means that the iterative process is beneficial between the decision gates. Yet, those decision points should still be present. The integration of systems engineering and agile to smart medical device development has been studied in the previous works (Guerineau, 2024). The MedTech-related software development through Simulink (Hoadley, 2010) enlarged the scope of systems engineering applications to healthcare. Those studies represent various discussions around the need for agility and systems approach in the healthcare sector, tackling different systems, products and application areas, but lacking such products as the MedTech-Pharma related ones.

The MBSE as an instrument to perform the systems engineering activities was applied to tackle the MedTech-related case studies. For instance, system modeling language (SysML) was used to couple the requirements to functions and physical architecture for the drug delivery system (Corns and Gibson, 2012). In that work the structure of the system of interest (drug delivery system) has been explored in-depth, limiting the holistic perspective to zoom-out the solution and to consider it in the context of the combination product, where such entities as drug itself and pharmaceutical company are present. The application of the MBSE approach to building the system model of the bioanalytical devices was studied in (Evin and Uludağ, 2020). The authors presented the approach to progress from the problem definition to the context definition to the system requirements definition, followed by the logical decomposition and physical decomposition. In (Malins et al., 2015) the authors have focused on the ISO standard for application of risk management to medical devices (ISO 14971:2019) to analyze the safety and risk management of the MedTech devices. Engaging the SysML and Business Process Modeling Notation (BPMN), the researchers applied MBSE to the critical requirements for the healthcare-oriented cyber-physical systems, in which human concerns are of special importance (Kotronis et al., 2019). Such application

allowed researchers to adhere human concerns, as well as "derive system criticalities from human concerns" (Kotronis et al., 2019). However, systems engineering was applied in a limited way to the MedTech-Pharma product development challenges, lacking holistic approach to the entire sector of combination products, which is estimated at ~ US$ 165 billion in 2025 (Market.Us, 2025). What remains as the challenge though is to explore the MedTech-Pharma interfaces for new combination product development, as it involves two different industries - medical technologies and pharmaceutical companies.

All those past works, developments and applications of systems engineering and MBSE to healthcare sector pave the way to address the challenges associated with the MedTech-Pharma combination product development, as it is heavily influenced and dependent on the communication and collaboration between the MedTech and pharmaceutical industries.

2.2 DSM in Healthcare

The Design Structure Matrix (DSM) utilizes a simple idea of constructing a table containing rows and columns representing complex systems relationships or organizational interdependencies. Interestingly, what was considered back in 1981 as the engineering design's involvement to accommodate "the specification of many variables which together define a product, how it is made, how it behaves" (Steward, 1981) is still relevant nowadays when the system architecture should be approached systematically. This challenge has even escalated due to increasingly more complex systems and products interwoven between different industries and applications. The significant increase in computational capabilities (Nordhaus, 2007) and the access of a much larger population to technological progress led to the analysis of even more relevant interdependencies today. Despite exceptional progress in generative design (Buonamici et al., 2020) during recent years, there is still a lack of systems and analytical approaches to how to design the product considering the human-systems integration (Boy, 2023; Menshenin and Pinquié, 2024) and the fact that the decision-making process is still facilitated and guided by the human mind. The broken digital engineering thread (Gerhard et al., 2022) only intensifies those issues, as the digital engineering solutions are potentially here to help, yet their practical implementation inherits the need to change the way of thinking, to which the design teams are resistant.

Steward (1981) called the underlying approach the "Design Structure System", which is close to what later happened to the DSM in reality. By adopting and exploiting the method in different industrial contexts and real-world applications, the DSM became the system itself, with its interconnections and entities. In this regard, the DSM has been significantly advanced and extended as the method, covering different applications in product architecture, process architecture, organization architecture, and multidomain architecture (Eppinger and Browning, 2012). Moreover, the DSM has been extended to map different system entities to each other through the Domain Mapping Matrix (DMM), which was formally defined as a "matrix-based approach, used to map between two different project domains" (Danilovich and Browning, 2007; Danilovich and Browning, 2004); while the Multi-Domain Matrix (MDM) allowed the domain mappings across DSMs and DMMs (Maurer, 2007; Lindemann et al., 2008). These research works made the DSM a system, as they extended the scope of its applicability not only to the specific industrial sectors but also to the community's understanding and practice regarding what can be done using DSM-based methods.

As one concrete example of the industry exploiting the DSM approach, the DSM-based methods were used in the automotive industry at various levels of system architecture – ranging from the entire system level to individual components. For example, the DSM was used to evaluate the strategy for CO2 emissions reduction (Schmidt et al., 2014). It was also utilized for the reliability systems method applied to a commercial truck (Lindén et al., 2015). The analysis of enterprise architecture data from commercial vehicle manufacturers, as studied by (Santana et al., 2016), led to the development of so-called diagnosis analysis approach, which can confirm the importance of the components and suggest other subsystems for further analysis. The automotive perspective is relevant because, unlike new product development in the healthcare sector, the automotive sector tends to favor co-design between partners. This approach assumes that a collaboration agreement is previously established. Successive waves of outsourcing have necessitated the ability to collaborate with suppliers and subcontractors possess know-how that manufacturers no longer have. The automotive industry is also well-known for its product development approaches, such as the Toyota Production Development System (Morgan and Liker, 2006).

Concerning the healthcare sector, the DSM-based methods have been used in various applications. The DSM and MDM applications to the exterior design process of a healthcare facility were studied in (Reichardt et al., 2012). In (Menshenin et al., 2023), the authors used DSM to define the role of the system architect in the early innovation phase of the MedTech new product development process. The matrix was used to encode the core activities at the "fuzzy front end" of innovation and to trace those activities to different functions within the MedTech company. The Swedish multi-project environment, such as healthcare organizations, has been studied to develop a new methodology for managing large-scale healthcare projects, such as digital patient journals (Grönevall and Danilovic, 2014). The enterprise-level research efforts with the DSM-based methods were also used for risk management activities, focusing on supporting auditors of global infrastructure projects (Dister et al., 2015). Software-based methods, such as the Agile approach to team collaboration, were introduced to analyze common patterns in cross-functional collaboration in microtiter plate development and propose

improvement measures (Schweigert-Recksiek et al., 2020). DSM has also been paired with other methods, such as “net benefit” from medicine, to engage both quantitative and qualitative criteria (Solberg et al., 2023).

The summary of the literature on the DSM-based applications demonstrates the wide spectrum of the method's application to different sectors, including healthcare. However, to the best of authors' knowledge, the DSM methods were not applied to the design challenges related to the MedTech-Pharma combination product development. Above there is a discussion regarding the lack of system approach and system models in the healthcare sector. Such a system model could, in the first place, approach the entire sector from the “holistic” perspective to clearly define the key actors and their interrelations. This would enable the establishment of proper interfaces and relationships between, for example, the pharmaceutical industry, MedTech providers, regulators, and hospitals, to name a few.

To perform systems engineering activities in a MedTech-Pharma holistic view, the role of system architect/systems engineer should be clearly defined in the context of MedTech-Pharma combination product. The previous work of the authors proposed the role of system architect within the MedTech organization (Menshenin et al., 2023). A similar approach should be undertaken to map the responsibilities and roles within the pharma company, especially within its device development teams, which are responsible for the communication with the MedTech partners.

In current work, the DMM is used to map the interfaces between the MedTech and pharma industries within the MBSE environment. The focus is on defining the core interfaces to support communication between both industries.

3 Research Method

The first step in the research method is to define interfaces critically important for the design and development of the drug delivery system as part of the combination product. Such interfaces are built in the MBSE environment to support the traceability of the core design inputs. The next step is encoding the interfaces-related data into the MBSE environment, particularly, in the block definition diagram of the SysML model in CATIA Magic software to be discussed later in Section 4. After this the traceability matrix is generated to trace the interfaces to the specific industry (either MedTech or pharma) which is responsible for providing the information on that interface to the partner. The purpose of those steps is not only technical, but also communication and collaboration: aligning engineering design teams within the specific industry (such as MedTech), and across the participating industries (such as MedTech and pharma) is a challenging, but necessary step.

4 MedTech-Pharma Combination Product Case Study

The introduction to the combination product as the result of the MedTech-Pharma interaction is presented in sub-section 4.1. This is followed by the sub-section 4.2 highlighting the complexity in the MedTech-Pharma communication during the new product development.

4.1 MedTech-Pharma Combination Product Introduction

The combination product is a well-established term, backed by the regulators overseeing the industry. The U.S. Food and Drug Administration (FDA) defines combination product as “therapeutic and diagnostic products that combine drugs, devices, and/or biological products” (FDA, 2019). There are different types of combination products, one of which is a drug/device that are both provided as individual constituent parts within the same package. This view is aligned with the European Medicines Agency (EMA) terminology referring “devices intended to administer a medicinal product, where the device and the medicinal product are placed on the market in such a way that they form a single integral product intended exclusively for use in the given combination and which is not reusable” (EMEA, 2021). Each of those constituent parts of the combination product (drug and device) is designed and developed by different industries - pharmaceutical and MedTech, respectively.

The examples of drug/device combination product are an on-body injector or autoinjector, storing the drug to be injected in the patient's body. Nowadays those products are becoming more and more complex, as they possess different capabilities enabled by technological advancements. Among those capabilities are embedded software, allowing a controlled drug delivery with a time delay; connected devices interfacing the product with a larger systems and environment; and traceability of drug delivery systems, to name a few. For the illustrative purpose within this paper, the imaginary drug delivery system (DDS) is explored. Such DDS is aimed at delivering a drug into the patient’s body with a time delay. The on-body injector can be placed on the patient's body and filled with drug by the healthcare professional in a hospital environment to enable an automatically run drug delivery by the system in a home environment hours after the on-body injector's placement at the hospital. This allows a safe drug delivery process without a need for the patient to return to the healthcare facility after the main treatment is completed. This also brings benefits to the healthcare systems funding sustainability: switching the drug delivery process from the hospital environment to the home environment is a key aspect to control overall healthcare costs for the society in a long term.

The harmonization of product development practices is a mutual interest for both industries - MedTech and pharma. We believe that such harmonization could be achieved through the holistic approach, which is well-known and well-practiced in systems engineering. For the MedTech industry developing the device constituent part of combination product, it is essential to understand the expectations of the pharma company, including drug parameters and other relevant specifications. For the pharmaceutical industry, the ability to provide the required data helps limit the potential delays in the product-to-market strategy. Even considering the pharma's preference having multiple suppliers of the device parts of combination products, supporting MedTech providers with sufficient inputs increases the likelihood of those device manufacturers to provide the right products on time.

Both industries, in the end, need to improve practices to satisfy the patient's needs. This goal is complicated due to a nature of the combination products which become more and more complex, as it is mentioned above in the description of the running case study. Considering an increasing complexity of the combination products landscape, the definitions of critical Design Inputs (such as needs, system requirements) should be made within a quality framework compliant with (ISO 13485:2016; 21 CFR Part 820). Therefore, it becomes critically important to enable the interface management and to establish the relationships between MedTech and pharma industries. In this paper the DSM and MBSE methods are purposefully exploited to suit those purposes.

Figure 1 represents a high-level combination product development system map, built in one of the MBSE tools - Dassault Systèmes CATIA Magic Cyber Systems Engineer software. The choice of the MBSE environment should be discussed between the respective partners in the MedTech and pharmaceutical industries. Whether the solution is Siemens-based, Dassault Systèmes-based, or IBM-based is not as critical. What is critical is the harmonization of this approach across respective partners, following the same logic and employing systems thinking approach.

As mentioned in the beginning of the manuscript, the examples of the combination products could be an on-body injector or autoinjector, with the drug inside the DDS. The DDS is a device constituent part of combination product, which is developed by MedTech. The function of such system is "Inject drug" (see the lower left part of Figure 1). The drug part of combination product is the second constituent of the combination product (see the lower right part of Figure 1). The drug part of the combination product is developed by pharma. The function of drug is "Treat disease". Eventually, in achieving the stated goal of injecting drug to treat disease, both patient and healthcare professional utilize the combination product. The combination product is exactly a product which the end-user purchases/receives in pharmacy, or which is stored in the healthcare facility. This underscores the critical importance of establishing clear interfaces between the drug developer (Pharma) and the device manufacturer (MedTech) to ensure the combination product is used safely and effectively by the end-user. While Pharma holds ultimate responsibility for regulatory approval, market launch, and post-market support of the combination product, MedTech's deep understanding of the device is essential for addressing technical issues and ensuring proper use which makes close collaboration between the two parties vital.

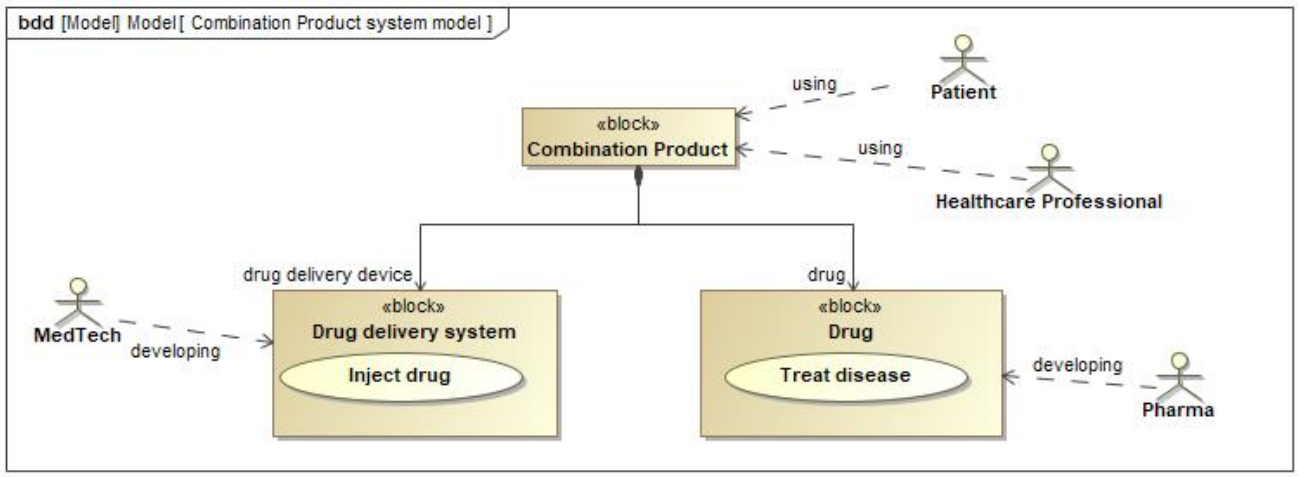

Figure 1. System Model: Combination Product comprising the drug delivery system (MedTech) and drug (pharma).

4.2 Complexity in the MedTech-Pharma Communication

Device developers and pharmaceutical companies must establish clear expectations regarding the information they need to share to ensure that combination drug-device products perform effectively for patients. Device companies typically possess extensive experience in research and development, as well as manufacturing capabilities, which enable them to create complex devices. On the other hand, pharmaceutical companies vary greatly in size and resources. Large, established firms may have well-known assets they wish to incorporate into devices or may seek platforms for early-stage or future drugs. However, they might be reluctant to share proprietary information with device developers due to competitive concerns. Similarly, device developers may hesitate to disclose too much, fearing that pharmaceutical

companies with their own device teams could gain a competitive edge. Smaller drug developers, often led by scientists and clinicians with limited experience in medical device development area of R&D, Quality or Regulatory Standards applicable to medical devices, may have only one or two drugs in their pipeline and lack in-house device expertise. They often focus on niche markets, such as orphan diseases and specialized treatments, leveraging their scientific expertise to drive innovation on molecule development. This imbalance in knowledge and capabilities related to current state of the art in devices highlights the need for strong collaboration to ensure both sides are aligned, fostering smoother and more efficient development processes.

Establishing clear expectations offers several benefits, including enhanced communication, streamlined development timelines, and improved product quality. By clearly defining the information to be shared, both parties can avoid misunderstandings and ensure that all necessary data is available. This transparency can lead to more efficient problem-solving and innovation, ultimately benefiting patients with better and safer products. However, information-sharing is not without risks. Both sides may fear that confidential data could be misused or exposed, jeopardizing their competitive standing. Additionally, negotiating these expectations can be time-intensive and require ongoing effort to build and maintain trust. Despite these challenges, the advantages of open, structured communication often outweigh the risks, paving the way for more successful and innovative drug-device combination products.

Understanding the relationships between functional parameters is crucial for both device developers and pharmaceutical companies to ensure that the combination drug-device product performs as intended. Functional parameters, such as dosage delivery, device mechanics, and patient usability, must be aligned to achieve optimal therapeutic outcomes. By comprehensively analyzing these parameters, both parties can identify potential issues early in the development process and implement necessary adjustments to enhance product performance. This collaborative approach helps in mitigating risks, improving safety, and ensuring regulatory compliance, ultimately leading to more effective and reliable combination products. Clear communication and mutual understanding of these functional relationships are essential for successful integration of drug and device components, fostering innovation and improving patient care.

Figure 2 proposes and encodes the generic interfaces for the DDS, enabling the communication between medical device developers and pharmaceutical companies. Those interfaces are established in collaboration with the domain experts in the MedTech sector. For this, the block definition diagram of SysML profile in CATIA Magic is utilized.

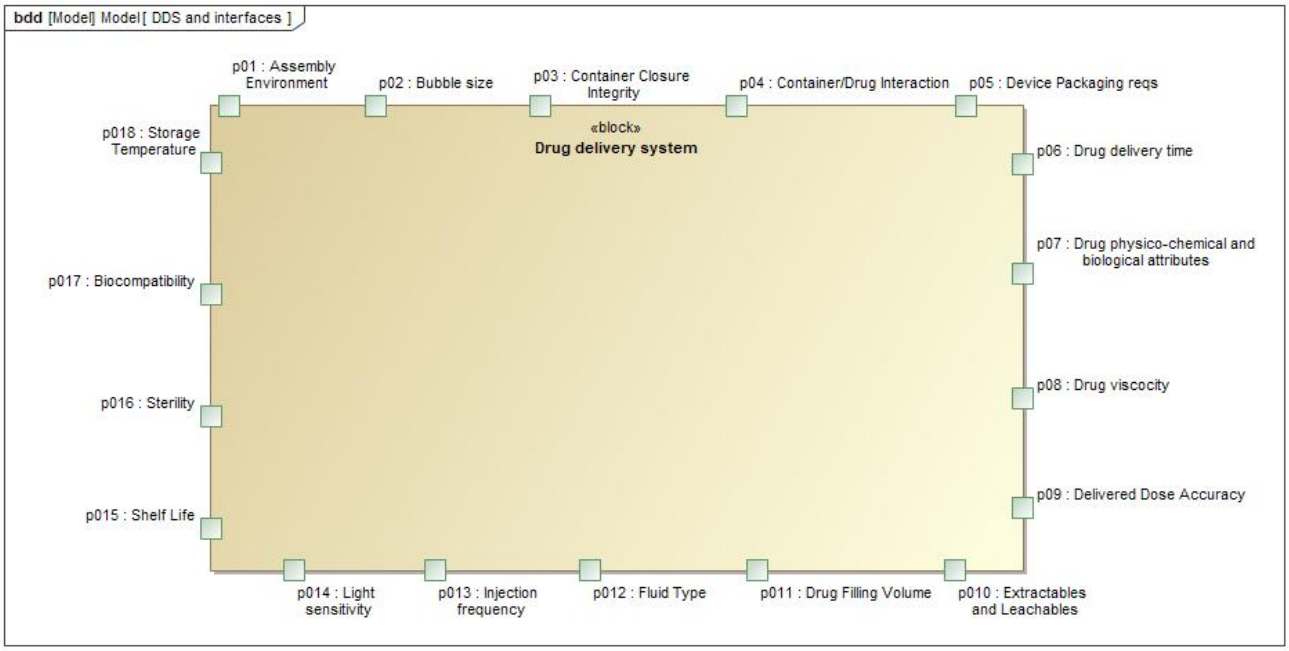

Figure 2. Interfaces establishment on drug delivery system.

In total, 18 generic interfaces were defined and encoded in Figure 2. The establishment of the interfaces in the MBSE environment leads to the definition of the responsibilities between MedTech and pharma functions. Such flows are represented in Figure 3 where the arrows illustrate which specific industry (MedTech or pharma) is responsible for providing which specific interface. For instance, the "Assembly Environment" interface is provided by MedTech to pharma; whereas the "Bubble size" interface is provided from the pharma to MedTech. In practice, MedTech likely develops their system with assumption around the nominal values and expected variation for both "Assembly Environment" and "Bubble size". Discussions around these parameters aim to drive conversations about alignment with pharma's (or their partners') capabilities and the impact of deviations on device performance.

The utility of the MBSE lies in the traceability of the interfaces defined in Figure 2 to the DMM-type of matrix represented in Figure 3. If the digital thread across MedTech and pharma industries is properly established, the DDS could be designed more efficiently, being supported by the iterative nature of the process as well. The interfaces to be provided from the MedTech side are to be primarily gathered by systems architect/systems engineer (Menshenin et al., 2023) in the R&D of the MedTech industry. This role has to communicate with the so-called device development teams, which are usually present in the pharma companies. Therefore, the establishment of the matrices as the one presented in Figure 3 would not only support the definition of the interfaces, but also allocation of the roles within the respective industries.

In practice, none of the interfaces work in isolation. The responsibility for the final combination product typically falls on the pharma company, as they are accountable for ensuring the product meets regulatory standards. For example, a MedTech provider may determine what maximum bubble size would keep the dose accuracy results within specific range. However, if the pharma partner's fill/stoppering process cannot achieve that range, the pharma company will likely request the MedTech partner to conduct a feasibility assessment to alter the design to accommodate.

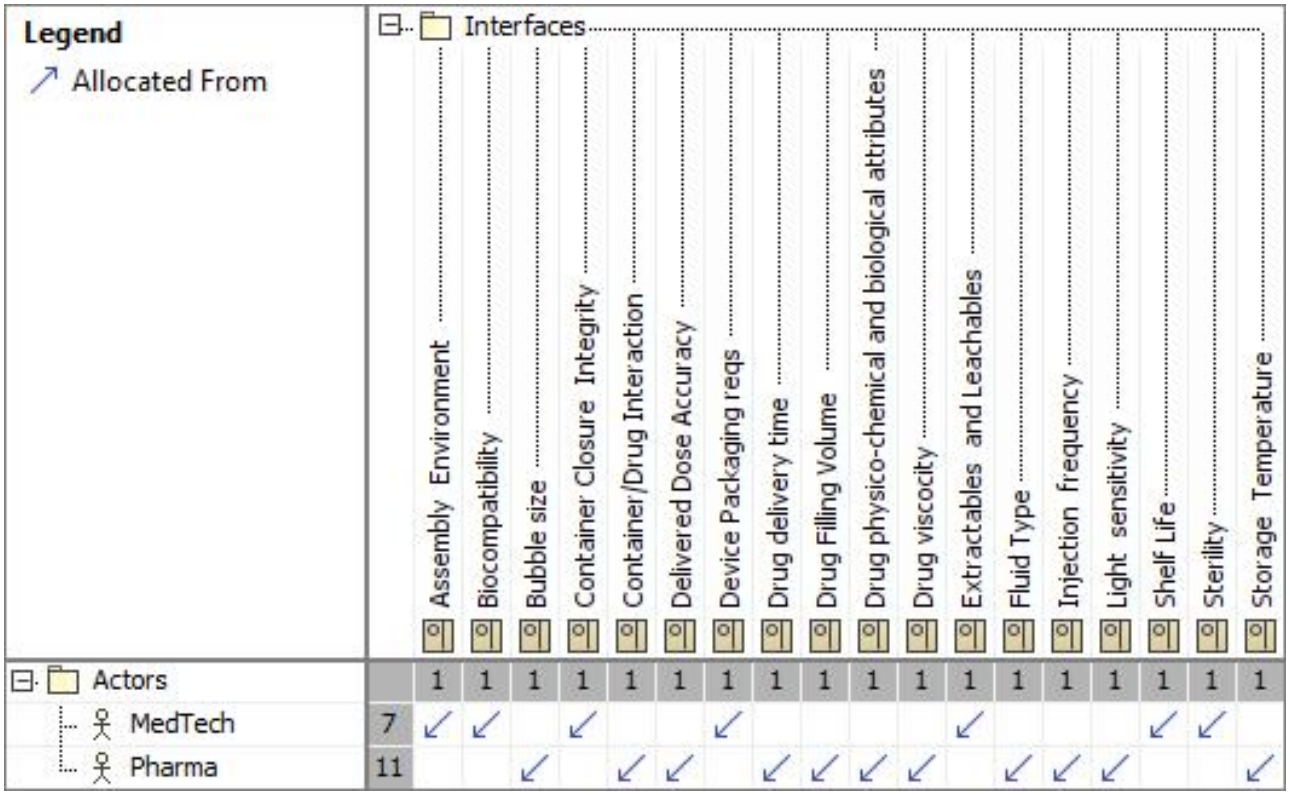

Figure 3. Establishment of the interfaces and the roles between MedTech and pharma industries.

5 Discussion

This work highlights the need for a structured systems engineering approach, supported by the MBSE solutions, to define the functions of combination products by decomposing them into two intrinsic subsystems: the device constituent part and the drug itself, each with its respective functional definition. For example, the drug delivery system (DDS) has the function "Inject drug", while the drug performs the function "Treat disease". Advancing toward interface definition, the systems architect or systems engineer should identify and define the core interfaces that need to be clarified and fulfilled in collaboration with the device development teams in pharma. Clear interface definition may serve as a framework for formalizing the collaboration agreement between MedTech and pharmaceutical partners, creating value for both parties involved in combination product development.

Therefore, we argue that a holistic approach is equally essential in the pharmaceutical industry to foster better integration and harmonization of practices, ultimately increasing the likelihood of improving time-to-market strategies. The value of this work is illustrated through a specific case study, namely, an imaginary on-body injector with delayed drug injection. The benefits of adopting a holistic system engineering perspective can be observed from multiple angles. For instance, a significant advantage lies in promoting the sustainability of healthcare system funding. Shifting drug delivery from hospital settings to home environments is a key step toward long-term control of overall healthcare costs at the societal level.

The MBSE approach is becoming increasingly instrumental in the development of MedTech-Pharma combination products. Within an MBSE environment, interface models are created and integrated into a Domain Mapping Matrix (DMM) type of DSM-based representation. This shift towards the model-based approach highlights a significant difference comparing to traditional document-based approaches, in which design information is often stored in Word or Excel files. While such conventional methods remain widespread, they limit teams' capabilities in tracking design changes and tracing design solutions throughout the product lifecycle.

It is also important to note that the same methodological approach should be applied at subsequent levels of interfaces between MedTech and pharmaceutical partner, as well as within the respective industry. Thus, work performed at the system level does not conclude the overall process of interface definition; rather it lays the foundation for sustainable, harmonized collaboration and communication across and within industries.

6 Conclusion

Several macro-trends are contributing to the growing importance of healthcare in society. One of the most significant is population ageing, which increases the need for effective drugs and drug delivery mechanisms over extended periods. Additionally, there is a rising emphasis on chronic disease management, which may become central to the future of healthcare. Chronic conditions often affect individuals over long periods, generating sustained demand for pharmaceutical products. More importantly, effective treatment of these diseases can slow or even prevent progression to more severe stages, which are typically more expensive to manage and carry greater health risks as patients get older. Pharmaceutical investment in such treatments highlights the industry's strategic shift toward long-term disease management and prevention, which will require collaboration with MedTech companies to develop devices for effective drug delivery.

MedTech products such as the combination products discussed in this manuscript are co-developed by two industries: MedTech and Pharma. While both can be considered under healthcare umbrella, their day-to-day focus differs. MedTech manufacturers primarily concentrate on the device constituent parts, whereas pharmaceutical companies focus on drug development. Since the final product must function as an integrated whole to deliver value to the end-user (patient), establishing and managing interfaces between MedTech and Pharma becomes a critical task. However, this remains a largely unexplored area from systems engineering perspective.

This paper examines the MedTech-Pharma combination product development process through the lens of systems engineering, supported by the MBSE environment. The choice of systems engineering and specifically the DSM method is motivated by the principle of holism, which is critical in the context of combination product development. As discussed throughout the manuscript, this development requires the integration of paradigms from both the MedTech and pharmaceutical industries. These two industries collaborate to develop a final combination product intended for end-users such as healthcare professionals, caregivers, and patients. However, their development processes are often not well aligned (Menshenin et al., 2023), resulting in the need for MedTech developers to design drug delivery systems under significant uncertainty regarding to the final specifications of the drug, which will be later integrated into the DDS to form the complete combination product.

Future work will focus on analyzing the next layer of roles responsible for managing specific interfaces within each of the two industries involved in combination product development - MedTech and Pharma. Ultimately, the authors believe that the proposed approach serves not only as a tool to support the technical development of combination products but also as a means to facilitate effective communication so much needed within the respective industry, be it MedTech or Pharma; or across both industries.

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Contact: Y. Menshenin, Univ. Grenoble Alpes, CNRS, Grenoble INP, G-SCOP, 46 Av. Félix Viallet, 38031 Grenoble, France, +33 7 66 899 507, yaroslav.menshenin@grenoble-inp.fr