Towards Computer Assisted Compliance Assessment in the Development of Software as a Medical Device

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Abstract: Medical devices (MDs) and Software as a Medical Device (SaMD) are essential for e-Health applications, but they must comply with strict standards and regulations to ensure their safety and effectiveness. However, there is a lack of tools to assist in conducting appraisals for compliance assessment and managing appraisal information. In this paper, after reviewing the most relevant standards and regulations for MD and SaMD certification, we propose a web platform to help technology companies that lack expertise in developing SaMD to create compliant and high-quality products for the e-Health market. The platform provides users with custom checklists or questionnaires depending on the selected regulations, standards, risk classes, and product parameters. Supporting a secure, incremental, and collaborative approach to completing the assessment process, the platform enables the attachment of notes, evidence, and improvement suggestions. It facilitates repeated assessments over time for data reuse and comparative analysis, enhancing the assessment process's efficiency and effectiveness.

1 INTRODUCTION

Numerous companies are engaged in the development of various types of software applications. However, when they enter the SaMD market, they often lack sufficient knowledge of the standards and regulations specific to SaMD. Various local and international rules and regulations control the medical device (MD) market. In order for an MD to be sold, it must comply with these regulations. The regulations are complex and strict, making it difficult for small and medium-sized enterprises (SMEs) to gain medical approval for their products.

To meet this challenge, we propose in this paper a web platform to help MD companies achieve compliance for their medical products. The platform will support the implementation of best practices for the development, testing, and validation of MDs and SaMD in the e-Health domain, taking into account regulatory requirements outlined in standards such as IEC 62304 (Jordan, 2006). The goal of this proposal is to create a tool that will help ensure compliance in the development of MDs, specifically software as a medical device (SaMD) (Group, 2019).

The remaining sections of the paper are structured as follows. A brief characterization of the different types of MDs is presented in Section 2. An overview of the standards and regulations for MD and SaMD certification is presented in section 3. Section 4 provides a brief overview of existing compliance assessment tools. A description of the proposed web platform for compliance assessment is provided in section 5. Lastly, section 6 concludes the paper.

2 TYPES OF MDs

An MD can be defined as any instrument, device, software, implant, material, or other article that is intended by the manufacturer to be used for medical purposes in or on the human body (Teferra, 2017). These purposes may include the diagnosis, prevention, monitoring, prediction, prognosis, treatment, or alleviation of disease; the diagnosis, monitoring, treatment, alleviation, or compensation for injury or disability; the investigation, replacement, or modifi-

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cation of the anatomy or physiology; or the provision of information through the examination of specimens.

An Active Medical Device (AMD)(Group, 2019) (IMDRF, 2018) is a type of MD that uses energy to function. AMDs are typically used to diagnose, prevent, monitor, or treat a medical condition or disease. AMDs can be either invasive (meaning they involve some type of penetration into the body) or non-invasive (meaning they do not come into direct contact with the body). Some examples of AMDs include ultrasound machines, x-ray machines, and laser surgery devices. AMDs are regulated by authorities such as the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) to ensure their safety and effectiveness.

An In Vitro Diagnostic Medical Device (IVD) (Group, 2019) is a type of MD used to perform diagnostic tests on samples of bodily fluids or tissues taken from the human body in order to detect diseases, infections, or other conditions. These devices are regulated by government agencies to ensure their accuracy and safety and must comply with the regulations and standards.

Software as Medical Device (SaMD) (Group, 2019) is a type of software that is intended to be used for one or more medical purposes, such as diagnosis, prevention, monitoring, or treatment of a medical condition or disease. SaMD is classified as an MD and includes IVDs. It can be run on general-purpose computing platforms and does not need to be part of a hardware MD in order to perform its intended medical functions. However, if the software's primary purpose is to drive a hardware MD, it is not considered SaMD. SaMD may be used in combination with other products, including MDs, and may be interfaced with other MDs and software. Besides generic regulations for MDs, SaMD is also subject to specific regulations.

3 REGULATIONS FOR MD AND SaMD CERTIFICATION

MDs and SaMD must follow standards that are set by the International Organization for Standardization (ISO) (Heires, 2008) (iso,), the International Electrotechnical Commission (IEC) (iec, b), the European Union regulation bodies (Kramer et al., 2012), the Food and Drug Administration (FDA)., and the International Medical Device Regulators Forum (IMDRF) (Group et al., 2020). These standards are used to ensure the safety and effectiveness of these products.

The International Medical Device Regulators Forum (IMDRF) (Group et al., 2020) is a global organization that brings together MD regulators from around the world to collaborate on the development of international guidelines and standards for the regulation of MDs. The IMDRF was founded in 2011 as a successor to the Global Harmonization Task Force on Medical Devices (GHTF) (Gagliardi, 2009). The organization aims to promote the safety, quality, and performance of MDs by facilitating the development of internationally recognized standards and guidelines for the regulation of MDs.

The applicable standards and regulations for SaMD and MDs are described next.

3.1 EU MDR

The European Union Medical Device Regulation (EU MDR) (Kramer et al., 2012) sets out the rules for the design, production, and performance of MDs in the EU. It replaces the Medical Devices Directive (MDD), which had been in place since 1993. The MDR aims to improve the safety and performance of MDs and to increase transparency and accountability in the MD market.

The EU MDR applies to all MDs that are placed on the EU market, regardless of where they are manufactured. It covers a wide range of products, including everything from simple bandages and tongue depressors to complex diagnostic and therapeutic devices such as pacemakers and MRI machines.

The EU MDR requires MD manufacturers to demonstrate the safety and effectiveness of their products through clinical data and other evidence. It also establishes a new regulatory framework for innovative MDs, including those that use software or rely on digital technologies.

It includes 17 annexes that cover different aspects of MDs (med,), such as: general safety and performance requirements; essential principles of safety and performance; clinical evaluation; classification of MDs; conformity assessment procedures; marking and labeling of MDs; vigilance and market surveillance; registration of manufacturers, authorized representatives, and importers; clinical investigations; transitional provisions; specific requirements for IVDRs; specific rules on the safety and performance of custom-made and investigational MDs, active implantable medical devices, MDs meant to administer medicinal products, MDs meant to be used in contact with blood, body fluids or tissues, MDs meant to be used for dental purposes, and MDs meant to be used for human reproduction.

To help determine if a given product is in the scope of the EU MDR, specific guidance is provided in (Group, 2019), in the form of a decision procedure schematized in Fig. 1.

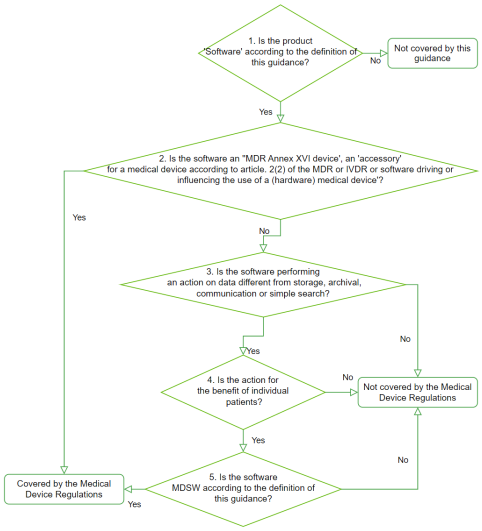

Figure 1: Decision steps to assist qualification of SaMD according to (Group, 2019).

3.2 FDA Regulations

FDA is a federal agency within the United States Department of Health and Human Services (fda,). It is responsible for protecting public health by ensuring the safety, efficacy, and security of human and veterinary drugs, biological products, and MDs.

The FDA's regulation of these products covers the following areas:

- **Premarket Review and Clearance/Approval** - Before a drug, biological product, or MD can be marketed in the U.S., it must go through a premarket review process to ensure that it is safe and effective. The FDA will clear or approve the product depending on the level of risk it poses to patients.
- **Postmarket Surveillance** - After a product is on the market, the FDA will continue to monitor its safety and efficacy through postmarket surveillance. This includes monitoring reports of adverse events and taking action if necessary.
- **Manufacturing and Quality Control** - The FDA sets standards for the manufacturing and quality control of drugs, biological products, and MDs to ensure that they meet certain quality standards.
- **Labeling and Advertising** - The FDA regulates the labeling and advertising of drugs, biological products, and MDs to ensure that they are truthful and not misleading.

3.3 IEC 62304

IEC 62304 is an international standard that provides guidance on the development of medical software. It covers the entire lifecycle of medical software, including design, development, testing, maintenance, and decommissioning. The standard is intended to help organizations ensure that their medical software is safe and effective for use in the healthcare environment.

The standard consists of a number of different sections, each of which covers a specific aspect of medical software development.

The standard mandates organizations to identify and evaluate the risks associated with their medical software, and put in place appropriate controls to manage these risks. The software systems are classified into three categories, Class A, Class B, or Class C, based on their potential impact on patient safety (see Fig. 2). Class A systems pose a minimal risk, Class B pose a moderate risk, and Class C poses a high risk to patients.

The standard also provides guidance on how to plan, design, implement, test, and maintain medical software, and the use of configuration management and change control processes. It also requires organizations to verify and validate their medical software at various stages of the development process and provides guidance on how to maintain and decommission the software when it is no longer needed, including the handling of data and disposal of hardware.

3.4 ISO 14971

ISO 14971 (Teferra, 2017) is an international standard that provides guidance on the application of risk management to the design and development of MDs. It outlines a systematic approach for identifying, evaluating, and mitigating risks associated with the use of MDs. The standard is intended to help manufacturers ensure that their products are safe and effective for their intended use, and to provide a common framework for regulators to evaluate the risk management processes of MD manufacturers.

According to ISO 14971, risks associated with MDs can be classified into several categories, including:

- **Physical Risks** - which relate to the physical properties of the device or its components, and may include risks such as electrical shock, mechanical failure, or chemical exposure.
- **Performance Risks** - which relate to the device's ability to function as intended, and may include

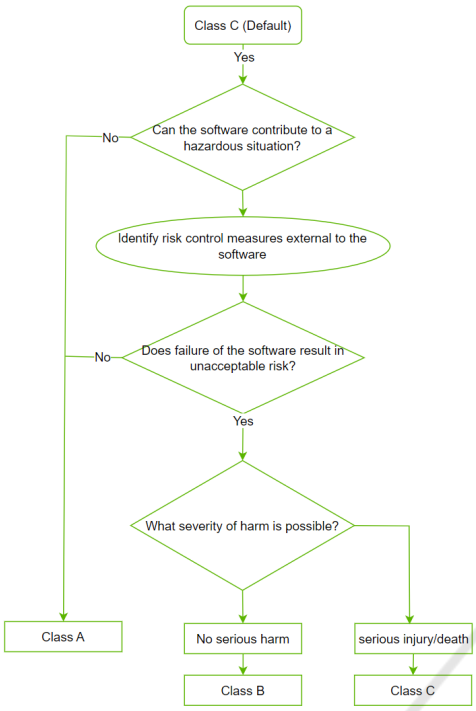

Figure 2: Risk classification according to IEC 62304.

risks such as incorrect diagnosis, incorrect treatment, or inadequate performance.

- **Use-Related Risks** - which relate to the way in which the device is used, and may include risks such as incorrect handling, incorrect maintenance, or incorrect disposal.
- **Human Factors Risks** - which relate to the interaction between the device and its users, and may include risks such as user error, user fatigue, or user confusion.
- **Environmental Risks** - which relate to the external environment in which the device is used, and may include risks such as extreme temperatures, humidity, or radiation.

There are several ways to classify risks based on their likelihood and severity. One common approach is to use a matrix or grid to plot the likelihood and severity of risks, with the resulting quadrants indicating the overall level of risk. For example, a risk might be classified as high likelihood and high severity (a high-risk situation), low likelihood and low severity (a low-risk situation), or anywhere in between.

3.5 ISO 13485

ISO 13485 is an international standard that specifies requirements for a quality management system (QMS) in the design, development, production, installation and servicing of MDs. The standard is intended to help organizations in the MD industry meet the applicable regulatory requirements and to demonstrate their ability to provide MDs and related services that consistently meet customer and applicable regulatory requirements.

The standard is based on the ISO 9001:2015 standard for quality management systems, with additional requirements specific to the MD industry. These include requirements for risk management, design and development, production, installation, and servicing, as well as regulatory and legal compliance.

The ISO 13485 standard is widely recognized and used by MD manufacturers and other organizations around the world as a means of demonstrating their commitment to quality and safety in the design, production, and servicing of MDs. It is also often required by regulatory authorities as a means of demonstrating compliance with relevant regulations and standards (Bos, 2018).

This standard requires the organization to meet a number of requirements specified in it. Organizations must establish, document, implement, maintain, and continuously improve a Quality Management System (QMS) that meets the requirements of the standard. Senior management must demonstrate their commitment to the development and implementation of the QMS and to the continuous improvement of the organization's products and processes. The organization must provide the necessary resources to implement and maintain the QMS, including personnel, infrastructure, and work environment. The organization must plan, develop, produce, and deliver MDs that meet customer and regulatory requirements. They must monitor, measure, and analyze its processes and products to identify opportunities for improvement and take appropriate corrective and preventive actions. The organization must conduct internal audits to verify that the QMS is being effectively implemented and maintained, and senior management must review the QMS at defined intervals to ensure its ongoing suitability, adequacy, and effectiveness.

3.6 In Vitro Diagnostic Regulation (IVDR)

The In Vitro Diagnostic Regulation (IVDR) is a European Union (EU) regulation that sets out the requirements for the design, production, and performance evaluation of IVD. The IVDR applies to all IVDs that are used for the examination of specimens, including blood, tissue, and other substances, taken from the human body for the purpose of providing information for the diagnosis, prevention, monitoring, or

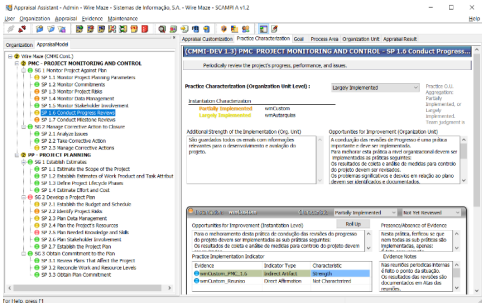

Figure 3: Appraiser Assistant.

prediction of a disease or condition. The regulation aims to ensure the safety, performance, and effectiveness of IVDs, as well as to provide a consistent and harmonized regulatory framework for their marketing and use in the EU. The IVDR replaces the previous In Vitro Diagnostic Directive (IVDD) and came into force on May 26, 2022. Some aspects covered by the IVDR include: risk classification of IVDs; conformity assessment procedures; clinical evidence; labeling and instructions for use; post-market surveillance; registration and listing of IVDs.

In addition to the above standards and regulations, MDs may also be subject to a variety of other national and regional regulations, depending on the country or region in which they are sold(Group, 2019).

4 COMPLIANCE ASSESSMENT RESOURCES

Currently, the only resources available for evaluating e-Health and SaMD products are checklists and desktop applications in related domains, such as Appraisal Assistant (app,) for CMMI (Chrissis et al., 2011). An example screen of this application is demonstrated in Fig. 3. However, these tools can be difficult for SMEs to use effectively when assessing SaMD products, as they must meet strict regulations. The lack of a web platform specifically designed for the e-Health and SaMD domain adds to the challenges faced by these businesses in the product assessment process.

In addition to the checklists and desktop applications mentioned earlier, some websites are available at the time this paper was written that offer consulting services to assist manufacturers of MD and SaMD devices with the assessment process. These websites served as an alternative option for companies seeking guidance and support with the assessment of their devices. To our knowledge, there are currently no web-based platforms available for the evaluation of e-Health and SaMD products.

Some commercial quality management software solutions are also available to aid organizations in the life sciences and medical device sectors in establishing quality management systems that enhance compliance with multiple regulations and standards. However, these solutions are generally not tailored for compliance assessments conducted by manufacturers or third-party entities. Our platform aims to fill this niche - it is designed specifically to facilitate thorough compliance assessments, setting it apart from conventional quality management tools.

5 PROPOSED COMPLIANCE ASSESSMENT PLATFORM

In order to facilitate the compliance assessment of MD and SaMD and the management of assessment information, we propose a web platform with the functionalities summarized in Fig. 4 and described next.

The main goals of the platform are to:

- provide to the user (appraiser) the applicable assessment checklist or questionnaire, depending on the selected regulation or standard, risk class, and other relevant parameters of the product under assessment;
- guide the users in conducting risk assessment and classification of a product under assessment based on relevant decision trees and checklists;
- provide an easily accessible platform for users to answer assessment checklists or questionnaires in a collaborative, secure, and incremental way;
- provide a way for users to attach explanatory notes and evidence to each item or answer so that relevant stakeholders can review them (including auditors in a formal certification process);
- support review and approval workflows;
- provide a way for users to attach improvement proposals to overcome issues identified;
- provide an easy way for users to visualize the overall results of finished assessments;
- allow users to export the assessment results and data to reports generated according to previously defined templates;
- allow users to conduct multiple assessments of the same product over time, possibly reusing data from previous assessments, and easily comparing their results.

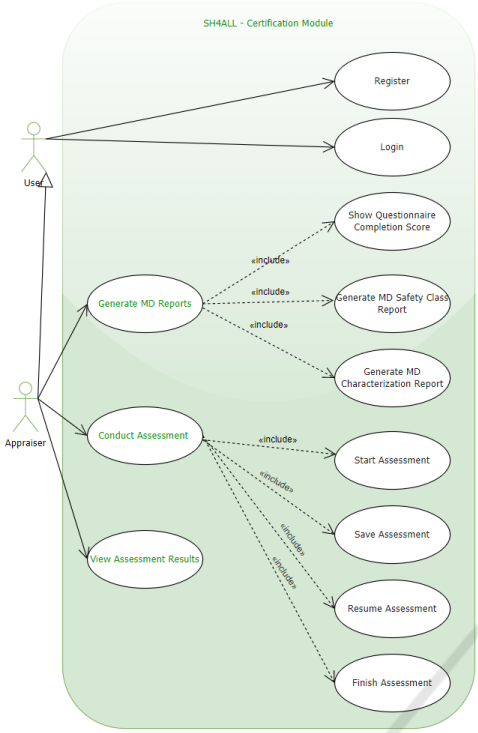

Figure 4: Use Case Diagram of the Proposed Web Platform.

5.1 Functionalities

The users (appraisers) can register and log in to the web platform, where they can conduct assessments after being authenticated. The assessment process can be saved and resumed by the user at a later time, and the module also has an auto-saving function that submits the answers to the questionnaire to the server and saves them in the backend data store. Upon completion of the assessment, the module generates the assessment result and characterizes the MD in a report. It also provides scores for the completion of the total questionnaire and the completion level of each section.

More specifically, the main functionalities provided to the user are:

1. **Register** - In order to be able to access the functionalities provided by the web platform, the user has first to register on the website, with appropriate credentials.
2. **Login** - Once registered in the web platform, the user can log in to the web platform and access the functionalities provided next.
3. **Conduct Assessment** - The appraiser can conduct an assessment by answering the questions of a questionnaire, dependent on a risk classification of the MD or SaMD under analysis.
4. **Start Assessment** - This use case is the first step in conducting an assessment. Appraiser starts answering the question.
5. **Save Assessment** - Since an assessment is rarely concluded in a single session, the user can save the assessment information defined so far.
6. **Resume Assessment** - The user can resume the assessment process.
7. **Finish Assessment** - An appraiser can conclude the assessment process, after answering the questionnaire provided by the system.
8. **Generate MD Report** - After concluding the questionnaire, multiple MD reports can be generated.
9. **View Assessment Result** - The user can see the assessment result.
10. **Show Questionnaire Completion Score** - After concluding a questionnaire, a score is generated indicating the completion level of the questionnaire.
11. **Generate MD Safety Class Report** - This report identifies the safety class of the MD, according to IEC 62304.

In conducting an assessment, the platform offers various features. Initially, only one standard is considered, and it can be extended to support more standards and regulations in the future as per requirements. The process of conducting an assessment begins by choosing a standard from a list of standards, which is illustrated in Fig. 5. The platform also supports multi-session assessment, enabling the appraiser to save progress and continue later. Additionally, multiple assessments for one device are supported. This enables the appraiser to assess their device based on various standards and regulations. On the platform dashboard, a list of the assessments and a summary of the assessments appears. Once the risk level of the MD under analysis is determined, the system presents a checklist with a series of questions for the appraiser to answer. These questions cover sections 4 to 9 of IEC 62304 (iec, a), illustrated in Fig. 6. To ensure the accuracy and completeness of the assessment, the appraiser can provide supportive evidence for each answer. If a question is not applicable, the appraiser can mark it with a comment explaining the reason. After the assessment is completed, the score is computed for each section and the entire assessment and then displayed to the appraiser. The score is shown to the appraisar as it is illustrated in Fig. 7.

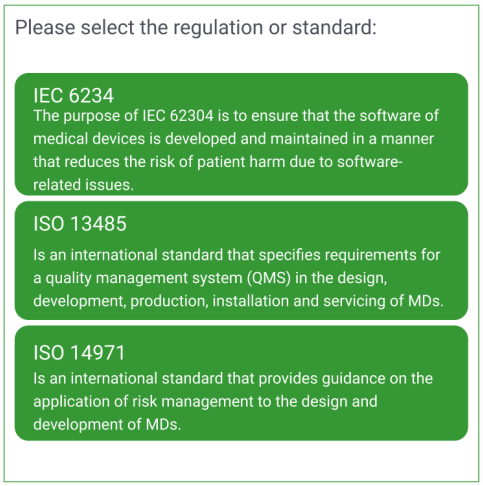

Figure 5: Certification Assessment Assistant, Standard Selection page.

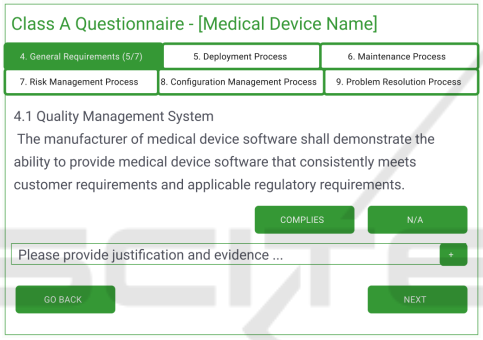

Figure 6: Certification Assessment Assistant, Questionnaire page.

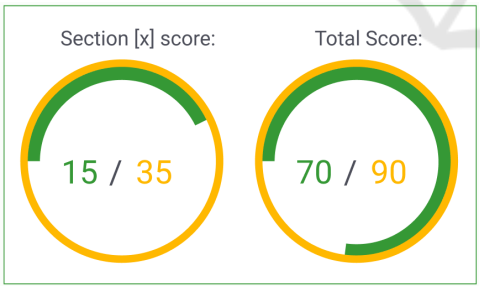

Figure 7: Certification Assessment Assistant, Score Result page.

5.2 Architecture

5.2.1 Frontend

The frontend will be built on Angular [1], an efficient framework for creating sophisticated single-page applications. Splitting a web portal into smaller Angular applications enables agile development and maintenance, independent deployment, and scalable server management.

5.2.2 Backend

To make business capabilities and functionalities accessible to the clients such as mobile and web portals, we will create small RESTful (Richardson and Ruby, 2008) services. These services will be developed using Kotlin (Jemerov and Isakova, 2017) in combination with Springboot (Walls, 2015) (spr,). By using Kotlin and Springboot, we can create lightweight services that clients can easily consume.

Kotlin is a programming language that combines object-oriented and functional programming concepts and is designed to be interoperable, safe, clear, and well-supported by tools. It was originally created for use with the Java Virtual Machine (JVM) (Yellin and Lindholm, 1996) and Android, but can also be used to create applications for JavaScript and native code. Kotlin was developed by JetBrains, the company behind the IntelliJ IDEA (Krochmalski, 2014) [2] development environment, and has been open source since 2012.

6 CONCLUSION AND FUTURE WORK

Before MDs can be released to the market, they must comply with various standards and regulations to ensure their safety and effectiveness. To do this, it is important to identify and assess the potential risks associated with the MD during the development process.

Multiple organizations such as ISO, IEC, and FDA provide guidelines and standards for MD development and certification. MDs are classified according to their usage, life cycle, and risk level, and manufacturers must certify their devices according to these guidelines.

A proposal for a web platform is made to help manufacturers ensure their devices meet the regulations. The initial step in developing an MD is to ensure that it meets the necessary qualifications. This is done by having an appraiser conduct a questionnaire based on the risk class of the device. The questionnaire is designed to evaluate the device's compliance with the relevant standards and regulations, and it serves as the first deliverable software product in the development process. The results of this questionnaire will be used to determine if the device meets the necessary qualifications and can proceed to the next stages of development.

[1] https://angular.io/guide/architecture/

[2] https://www.jetbrains.com/idea/

In future work, a decision tree will be implemented to aid in the classification of the risk associated with the MD. This decision tree will be used as a tool to assist in the identification and assessment of potential risks during the development process and to ensure that the device meets the necessary qualifications and complies with the relevant standards and regulations. Additionally, expanding the platform to support additional standards and regulations in the future, depending on the requirements, is possible.

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