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Regulatory Challenges of Software as a Medical Device

The healthcare industry is witnessing many changes in this digital era. One such trend is in software and its impact on how clinicians practice medicine, how consumers manage their own health, and how patients and healthcare providers interact. In particular, a recent revolutionary development in digital health technology is software that can perform complex medical functions - software as a medical device (SaMD).

In the past, software was simply an ancillary component of a medical device, which was based on hardware. These days, software frequently has a primary role, and in many cases, it is the core of the medical device. As a result, software is becoming more complex and the risk associated with it, compounded. More often than not, it is the main and only component of the device (i.e. SaMD).

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In fact, this is becoming so common that regulatory authorities such as the US FDA and the MHRA in the UK periodically publish guidance documents to assist manufacturers on SaMD's[1] regulatory process.

Alongside this evolution is the software development process which is characterized by a high rate of changes and ease of implementation. Well-known for its comprehensive regulations, stringent quality requirements and market pressure, the medical device industry is at times in conflict with this process.

What is a SaMD exactly?

Software has multiple functions. It can operate as an integral component of a medical device, as a standalone device, or, more recently, as an application on mobile devices. The term Software as a Medical Device is defined by the International Medical Device Regulators Forum (IMDRF) as "software intended to be used for one or more medical purposes that perform these purposes without being part of a hardware medical device.[2]" According to the IMDRF a medical purpose can be, but is not limited to, one or more of the following:

- Diagnosis, prevention, monitoring, treatment or alleviation of disease or an injury
- Supporting or sustaining life
- Providing information by means of in vitro examination of specimens derived from the human body

In addition to this, SaMD relates to both traditional as well as in vitro diagnostic (IVD) medical devices and can be used in many ways in the healthcare environment[3]:

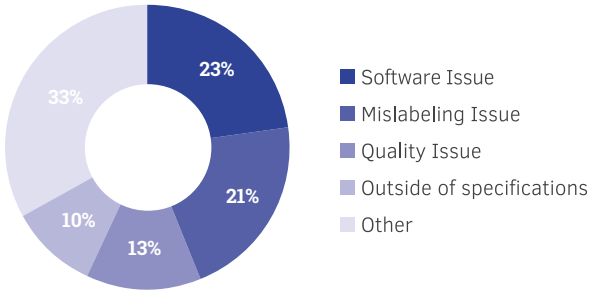
- Hospital Information Systems
- Decision Support Software
- Information Systems
- Communication Systems
- Web systems for monitoring of data
- In vitro diagnostic (IVD) software

It is important to remember that whereas SaMD may be interfaced with other medical devices (e.g. hardware medical devices and other SaMDs), software that is part of a hardware medical device does not meet the definition of Software as a Medical Device.
Here are some examples of what is considered SaMD:

- Software for a medical purpose that operates on a general-purpose computing platform. i.e., a software that uses an accelerometer embedded in a consumer digital camera or mobile phone for diagnosis of a condition
- Mobile medical apps that are used for diabetes management by controlling glucose meters used by an insulin-dependent diabetic patient
- Software that is connected to a hardware medical device, in order to allow additional function of the medical device (but is not needed by that hardware medical device to achieve its originally purpose)

What regulatory challenges do SaMD face?

SaMD is, by far, the biggest driver of all medical device recalls[4]. Why? The more complex the software, the more likely it is that developers do not account for all variables in the clinical environment, increasing the risk of bugs and errors. Manufacturers and regulatory authorities must join forces to minimize this risk. A balance must be struck between constantly testing and validating software and the clinical benefits of using the software.



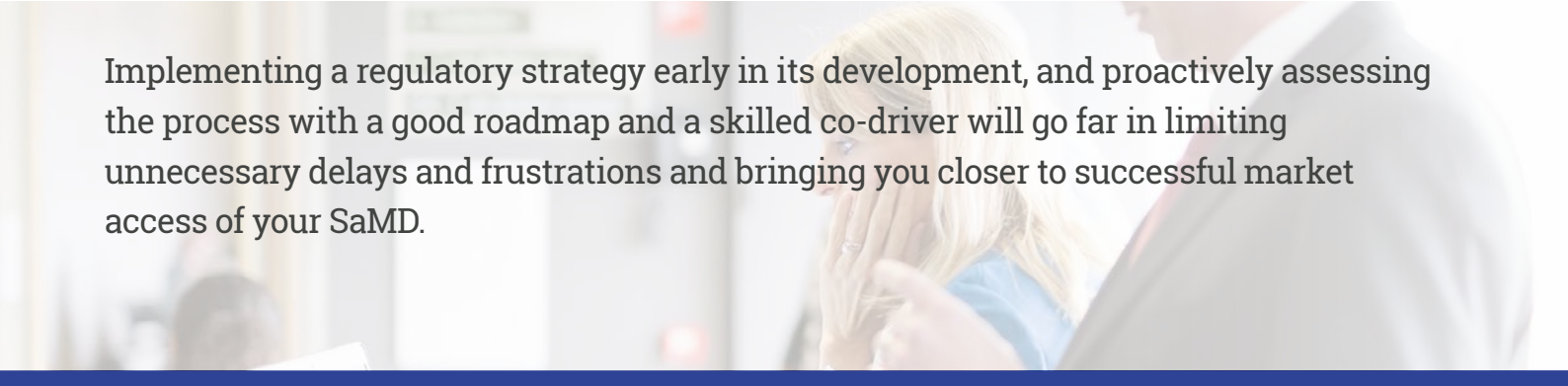
Causes of medical device recalls[4]

Protecting patient safety is top priority. That is why regulatory authorities have defined key principles for manufacturers to adopt when developing a SaMD product:

Risk Categorization and Risk Management

Software classification is based on software safety. In other words, the severity of possible harm to the patient. Software safety classification systems are outlined below:

- The FDA defines the Level of Concern of each software - Major, Moderate, or Minor. The Level of Concern is based on how the operation of the software affects the patient or user, directly or indirectly[5]
- Software can also be divided into three separate classes according to international standard IEC 62304[6] - Class A, Class B, and Class C. EU regulatory authorities accept these classifications.
- IMDRF has defined a SaMD risk categorization framework which is divided into four categories - I, II, III, and IV[7]. These categories are based on the levels of impact on the patient or public health in cases where data provided by the SaMD to treat or diagnose, is crucial to avoid death, long-term disability or other serious deterioration of health. Level IV has the highest impact on the patient or public health and Level I, the lowest.



Implementing a regulatory strategy early in its development, and proactively assessing the process with a good roadmap and a skilled co-driver will go far in limiting unnecessary delays and frustrations and bringing you closer to successful market access of your SaMD.

- Risk Management must play a crucial part in the development of your SaMD, and it is your duty to consider all hazards associated with the product's intended use.

Data Security and Data Privacy

Part of the Risk Management process includes account data security and privacy considerations. A data security and/or privacy risk entails the likelihood of a vulnerability (hazardous situation) being exploited and the likelihood of this vulnerability breach (hazardous situation) leading to exposure of health data in databases and/or damage to computer hardware or patients.
In addition to this, the GDPR Regulation (EU) 2016/679 on the protection of natural persons regarding the processing of personal data and on the free movement of such data, was ruled on May 24, 2016 and applied on 25 May 2018. Its purpose is to strengthen individuals' fundamental rights in the digital age and facilitate business by clarifying rules for companies and public bodies in the digital single market. The main GDPR requirements can include:

- Getting subjects' consent for data processing
- Anonymizing collected data to protect privacy
- Providing data breach notifications
- Safely handling the transfer of data out of the EU
- Appointing a Data Protection Officer (DPO) to oversee GDPR compliance

It is vital that every organization is aware of all information security regulations and GDPR requirements.

Clinical Evaluation

The Clinical Evaluation process is an ongoing procedure to collect, appraise and analyze clinical data pertaining to a medical device (not specifically referring to SaMD), and to evaluate whether there is sufficient clinical evidence to confirm compliance with relevant regulatory requirements for safety and performance. Published on May 5th 2017, the new EU Medical Device Regulation (MDR) has tightened requirements for clinical evaluations, expecting manufacturers to provide more clinical evidence and performance evaluation data.

Quality Management System

SaMD shall comply with regulatory requirements for medical devices manufacturers -- to establish, implement and have a Quality Management System (QMS) in place, in order to maintain and control the quality of products and manage unintentional outcomes related to patient safety. QMS requirements for medical devices are defined by regulatory agencies (e.g. FDA, EU authorities, etc.) and are detailed in international standard ISO 13485 - Medical Devices - Quality Management Systems - Requirements for Regulatory Purposes[8]. These requirements include amongst others[6]: documentation and record control, identification and traceability, changes control, and risk management.

Regulatory Approval

Before entering a specific market, manufacturers must comply with the regulatory requirements in the requested territory. Requirements can differ slightly between territories, but the general process involves submitting a technical documentation to the regulatory authority for approval -- either a CE mark certification in the EU or FDA clearance/approval in the U.S.

- ✔ Risk Categorization and Risk Management
- ✔ Data Security and Data Privacy
- ✔ Clinical Evaluation
- ✔ Quality Management System
- ✔ Regulatory Approval

Key principles to be adopted by manufacturers while developing a SaMD product

Conclusion

SaMD's tremendous growth is bringing exciting new innovations to the medical device industry and is a great opportunity for manufacturers. Having said that, the high rate of changes and ease of implementation challenges their ability to address regulatory requirements for medical devices, and SaMD in particular. Implementing a regulatory strategy early in its development, and proactively assessing the process with a good roadmap and a skilled co-driver will go far in limiting unnecessary delays and frustrations and bringing you closer to successful market access of your SaMD.

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