SOFTWARE AS MEDICAL DEVICE

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REVIEW ARTICLE

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ABSTRACT

The use of software in a medical device allows the manufacturer to concentrate on the application needed to run device-specific functions. The medical device manufacturer using software generally neglect software life cycle control, but still bears the responsibility for the continued safe and effective performance of the medical device. Software created for medical purposes and non-medical purpose is being used in healthcare. Earlier, hardware was more important; but in the recent times software one of the element for overall implementation has surpassed the prominence than hardware. Software is vital for the design, architecture and functionally of medical devices. Regulatory bodies have taken approaches in developing definitions and frameworks for software that have common public health goals, with variations in approach. Regulatory guidelines from such regulatory bodies for medical software established and implemented, serves as an environmental scan to provide direction on the guidelines on proposed regulatory framework for adoption, based on best practices. Medical software regulation is aimed to facilitate member economies to establish and harmonize an economic and effective approach for control of medical software in the interest of public health, in the continued innovation of medical software development.

Keywords: Software, Regulatory bodies, Medical device and Hardware.

INTRODUCTION

The terms medical software and medical device software are undefined terms that can designate any software, software item or system used within a medical context, depending on its intended use / indication for use. Software plays an increasingly important role in medical devices, especially in the field of mobile healthcare; however, the rapid evolution, particularly in relation to standalone software and mobile technology, presents new and complex challenges for regulatory agencies, globally.

A set of guidelines to allow member economies to assess the appropriate level of controls pertaining to software, and facilitate a harmonized approach to the regulation across member economies, is currently lacking. Regulatory bodies for medical software established and implemented, and serves as an environmental scan to provide direction on the guidelines on a proposed regulatory framework for adoption, based on best practices. (1)

OBJECTIVE

The Medical software regulation objective is to establish and harmonize an economic and effective approach to the control of medical software in the interest of public health and in the continued innovation of medical software development.

IMDRF

The IMDRF definition for "software as a medical device," or SaMD, as "software intended to be used for one or more medical purposes that perform these purposes without being part of a hardware medical devices." In defining SaMD, the guidance highlights a list of characteristics of SaMD:

- SaMD is a medical device and includes in-vitro diagnostic (IVD) medical device.
- SaMD is capable of running on general purpose computing platforms
- Software not necessary for a hardware medical device to achieve its intended

medical purpose;

- Software does not meet the definition of SaMD if its intended purpose is to drive a hardware medical device.
- SaMD may be used in combination with other products including medical devices;
- SaMD may be interfaced with other medical devices, including hardware medical devices and other SaMD software, as well as general purpose software.
- SaMD includes mobile apps that meet the definition of a SaMD as set out in the guidance.

Stand-alone software

Defined as an active medical device if it fulfils the definition of a medical device. Medical software may perform, primarily qualifying software that perform medical purposes within the scope of the medical device and *In Vitro* Diagnostic (IVD) medical device definitions. This includes software that can perform, or aid in the course of, the diagnosis, monitoring or treatment of, physiological status, predisposition or disease. The guidance also briefly mentions on possible changes to SaMD during its lifecycle, which includes changes as part of the software maintenance phase. Such maintenance changes may be adaptive, perfective, corrective or preventive. (2)

Classification for Medical Device Software

Any software that drives a device or influences the use of a device falls automatically in the same classification. Clearly, software may be viewed as a medical device or an accessory to a medical device or as a component and integral part of a medical device.

The function of the software guides the classification of the software medical device. If the software is a medical device, it may be classified as Class I; however, if the software medical device is an integral component of a device as indicated above, it assumes the classification of the device. For example, software that is part of a Class III medical device is viewed as a Class III device. (1, 3)

Types of Software that are Regulated as Medical Devices

Software which fall under the respective jurisdiction's medical device definition are regulated as medical devices. It is noted that the medical device definitions, although vary in wording between jurisdictions, in general encompass products intended to be used in the treatment, mitigation, diagnosis, monitoring or prevention of a disease or abnormal physical condition.

As the medical device definitions are high level criteria that broadly cover forms, presentations and scope of intended use, relying solely on the definition would mean a substantial level of granularity would be lacking in determining whether certain software should be qualified as medical device.

As such, in addition to the medical device definition, regulatory bodies have found it necessary to publish specific guidelines in relation to software qualification and classification, providing clarity on types of software that would be regulated as medical devices in their jurisdiction. (4, 5)

Forms of Medical Device Software

Software presents in a range of forms and functionality. There may be need to identify the form of medical software currently in the market such that controls may then be tailored based on the understanding of software forms and distribution modes on the market.

The identification of software forms should be an on-going process due to rapid advancements in software development and regulatory bodies would need to continue to keep abreast of developments in medical device technology. This is done to achieve and maintain a reasonable level of control, as a balance between ensuring public health and safety and avoid stifling of innovation and development of new technology. Medical software can be broadly classified into three categories:

a. Software that drives a medical device or influences the use of a device. This typically refers to embedded software, incorporated as a component or part of accessory of a medical device.

E.g. imaging software in diagnostic ultrasound system, software in pacemaker, mobile software that controls insulin pump delivery rate.

b. Software intended to be an accessory to a medical device

E.g. Software that accepts data transmitted from medical devices.

c. Software that is a medical device in its own right Software related to the functioning of a medical device may be part of a device or a device in its own right if it is placed on the market separately from the related device.

E.g. Treatment planning software, data analysis software for the purpose of directly aiding in the treatment or diagnosis of a patient

The above-stated categories include such software that is able to perform its medical purpose without being embedded in a hardware medical device or being dependent on specific or proprietary medical purpose hardware. This would refer to software capable of running on general purpose (non-medical purpose) computing platforms. The current IMDRF guidance defined such software as 'software as a medical device (SaMD)

Two modes of presentation of SaMD identified are recognized below

a. Software applications that are supplied via download, transfer and/or installation directly to the end-user, and may be used as an accessory to a regulated medical device, or transform a general purpose platform (e.g. mobile platform) into a regulated medical device

b. Web-based software which is executed on a server, such as a web browser. A web-based software would involve the delivery of computing as a service rather than a product. (6, 7)

A web system for the monitoring of clinical data may interact with a medical device, and uses a transmitter to send the information over the internet, a landline telephone or a mobile network. The information is collected and stored on a web server usually run by an external party who is generally the manufacturer of the system. The information can be reached by authorized health professionals or the patient through an internet connection.

Of the above two modes of presentation for SaMDs, while the general principles of software qualification, classification and design verification and validation do not differ, it is however noted there are potential differences in mechanisms employed for their post-market control, including traceability of end-users.

As per IMDRF guidelines, existing regulations adequately address public health risks of software when embedded in a traditional medical device. However, existing regulations do not readily translate or address the unique public health risks posed by standalone software nor assure an appropriate balance between patient/consumer protection and promoting public health by facilitating innovation.

Existing regulatory controls may have limited applicability when software can be developed, distributed, and accessed in a distributed environment through the internet. The below environment scan will cover controls in place for SaMD in other regulatory agencies.

European Union

European Commission refers to "standalone software" for medical device qualification. Such software would first need to have a medical purpose to be qualified as medical device. It is clarified that only the intended purpose as described by the manufacturer of the product is relevant for the qualification and classification of any device. The guidance also

clarifies some criteria for the qualification of standalone software as medical devices. Some qualification criteria are highlighted in the guidance:

- Not all standalone software used within healthcare can be qualified as a medical device.
- Standalone software can directly control an apparatus which provide immediate decision triggering information or provide support for healthcare professionals.
- The operating systems or virtual environments on which a software may run do not Impact the qualification criteria.
- Standalone software might also be an accessory of a medical device.
- The risk related to a malfunction of the standalone software used within healthcare is in itself not a criterion for its qualification or not as a medical device.

Software may comprise of a number of applications, where each of these applications are correlated with a module, some of which may have a medical purpose and some may not. In EU, medical device modules must comply with the medical device requirements while non- medical device modules are not subject to these requirements. However, if the modules are intended for use in combination with other modules of the whole software structure or other devices, the whole combination, including the connection system, must be safe and must not impair the specified performances of the modules which are subject to the Medical Device Directives.

Risk classification

The risk classification of medical devices in EU is via a risk-based system based on the vulnerability of the human body taking account of the potential risks associated with the devices.

Tables 1 & 2 contains some examples on EU qualification for software with specific intended use. The medical device guidance clarifies that the examples given were drafted in the light of today's state of the art and there may be more examples added in future in medical device guidance's in light of technological progress. (1, 2)

US FDA

The US FDA regulations for medical devices, any software that meets the legal definition of a device under section 201(h) of the Federal Food Drug & Cosmetic (FD&C) Act, is deemed a device and is known as medical device software. Similar to the EU, there are further general criteria specified by the US FDA to be considered for qualification of medical device software:

- Operating systems or virtual environments on which a software may run do not impact the qualification criteria.
- Qualification is based on the intent of the product, and is not based on the engineering definition of software functionality

If software intent falls under the legal definition, software is still a device regardless of the means by which the software is delivered to the end user with the Mobile Medical Applications guidance published in Sept 2013 by the US FDA, the agency has broadly categorized mobile applications (MAs) as

(1) MAs that are the focus of FDA's regulatory oversight,
(2) MAs that are not medical devices and
(3) MAs that, although qualify as medical device,

FDA intends to exercise enforcement discretion as they pose a low risk to patients

Table 1: Examples of software types and their qualification as general medical devices in EU

Software type	Hospital Information Systems (HIS)	Information Systems		Communication Systems (Tele-medicine)		Web Systems for monitoring of data		Decision Support Software
		Electronics Patient Record	Additional modules in Electronics Patient Record for diagnosis, therapy and follow-up					
Intended use	Patient admission, scheduling patient appointments, insurance and billing purpose	Store & transfer electronic patient records. Archives all kinds of documents & data related to a specific patient (e.g. vital parameters, patient identification, scheduling, examination results, image identification details & other Documented clinical observations. - Clinical Information Systems (CIS)/ Patient Data Management Systems (PDMS) - Pre-hospital ECG System - Radiological Information Systems	Modules that are intended to provide additional information that contributes to diagnosis, therapy and follow-up, e.g. - Image viewer with functionality for diagnosis - Medication module - Generate alarms - Provide information to start patient's treatment to paramedics when patient is transported	General communication systems (email, mobile, video, paging etc.) for general purposes - Home care monitoring - Video appointment	Tele surgery software - intended to conduct a surgical procedure from a remote location. Remote control software used in combination with telesurgery robots.	Monitoring of non-medical performance of medical devices (software monitoring medical devices in hospital for maintenance & report)	Monitoring of performance of medical devices	Computer based tools which combine medical knowledge databases and algorithms with patient specific data e.g. Radiotherapy treatment planning systems (calculate ionizing irradiation dosage), drug/chemotherapy planning systems (calculate drug dosage administration) & Computer aided detection system (automatically read x-ray images or interpret ECG)
EU qualification	**Not MD**	**Not MD**	**MD (modules only)**	**Not MD**	**MD**	**Not MD**	**MD**	**MD**

- **MD- Medical Device**

Table 2: Examples of IVD software types and their qualification as IVD medical devices in EU

Software type	Laboratory Information Systems (LIS) and Work Area Managers (WAM)	Expert System	Interpretation of raw data	Home care monitoring
Intended use	Support the process from patient sample to patient result. Management & validation of incoming information from IVD analysers (e.g. calibration, QC, product expiry, feedback) through interconnection with various analytical Instruments. Takes care of communication of data (results, statistics) to external databases. Results are available, readable and Understand able without the intervention of the software.	Intended to capture and analyse together several results obtained for one patient by 1 or more IVD devices, to provide information falling within the definition of an IVD medical device e.g. differential diagnosis. e.g.- Software that uses algorithm to characterize viral resistance to various drugs, passed on nucleotide sequence generated by genotyping assays	Used to render raw data (obtained from an IVD test) readable for the user	Intended for archiving patient results or for transferring results from home to healthcare provider. Results are available, readable and understandable by the user without the intervention of the software.
EU qualification*	**Not MD**	**IVD MD**	**IVD MD**	**Not MD**

Table 3: Examples of software types and their qualification as medical devices in US FDA

Software type	Hospital Information Systems (HIS)	Information Systems			Communication Systems (Tele-medicine)			Decision Support Software		Mobile apps that transform mobile platforms into medical devices	Automate tasks for health care providers
		Medical Device Data System	Patient management/ information	Access electronic/ public health records							
Intended use	Patient admission, scheduling patient appointments, insurance and billing purpose	Software that display, store, or transfer medical device data in its original format	Help patients: Self-management disease/ conditions without providing specific treatment or suggestions • Organize and track their health information • Access information related to their health conditions or treatments • Document, show, or communicate potential medical conditions to health care providers	Enable individuals to interact with PHR systems or EHR systems	Display medical device data to perform active patient monitoring	General communication systems (email, mobile, video, paging etc.) for general purposes - *Video appointment*	Remote Medication Management System software intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease Mobile apps that connect to an existing device type for purposes of controlling its operation, function, or energy source	Computer based tools which combine medical knowledge databases and algorithms with patient specific data *e.g. Radiotherapy Treatment planning Systems (calculate Ionizing irradiation dosage), drug/ chemotherapy planning systems (calculate drug Dosage administration) & Computer aided detection system (automatically read x-ray images or interpret ECG)*	Perform simple calculations routinely used in clinical practice ∟ Body Mass Index (BMI) ∟ Total Body Water / Urea Volume of Distribution ∟ Mean arterial pressure ∟ Glasgow Coma Scale score ∟ APGAR score ∟ NIH Stroke Scale ∟ Delivery date estimator	Mobile apps that transform the mobile platform into a regulated medical device by using attachments, display screens, or sensors or by including functionalities similar to those of currently regulated medical devices	*Automate simple tasks for health care providers*
US FDA qualification	**Not MD**	**MD (Class I, 21CFR 880.6310)**	**MD (Enforcement discretion applied to not regulate)**	**MD (Enforcement discretion applied to not regulate)**	**MD**	**MD (Enforcement discretion applied to not regulate)**	**MD**	**MD**	**MD (Enforcement discretion applied to not regulate)**	**MD**	**MD (Enforcement discretion applied to not regulate)**

Risk classification

Medical devices are categorised into 3 classes, Class I, II, III, based on the device's risk. Rather than providing a set of general guidelines as other reference agencies, the FDA defines specific device categories under Title 21 of the Code of Federal Regulations, each of which has a regulation number, and assigns the risk classification accordingly.

The Mobile Medical Applications guidance provides a consolidated list of already existing classifications for regulated medical devices, which pertain to devices that potentially contain or are presented as software, the Class according to which they are regulated and the corresponding submission type to the US FDA. The list is noted as a reference starting point for mobile medical app manufacturers in identifying regulated medical devices and is likely not meant to be exhaustive. (8, 9)

SUMMARY

With the enormous complexity and rapid advancements in software technology, it would be appropriate to follow suit and avoid defining software forms in any guidelines on software qualification to be developed. The focus of determining regulatory control has been emphasized to be passed on the intended use of the software, and hence the degree of risk to the user.

Additionally specified that general platforms, on which such medical software may run or be distributed, are not intended by their manufacturer to be used for therapeutic purposes would not be regulated as a medical devices. Such examples of platforms include general-use mobile phones, computers and tablets, which are not entities that exclusively distribute medical software.

In regards to specific software types, a similar trend is observed in qualification of types of software as medical devices, although guidelines from each jurisdiction may specify certain software types that are not identified in other jurisdictions' guidelines, while some software types addressed differ in qualification status across jurisdictions.

CONCLUSION

Software standards that are currently available may facilitate regulators' and manufacturers' compliance to medical device safety and performance requirements. It has always been a challenge for regulatory authorities and standardization bodies to keep well-informed with the rate of development in technology. A potential impact towards patient safety due to an unregulated technology/ market can cause significant changes in device industry; forcing authorities to implement stringent norms in software development and application.

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CONFLICTS OF INTEREST

The author declares that there are no conflicts of interest.

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