Medical Software: a literature review and commentary on the importance of regulations and standards for its development towards market entry

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Introduction

Medical software has been in circulation since the 1980s and is estimated that 50% of all medical devices require software (Branstetter, Drev and Kwon, 2018). The increasing popularity of medical software, mHealth, medical apps, raises questions on their safety and quality. Regulations covering medical software do exist and are designed to promote the safety of the public and ensure that these software based products are effective in their intended use (Özcan-Top and McCaffery, 2018). It may be that awareness of software developers on the relevant regulations may be lacking (Censi et al., 2015). This paper discusses legal definitions and regulations relevant to medical software.

Methods

Literature review covering EU regulations and guidance documents relevant to medical software

Results and Discussion

Within the European context regulatory oversight of medical software begins with the legal definitions on what constitutes a medical device, software, stand alone, software-as-a-medical device, expert function, intended purpose, and manufacturer as contained in table 1.

Taking all these definitions together in table 1, software developers that market and own their own software can be considered manufacturers. As manufacturers, developers must be able to articulate what the intended purpose of their product is/are. Following that if the software to be marketed fits the definition of a medical device, software manufacturers are mandated to conform to the requirements set by the relevant authorities.

The essential principles guiding regulatory systems is risk management and quality management systems. Based on its intended purpose, manufacturers are tasked to appreciably demonstrate to authorities the safety, quality and effectiveness of their products. Standards while not compulsory, act as a benchmark for best practice with which regulators will use to assess manufacturers seeking a CE mark or proof of conformity assessing to the quality and safety of the products that are to be marketed and sold in the single market**. As such there are several standards that would best apply to medical software and apps stated in figure 1.**

One of the standards in figure 1 is IEC 62304. Contained within this standard is a software lifecycle process that implements principles of quality and risk management as detailed in ISO 13485 and ISO 14971. The phases of this process are 1) Development planning, 2) Requirements analysis, 3) Architectural design, 4) Detailed design, 5) Unit implementation and verification, 6) Software integration and integration testing, 7) Systems testing, 8) Release. After these 8 stages there is also the expectation on manufacturers to do post-market surveillance and vigilance on their products for continuous improvement and to detect and monitor potential failures and ongoing risks. These steps closely mirror the US FDA design control guide (US FDA, 1997).

The adoption and implementation of these processes and standards can greatly improve regulatory compliance, decrease development time, lower development costs, reduce defects, improve testing and enhance the quality of the product developed, although there is a recognized learning curve for manufacturers (Hrgarek, 2012; Höss et al., 2014).

It is acknowledged however, that there may be software that does not completely fall into the definition of a medical device, especially with software providing different functions. Guidance is available both from the EU and its member states. An example of which is the UK MHRA guidance on standalone medical software and apps. It provides specific instructions for manufacturers to determine whether their product is considered a medical device. It also refers to other specific guidance for borderline cases (Medicines and Healthcare Products Regulatory Agency, 2014).

Conclusion and Recommendations

What this discussion illustrates is that medical software and apps are covered by the existing regulations. This puts the onus on software developers as manufacturers, to implement the necessary planning and foresight to make themselves aware of the legal framework and to conform to the requirements. Conformance is not only a way to put their products into the market but provides a pathway to learn from best practice, in the form of standards, and to assure end-users and patients that their software is safe, of good quality, and effective in their intended purpose. Other benefits in conforming to the standard is that they decrease development time, optimize costs, reduce defects, and improving testing.

Table 1. Regulatory and Legal Terminology, adapted from EU 2017/745 and MEDDEV 2.1/6

Terminology	Definition
Medical Device	Any instrument, apparatus, appliance, software, implant, reagent, material or other article intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the following specific medical purposes: • Diagnosis, prevention, monitoring, prediction, prognosis, treatment or alleviation of disease • diagnosis, monitoring, treatment, alleviation of, or compensation for, an injury or disability • investigation, replacement or modification of the anatomy or of a physiological or pathological process or state • providing information by means of in vitro examination of specimens derived from the human body, including organ, blood and tissue donations and which does not achieve its principal intended action by pharmacological, immunological or metabolic means, in or on the human body, but which may be assisted in its function by such means (European Union, 2017)
Software	A set of instructions that processes input data and creates output data (MEDDEV 2.1/6, 2016)
Stand Alone	Software not incorporated into the device at the time of placing onto the market (MEDDEV 2.1/6, 2016)
Software as a Medical Device (SaMD)	Software intended to be used for a single or multiple medical purpose without being part of a hardware medical device (MEDDEV 2.1/6, 2016).
Expert Function Software	Software able to analyse information according to the use of the software (MEDDEV 2.1/6, 2016).
Intended Purpose	The use for which a device is intended according to the data supplied by the manufacturer on the label, in the instructions for use or in promotional or sales materials or statements and as specified by the manufacturer in the clinical evaluation (European Union, 2017).
Manufacturer	The natural or legal person who manufactures or fully refurbishes a device or has a device designed, manufactured or fully refurbished, and markets that device under its name or trademark (European Union, 2017)
Standards	Technical specification, adopted by a recognized standardization body, for repeated or continuous application, with which compliance is not compulsory (European Commission, 2012)

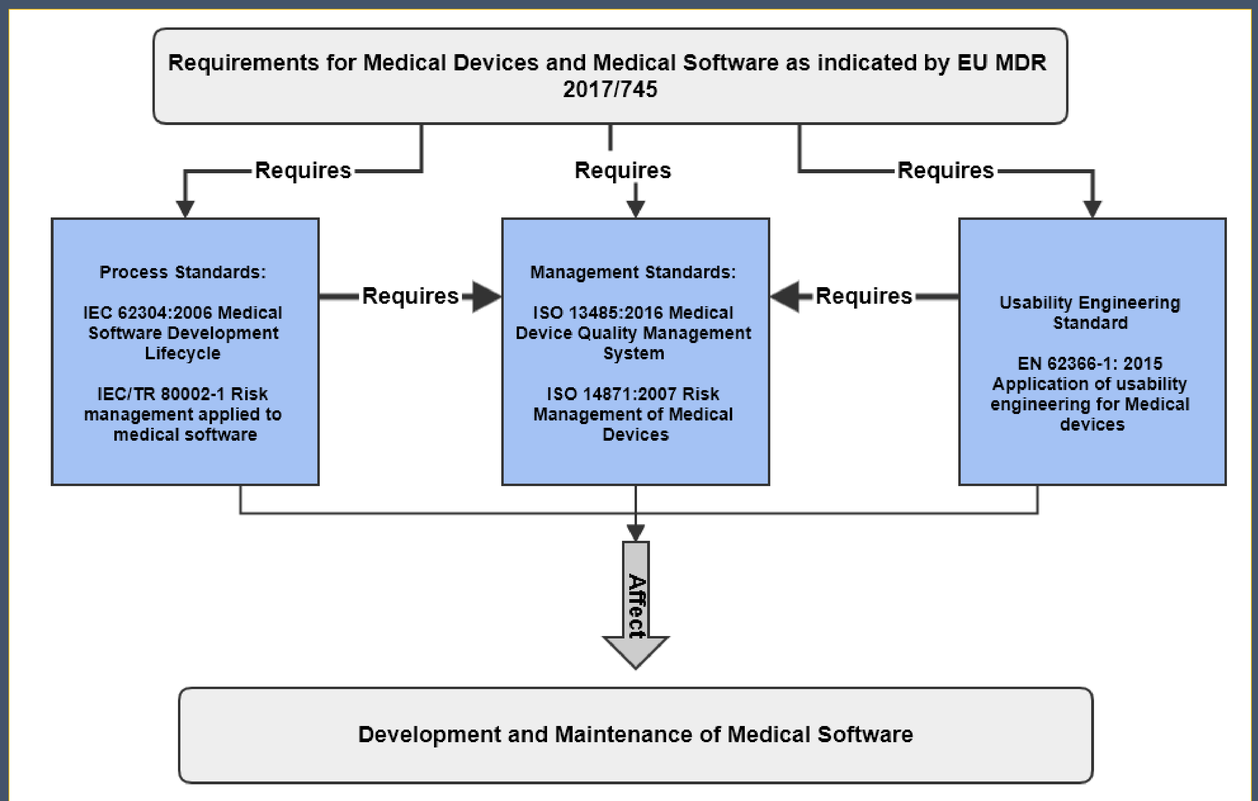

Figure1. Mapping of IEC 62304, ISO13485:2016 and ISO 14971:2007 to MDR 2017/745 and how they affect Medical Software development (Adapted from *Höss* et al*., 2014*)

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