When does healthcare stand-alone software become a medical device?

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Abstract

Mobile phone applications ("apps") are being used more and more widely in the healthcare sector. Health apps are typically intended to better inform patients about their conditions through raising awareness of safety and efficacy or reduce costs of use for health products. They can help healthcare organisations to better communicate between parties and improve their cost/effectiveness ratio. However, the regulatory status of such health apps must be clarified on a case-by-case basis, as some of them could be categorised as medical devices.

[Note: In vitro diagnostic medical devices regulated by Directive 98/79/EC are not considered in the context of this article.]

Mobile phones are primarily intended for communication purposes. However their ability to run stand-alone software has extended their use. Accordingly, there has been considerable growth in this new technology, and this has included the use of health applications (apps). The top ten countries for downloads of the top 200 most popular free apps are the US, China, Japan, the UK, Germany, France, Canada, Italy, Australia and South Korea. Emerging app markets are Russia, Brazil, Mexico and Turkey. The potential for developers has grown over the past two years, as evidenced by the increase in daily downloads from 7.7 million to 16.8 million for the top 200 most popular free apps. Looking at the aggregated revenue among the top 100 highest grossing apps in all countries, the total revenue has more than tripled over the past two years to reach US$2 billion.[1] The biggest category was games (16%), and it is estimated that this category was responsible for over 50% of app sales. The "medical" and "healthcare & fitness" categories are today modest by comparison, each making up approximately 2% of the app store, for a combined total of more than 21,000 apps.[2] The use of apps for healthcare purposes is not limited to healthcare professionals. This technology has huge potential to support the population as a whole. Developers and users are only just beginning to explore their potential use, but popular apps to date include those that support healthier living, help manage a long-term condition, or provide initial advice on an emerging medical problem.

The rising popularity of smart phones and app use is both an opportunity and a threat for healthcare organisations and healthcare companies but the regulatory status of this new technology is not always clear.[2]

A healthcare improvement opportunity

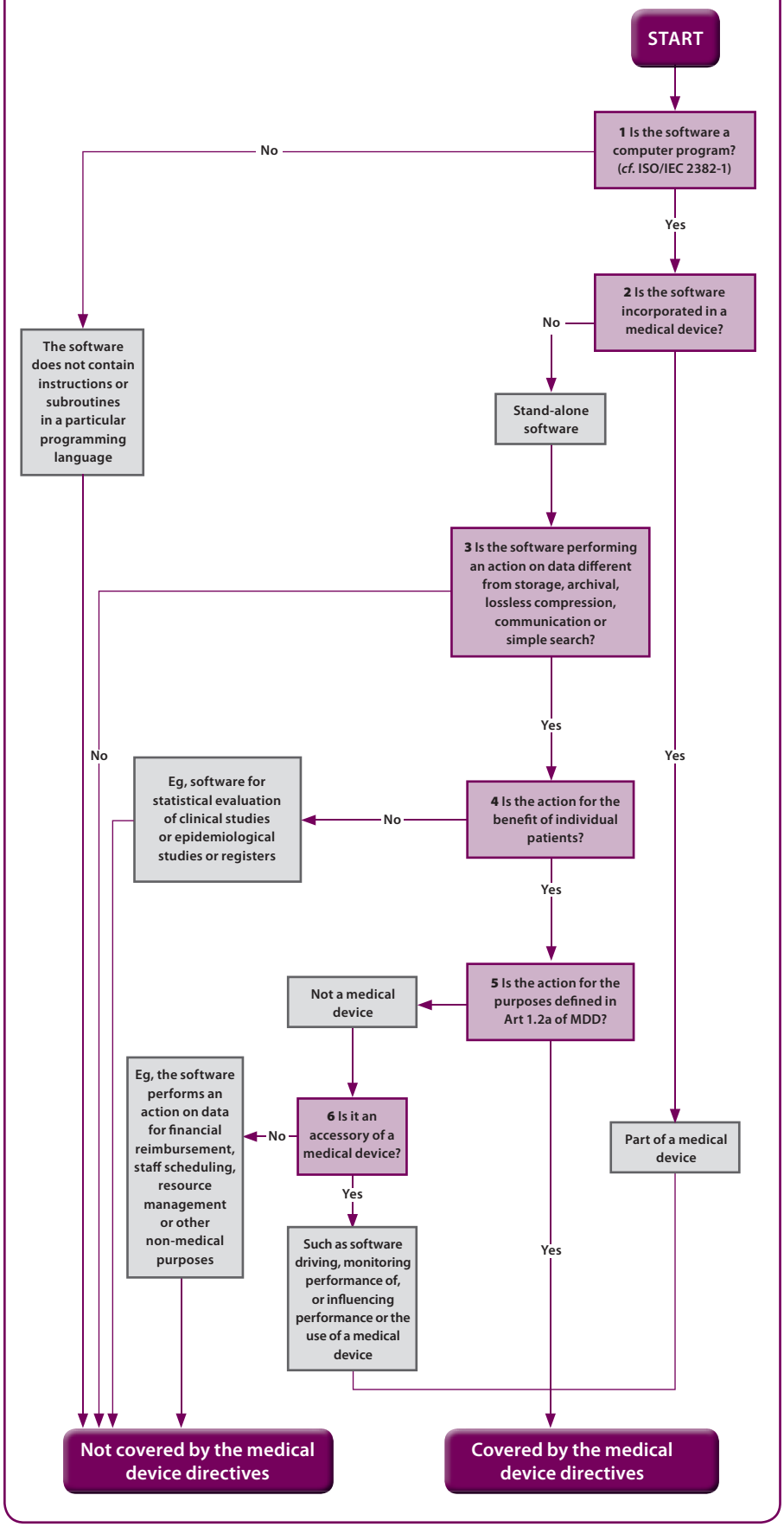
For many drugmakers, apps serve as tools within broader digital strategies that follow the trend for doctors and patients to go online or turn to their mobile devices for information about health and medicines. They rarely promote products with these consumer-friendly apps (possible in the US, but illegal in the EU), but the company name stays in front of their target audiences.[3] Many apps provide visual and audible information to help patients better understand their health condition and how a prescribed drug works within their body. Patients with diseases such as hepatitis C, autoimmune disorders, haemophilia and multiple sclerosis can benefit from knowing as much as possible about their illness, their medication and any potential side-effects, and apps can provide such information in situations where accessing and remembering trusted information can otherwise be a challenge.[4] A survey of more than 1,800 US doctors also found reps that used iPads were more likely to influence physician behaviour.[5]

Care organisations are also involved. As an example, healthcare delivery is a complex enterprise that involves multiple interactions among multiple stakeholders. Effective communication between these dispersed parties is critical to ensuring quality and safety and improves operational efficiencies. Time-and-motion studies in hospital settings provide strong evidence that doctors and nurses spend a significant proportion of their time obtaining or providing information (ie, communicating). In a 2010 article entitled: "Quantifying the economic impact of communication inefficiencies in US hospitals",[6] Agarwal *et al* found that "US hospitals waste over $12 billion annually as a result of communication inefficiency among healthcare providers. Increase in length of stay accounts for 53% of the annual economic burden. A 500-bed hospital loses over $4 million annually as a result of communication inefficiencies". It has been estimated that poor communication costs NHS hospitals in England alone in excess of £1 billion.[2] Agarwal *et al* also note that their "estimates are conservative as they do not include all dimensions of economic waste arising from poor communications. The economic burden of communication inefficiency in US hospitals is substantial. Information technologies and process redesign may help alleviate some of this burden".[6]

The market for health apps is growing in terms of the supply of apps and the number of downloads. Involved healthcare stakeholders should encourage greater use of mobile devices in the workplace, which would have a positive impact on:

- Improving patient safety, care and outcomes

Figure 1: Decision diagram to assist qualification of software as medical device.



- Reducing the cost of ownership for the individual
- Raising security awareness and compliance
- Enhancing productivity and effectiveness.[2]

However:

- Healthcare professionals should carefully consider the risks when using apps to support a patient's care
- Developers should test their apps thoroughly and maintain adequate technical documentation to demonstrate this
- Publishers should ensure compliance with the necessary regulations before releasing apps on to the market.[2]

As the popularity of running software applications on mobile devices continues to increase, it can be anticipated that the use of apps to aid medical diagnosis and treatment will gain in popularity, with a corresponding increase in risk to the general public. Specific regulation for this new technology should not be ignored.[2]

Requirements to be categorised as a medical device

Medical Devices Directive 93/42/EEC and, more recently, MEDDEV 2.1/6[7] entitled "Guidelines on the qualification and classification of stand-alone software used in healthcare within the regulatory framework of medical devices" provide the following definitions:

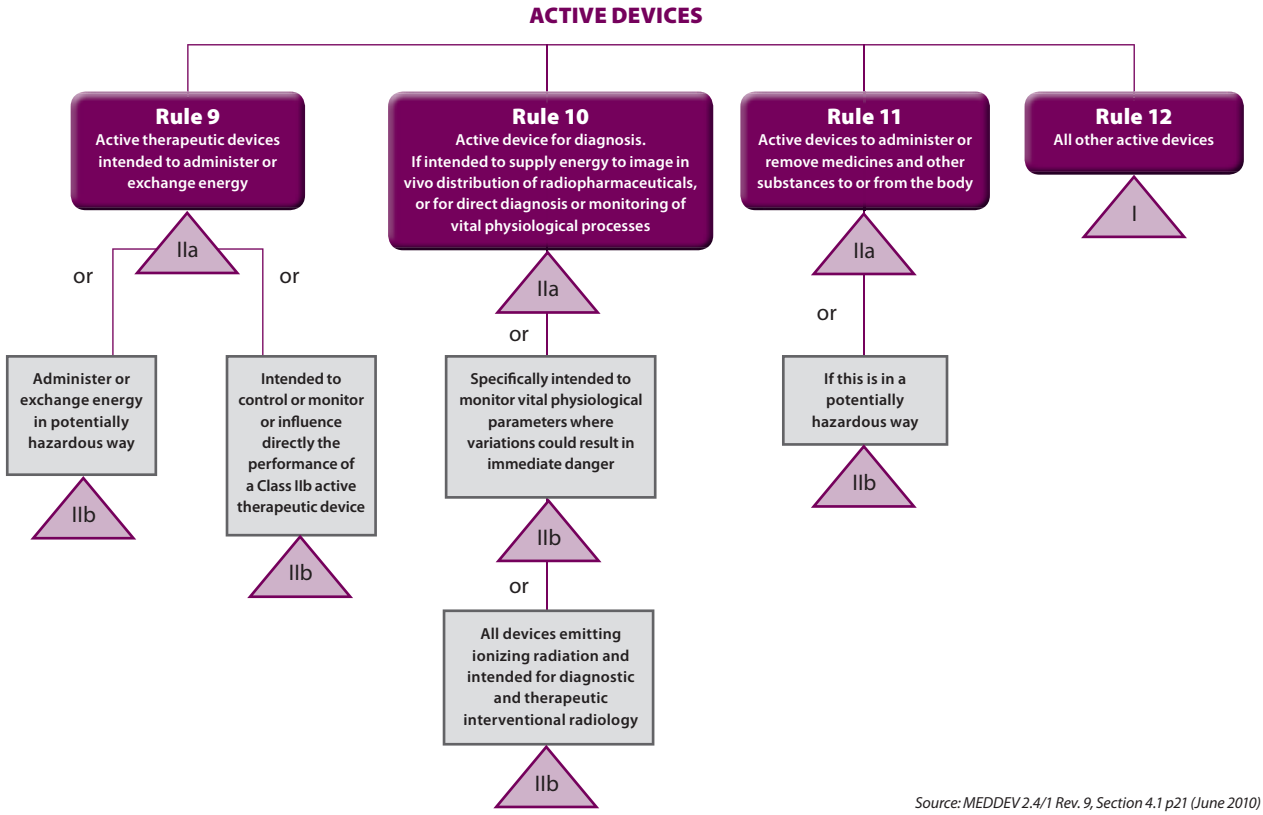
"Medical device" means any instrument, apparatus, appliance, software, material or other article, whether used alone or in combination, including the software intended by its manufacturer to be used specifically for diagnostic and/or therapeutic purposes and necessary for its proper application, intended by the manufacturer to be used for human beings for the purpose of:

- Diagnosis, prevention, monitoring, treatment or alleviation of disease
- Diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap
- Investigation, replacement or modification of the anatomy or of a physiological process
- control of conception

and which does not achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its function by such means.

"Active medical device" means any medical device, the operation of which depends on a source of electrical energy or any source of power other than that directly

Figure 2: Classification of active medical devices as described in rules 9–12 of Annex IX to Directive 93/42/EEC.



Source: MEDDEV 2.4/1 Rev. 9, Section 4.1 p21 (June 2010)

generated by the human body or gravity and which acts by converting this energy. Medical devices intended to transmit energy, substances or other elements between an active medical device and the patient without any significant change, are not considered to be active medical devices.

According to the MEDDEV 2.1/6, stand-alone software must have a medical purpose to be qualified as medical device. When it is the case, stand-alone software is considered to be an active medical device.[7]

Stand-alone software can directly control an apparatus (eg, radiotherapy treatment), or provide immediate decision-triggering information (eg, resuscitation equipment), or provide support for healthcare professionals (eg, electrocardiogram interpretation). Stand-alone software may run on different operating systems or in virtual environments. These operating systems or virtual environments do not impact the qualification criteria.

An example of stand-alone software having a medical purpose is a clinical tool for estimating burn area percentages and recording patients' details. The app works on the Apple iPad, iPhone and iPod Touch. With this app, a physician can graphically highlight the areas of the patient that are burned and enter some basic statistics such as their age, height and weight. The app then calculates the necessary fluids protocol to be administered over the 24 hours following burn injury. The information entered and the results calculated can then be emailed, for example, from an outlying hospital to a specialist Burns Unit.[2]

Stand-alone software that does not meet the definition of a medical device but is intended by the manufacturer to be an accessory to a medical device also falls under the scope of Directive 93/42/EEC. It means that stand-alone software may be an accessory of a medical device.

However, the risk related to a malfunction of the stand-alone software used within healthcare is not in itself a criterion for its qualification as a medical device. Not all stand-alone software used within healthcare can be qualified as a medical device.

Where a given product does not fall under the definition of 'medical device', or is excluded by the scope of the Directives, other Community and/or national legislation may be applicable.

Figure 1 is a decision diagram which gives some guidance regarding the necessary steps to qualify stand-alone software as medical device.[7]

Main decision steps can be summarised as follows according to MEDDEV 2.1/6:[7]

- **Decision step 1:** If the stand-alone software is a computer programme, then it may be a medical device. If the software is not a computer programme, then it is a digital document and therefore not a medical device. Examples of computer programmes are software applications, macros, scripts, dynamically linked libraries, batch files, style sheets and any document containing active formatting or filtering instructions. Examples of digital documents are image files, DICOM (Digital Imaging and Communications in Medicine) files, digital ECG recordings, numerical results from tests and electronic health records (EHRs). While the EHR is usually not a computer programme, the EHR system, ie, the software writing, retrieving, representing, etc, the information in the EHR, is a computer programme. This is similar as for DICOM files versus a PACS (picture archiving and communication system).

Table 1: Conformity assessment procedures dependent upon class of device.

Class	Procedure	Combined with
Class III	Annex II, Full quality management system	None
	Annex III, Final design review, with:	Annex IV, Unit or sample review, or Annex V, Production quality procedures
Class IIb	Annex II (w/o 4), Full quality management System, excepted design procedure	None
	Annex III, Final design review, with:	Annex IV, Unit or sample review, or Annex V, Production quality procedures, or Annex VI, Final test quality procedures
Class IIa	Annex II (w/o 4), Full quality management System, excepted design procedure	None
	Annex VII, Final design review, with:	Annex IV, Unit or sample review, or Annex V, Production quality procedures, or Annex VI, Final test quality procedures
Class I	Annex VII, Final design review (less comprehensive than other classes)	None

- **Decision step 2**: If the software is incorporated into a medical device rather than stand-alone software, it must be considered as part of that medical device in the regulatory process of that device. If it is stand-alone software, proceed to decision step 3. Altering the representation of data for embellishment purposes does not make the software a medical device. In other cases, including where the software alters the representation of data for a medical purpose, it could be a medical device.
- **Decision step 3:** If the software does not perform an action on data, or performs an action limited to storage, archival, communication, 'simple search' or lossless compression (ie, using a compression procedure that allows the exact reconstruction of the original data) it is not a medical device. 'Simple search' refers to the retrieval of records by matching record metadata against record search criteria, eg, library functions. Simple search does not include software which provides interpretative search results, eg, to identify medical findings in health records or on medical images.

Final decision steps are:

- **Decision step 4:** The action must be for the benefit of individual patients. One example is software intended for the evaluation of patient data to support or influence the medical care provided to that patient. Examples of software not considered as being for the benefit of individual patients are those which aggregate population data, provide generic diagnostic or treatment pathways, scientific literature, medical atlases, models and templates as well as software for epidemiologic studies or registers.
- **Decision step 5:** The intended use must be within the purposes of the medical device. The legal manufacturer must intend the software to be used for any of the purposes listed in Article 1(2)a of Directive 93/42/EEC; then the software shall be qualified as a medical device. If only a non-medical purpose is intended by the manufacturer, it is not a medical device. Tasks such as emailing, web or voice messaging, data parsing, word processing, invoicing, staff planning or back-up are not in themselves considered as being medical purposes, according to Directive 93/42/EEC.

Rules applicable to stand-alone software as a medical device

Regarding the classification, stand-alone software that meets the definition of a medical device shall be considered as an "active medical device". This means that rules 9, 10, 11 and 12 of Annex IX to Directive 93/42/EEC may apply as indicated in Figure 2.

In addition, clause 2.3 of the implementing rules in Annex IX states that software "which drives a medical device or influences the use of a device, falls automatically into the same class, as the device it drives".

Examples of active medical devices referred to in rules 9–12 include:[8]

Rule 9:

- Software linked to a muscle stimulator, an incubator, a laser, etc
- Software monitoring physiotherapy equipment

Rule 10:

- Software installed in any imaging apparatus (ultrasound, X-Ray, MRI, scanner)
- Software connected to a diagnosis device, eg, PACS.

Rule 11:

- Software installed in dialysis equipment
- Software connected to a device delivering or administering medicinal products.

Rule 12:

- Software installed in a hospital bed
- Software used to monitor or control a class I device.

As with all medical devices, conformity assessment procedures differ with the class of the device (see Table 1).[8]

The main difference between Annex II and other annexes is linked to the organisation of the manufacturer:

- Annex II is applied to the whole company, for every product (except derogations with justification). In most cases the company is ISO 13485 certified and has an activity in medical devices only
- Annex III, VII and V is most often applied to a subset of products delivered by the company.[8]

Class I devices do not require European notified body approval except for sterility or metrology aspects where applicable. The conformity assessment procedures for Classes IIa, IIb and III require previous notified body approval. The latter two are heavier to manage and more onerous.

In any case, the legal manufacturer should:

- Demonstrate that his device meets applicable Essential Requirements (Annex I of the Medical Device Directive) notably by conforming to the IEC 63204 standard which defines the minimum activities and tasks to be performed, to provide confidence that the software has been developed in a manner that is likely to produce highly reliable and safe software products
- Perform a risk analysis according to EN ISO 14971 standard resulting in an acceptable global result
- Implement and maintain a quality management system including vigilance procedures and procedures for preventive or corrective action (CAPA)
- Obtain notified body approval where applicable
- Draw up the "EC Declaration of Conformity" before applying the CE mark to the device
- Register with the competent authority where the legal manufacturer is located
- Manage post-production data and risk management file
- Make available relevant documentation at any time on request of the competent authority
- Comply with the national rules for advertising.

Relevant standards for software development are IEC 62304, IEC 62366 and IEC60610-1. All three standards require manufacturers to have a design control procedure for software. Only the level of scrutiny of design will change, given the class of software – IEC 62304 is very clear about this. Only a part of the standard is mandatory for software with a low level of risk, whereas the full standard is mandatory for software with high levels of risk.[8]

Who is the legal manufacturer?

In the end, the key question arises: who is the legal manufacturer under the Medical Device Directive – the developer or the publisher?

According to Council Directive 93/42 EEC, "legal manufacturer" means the natural or legal person with responsibility for the design, manufacture, packaging and labelling of a device before it is placed on the market under his own name, regardless of whether these operations are carried out by that person himself or on his behalf by a third party.

Reading the above definition it appears that the publisher of the app (ie, the organisation which places the device on the market in its own name) is deemed the legal manufacturer and is obliged to follow the directive requirements and to implement post-market surveillance. Accordingly, publishers have the legal obligation under the Medical Device Directive to exercise sufficient control over the developers/subcontractors in order that they comply to applicable essential requirements of the directive for design, testing and manufacturing and/or be able to take corrective action where necessary (eg, "bug" reporting and resolution). The contract between the publisher and developer/subcontractor should therefore consider these issues, and the design of the app may want to include the ability to notify users or even terminate use if corrective action is required.[2]

Conclusion

When an app is associated with, contributes to, or makes, a clinical decision, it will be classified as a medical device and therefore must conform to the relevant regulation. In addition, the publisher will be obliged to release updates to preserve its relevance.

Within the EU, further regulatory considerations in addition to the Medical Device Directive include the following:

- Liability for defective products (1985/374/EC &1999/34/EC)
- General product safety (2001/95/EC)
- Sale of consumer goods (1999/44/EC)
- Information society services and e-commerce (2000/31/EC)
- Data protection (1995/46/EC)
- Misleading and comparative advertising (2006/114/EC)
- Unfair business-to-consumer commercial practices (2005/29/EC).

Given the range of legal issues concerned, and the potential sources of liability that manufacturers of apps face, publishers should seek legal advice to ensure they conform to all relevant regulations. They will also need to ensure they are not infringing the intellectual property rights of others. This could be done via patents, trademarks or material under copyright.[2]

The "app mentality" represents a new paradigm. In the healthcare field, apps can promote more efficient clinical communication and also have the potential to deliver more efficient decision-making. They also may demand greater responsibility from the publishers and/or from patients with regard to managing their own diagnosis and treatment.

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