Do mobile medical apps need to follow European and US regulations or not: decisions exemplified by diabetes management app

Anna Holubová[abc], Meghan Bradway[c], Eirik Årsand[c], Daniel Hallgren[c], Gunnar Hartvigsen[bc]

[a]Faculty of Biomedical Engineering, Czech Technical University in Prague, Kladno, Czech Republic
[b]Department of Computer Science, University of Tromsø - The Arctic University of Norway, Tromsø, Norway
[c]Norwegian Centre for Integrated Care and Telemedicine (NST), University Hospital of North Norway, Tromsø, Norway

Abstract

Rapid development of medical and health-related mobile applications (apps) has caught the attention of the regulatory institutions. Despite the fact that we have valid sources of information regarding related legislative issues, it is not easy for developers to interpret specific laws, directives and definitions. To clarify this situation, we summarize the main points of EU and US medical device directives and regulations for developers of mobile medical-oriented applications. To help developers decide whether their app should be considered under these regulations or not, we describe the process of evaluating the mobile phone app called Diabetes Diary (Diabetesdagboka) for classification as a medical device. In addition, we also highlight some serious issues the developers and regulatory bodies should keep in mind when inventing or encountering a new product.

Keywords:

Mobile Medical Application, mHealth regulations, classification of stand-alone software, diabetes.

Introduction

Mobile medical apps have become more and more useful and desired not only within the general population, but also as part of medical diagnosis and treatment within healthcare systems around the world [1][2]. Nowadays, smartphones are capable of communicating to sensors and medical devices to track users' physiological parameters such as motion, heart rate, blood pressure, blood glucose, oxygen saturation, and even ECG signals [1][3]. Moreover, integrated MEMS (Micro-Electro-Mechanical Systems) [3] based sensors are possible to be used for fitness and health tracking. These integrated technologies, which are cost-effective for healthcare systems and more affordable to the common population, have begun to play a dominant role in personalized medicine [4][5]. The rapid development of fitness and medical app functionalities, which include inter-communication between devices, enables the user to transfer and store all tracking data from multiple sensors into one central app. Individuals as well as health care authorities have recognized the potential for these integrated tools to benefit individuals with chronic diseases, enabling them to better self-manage.

In the case of diabetes care, integrated data from multiple devices can significantly ease data interpretation, and thus improve the lives of patients with diabetes. Instead of controlling and tracking each particular parameter, such as insulin doses, blood glucose or intensity of physical activity, via different devices, such as insulin pumps, glucose meters or activity trackers, it is highly desirable to let these devices communicate with each other and arrange all the necessary data in one place using one diabetes app. [6]

Another issue is on the one hand, the continuous increase of new non-medical apps, while on the other hand, much fewer medical certified apps, since approval often take a substantial amount of time and they are also often not thought of as necessary by the developers. Therefore, it is even more difficult for policy makers to find medical certified apps.

Institutions responsible for regulating medical devices are responding to this situation by preparing documentation describing which applications fall into these regulations and which do not. Although these institutions frequently issue new guidelines for developers, in attempts to adequately react to this rapid development of medical software, there are still some details for app classification which may be unclear.

Therefore, the aim of this article is to summarize and clearly explain the main points of medical device directives and regulations established in the EU and US for the developers of medical mobile apps. An example of a concrete mobile app, the Diabetes Diary (Norwegian name: Diabetesdagboka, developed at the Norwegian Centre for Integrated Care and Telemedicine (NST)), will be used to illustrate the process of classifying a mobile app as a medical device.

Regulations of mobile medical applications

Regulatory system in EU

Summary of relevant Medical Device directives

In the European area, the main organization responsible for medical device regulations is the European Commission. There are three Medical Device Directives in place, the Directive of Active Implantable Medical Devices (90/385/EEC), the Medical Devices Directive (93/42/EEC), and the Directive of In Vitro Diagnostic Medical Devices (98/79/EC) [7]. The document that specifically covers the European classification of medical devices and their accessories is the Medical Device Directive (MDD, Council Directive) 93/42/EEC [8].

This document describes the meaning of the terms "medical device" and "accessory", their classification, essential requirements, and other issues including their production. Fol-

lowing this directive, "accessories" are treated as "medical devices in their own rights" [8]. It means they are produced in order to be used together with a device to meet the requirements of use of such a device (e.g. electrodes for ECG monitors are considered to be an accessory) but they can also be marketed separately. A product can be considered an accessory if the manufacturer intends for it to be used "*in conjunction with one or several medical devices*" [9].

With respect to the classification of medical devices, the most pertinent section is *Article 9* (and its corresponding *Annex IX*), which dictates 4 classes in total – Class I, IIa, IIb and III, according to the risk of harm to the patient when using a certain medical device. The process of deciding whether a given device should be classified, and then in which class, is facilitated by rules defined according to the device's invasiveness (invasive, non-invasive), duration of contact with a body (transient, short term, long term), dependence on an electrical source (i.e. active medical devices) and others.

Regulations applied to mobile applications

With respect to regulations of mobile medical apps, EU is "*less centralized and more efficient*" [10] in comparison with the US. Most medical apps determined as a medical device are usually qualified as Class 1, which represents the lowest risk of potential patient's harm. This specific device class does not require so many legislative processes to be approved [11].

Unfortunately, the Medical Device Directive is not comprehensive enough for properly classifying health apps, or software in general. For this purpose, "Guidelines on the Qualification and Classification of Stand Alone Software Used in Healthcare within the Regulatory Framework of Medical Devices" (MEDDEV 2.1/6, last updated on January 2012) [12] has been issued separately. Here, we can find more detailed classification of stand-alone software used for medical purposes and also some decision steps that can help us to decide whether our software is or is not to be covered by MDD.

According to this document [12], a mobile medical app can meet both the definition of a "medical device" as well as an "accessory", depending on its intended use. In addition, if the app is not incorporated into a medical device, it is determined as "stand-alone software" which belongs to the group of "active medical devices". If categorized as a medical device, it has to have a medical purpose, but there are also some exceptions [12].

One of the main criterions for determining whether an app is classified by medical device regulations is a type of action performed on a medical data. Software that is simply a patient management system or a records storage system is not considered to be regulated [13]. To be more specific, it means that if the application is used only for storing, archiving, simple searching (similar to a library system, but not in case of identifying medical findings or medical images in health records), or it is used for communicational purposes, or if it enables lossless data compression, it is not considered to be a medical device [12][13]. Any design implementation used for embellishment purposes does not make the software to be classified as a medical device either, if its improvement is not made for medical purpose (i.e. better visualization of medical images used for a patient diagnosis) [12].

Whether the software is used to support patients or influence medical care and performs some action on data, it is necessary to check the Council Directive 93/42/EEC in Article 1(2)a,b, which describes the definition of medical devices and their accessories, and check whether its intended purpose of use appears there. Here, the medical device also means "*[software] 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,...*" [8].

In case the definition of medical device does not fit to one in Article 1(2)a, but the software is an accessory to a medical device with a function of driving, monitoring performance of this device or influence the actions of medical device, it is covered by the MDD. In other cases, the software might not fall into the medical device directives. As an example, such software can be used for financial purposes, resource management and other non-medical purposes. [12]

When deciding which class the app should have, if it has already been evaluated as an active medical device, we have to follow the classification of medical devices (MEDDEV 2. 4/1 Rev. 9, June 2010), specifically Rules 9-12 describing active medical devices. If Rules 9, 10 or 11 that describe the functionality and purpose of the stand-alone software apply, then software is classified as IIa or IIb, according to the potential harm it may cause. Otherwise, Rule 12 classifies all other active medical devices as Class I, determined by their low risk or potential for harm to the patient. [14]

Steps for correct classification of the Diabetes Diary app

To illustrate this classification process, the mobile Diabetes Diary app has been used. This app is currently in the process of self-classification as a medical device, including gathering necessary documentation needed for CE-marking.

This app serves primarily as a logbook for diabetic patients. Users can make registrations about their daily food and insulin intake, blood glucose values and physical activity, including the possibility to enter notes regarding these registrations. The goal of the app is to encourage the patients to reflect upon their own entered data, thus learning how their lifestyle habits affect their blood glucose, or disease state. Due to its primary function as a logbook, this app would normally not be considered for regulation. However, there are other functions which change the classification of this app, including the ability to automatically transfer blood glucose values via Bluetooth from glucose meters, analyze input data and visualize it providing graphical feedback on a screen, approximation of BG values and calculations of blood glucose variations over a standard day. Furthermore, there is also a function that helps a user to decide insulin dosage. This function is based on simple searching in the history of the patient´s registrations within the app to find the most similar historic situation to their current situation based upon similar time, blood glucose before meal, dose of carbohydrates, and previous insulin taken. The results of this function presents the 20 most similar historic insulin dosages in the user's history.

There were also some clinical trials applied to this app, the latest one of which was related to its use by Type 1 diabetic patients [15].

Based upon these outlined functions and features, we will use the decision diagram, and the guidelines for stand-alone software (MEDDEV 2.1/6), to determine whether the Diabetes Diary app should be classified as a medical device and, therefore, covered by the MDD. If we conclude that the app should be considered as a medical device, then the next step is to determine the correct class for the app, according to the classification of medical devices document (MEDDEV 2. 4/1). An-

other useful guidance for mobile apps was published by Nictiz in November 2013 [16]. Nictiz is the "centre of expertise for standardization and eHealth" placed in Netherlands and financed by the government. This institution assists with implementation of IT standards in healthcare, and also publishes many practical overviews connected to standards, laws and regulation within this sector. [17]

Table 1 summarizes the main decision steps for classifying the Diabetes Diary app, based on combination of the float chart described by Nictiz [16] and one provided by the MEDDEV 2.1/6 [12].

Table 1 - Determination of the Diabetes Diary as a medical device and its subsequent classification [12][16]

Step	Question	Answer	Comments
Determination of Medical Device status			
1.	*Is the SW a computer program?*	Yes	A mobile health application is a computer program (according to ISO/IEC 2382-1: 1993)
2.	*Is the SW incorporated in a medical device?*	No	Since it is not incorporated, it falls under the definition of stand-alone software. If it was incorporated, the software would have to be classified according to the classification of the medical device it is part of.
3.	*Is the software performing an action on data different from storage, archival, lossless compression, communication or simple search?*	Yes	All these cases have already been explained above. However, it is important to make clear which types of actions are covered when altering the data. According to the MEDDEV 2.1/6 [12], "*...alterations may include reconstruction, lossy compression, filtering, pattern recognition, modelling, interpolation, transformation, classification, segmentation, registration (e.g. mapping a data set to a model or to another data set), calculations, quantification, qualification (e.g. comparison of data against references), rendering, visualisation, interpretation, etc.*. ". In our case, we uses some of these alterations. Thus, the software is performing an action on data.
4.	*Is the action for the benefit of individual patients?*	Yes	The app is used for gathering and evaluating the data, to help individuals manage their diabetes, with the potential to help healthcare providers make better clinical decision, if allowed, to browse through the patient's data stored in the app.
5.	*Is the action for the purposes defined in art 1.2a of MDD?*	Yes	The purpose of the app's functionalities include *"monitoring, treatment or alleviation of disease",* in this case of one's own diabetes, which fall under one of the categories defined by Article 1.2a of MDD [8]. These functionalities include monitoring the patient´s diabetes, helping the patient to manage necessary parameters (blood glucose, insulin doses, meal, and activity), and guiding an individual to make decisions regarding insulin or carbohydrates dosage.
6.	*Is it an accessory of a medical device?*	Yes	This step follows in case the previous question was answered "NO". While we did answer "YES" it is under discussion if our app could be considered as an accessory, since it is capable of transferring data from some blood glucose meters via Bluetooth. The decision depends on its intended use, since "*a product can only become an accessory to a medical device if the manufacturer of such a product establishes an intended use in conjunction with one or several medical devices*" (MEDDEV 2.1/1) [9]. Based upon either step 5 or 6, we still continue to step 7.
7.	***Result no.1: Medical device (stand-alone software) covered by MDD Annex IX as active medical device***		
Classification of the Diabetes Diary: active medical device			
8.	*Does the app contain a measurement function?*	No	For the actual state of our app, we do not use any measurement function. However, there might be some potential to use some sensors integrated into a smartphone, such as motion sensor, camera, etc. In this case we would have to verify this issue more properly. If we finally consider incorporating any measurement function into our app, we have to follow step 9.
9.	*Does the app have one of the following medical purposes:* *a. intended to administer, supply or exchange energy;* *b. intended to control, monitor or influence directly the performance of a class IIb active medical device;* *c. administer or remove medicine, energy or other substance to or from the body;* *d. intended for direct diagnosis or monitoring of vital physiological processes?*	No	As we can see, no one of the purposes described in step 9 fits to our app. However, if we decided to cover a function "*to obtain readings of vital physiological signals in routine check-ups and in self-monitoring of physiological parameters*" [14] (such as "*respiration, heart rate, cerebral functions, blood gases, blood pressure and body temperature*" [14]) it would have to be classified as Class IIa active medical device.
10.	***Result no. 2: Class 1 medical device, self-certification without intervention of notified body is allowed for CE-marking***		

After step 2 in Table 1, we can conclude that our health app is a stand-alone software falling within active medical device directives. At the end of the step 6, we have concluded that the app falls under the discretion of the MDD.

Then we can follow additional rules for active devices (9-12) of the classification of medical devices document (MEDDEV 2.4/1, Annex IX, section III.3). This part is also included in the Nictiz flowchart [16] (starting with the step no. 8) and where the most important part of the MDD´s rules applied on health apps is extracted.

Since the app does not have any measurement function, rules 9-11 of MEDDEV 2.4/1 do not apply, and we, therefore, must follow rule 12 which classifies this software as a Class I medical device. According to these observations we suggest that the app should be considered as a medical device with a low risk, which only requires self-certification [16].

If we consider incorporating a measurement function, during potential future development of the app, we would have to follow step 9, which would require the device to be validated by a notified body and assigned a CE mark [16].

Regulatory system in US

Summary of relevant Medical Device directives

In the US, the main organization responsible for medical devices regulations is The U.S. Food and Drug Administration (FDA). Nowadays, the regulation system distinguishes approximately 1,700 different types of devices separated into 16 specific groups called "panels" according to their intended use (e.g. General Hospital, Haematology, Neurology,...) [18].

The main document covering medical device regulations is the Federal Food Drug & Cosmetic (FD&C) Act [19].

This Act distinguishes three general classes of medical devices "*based on the level of control necessary to assure the safety and effectiveness of the device*" [20]. Class I requires only general controls; Class II requires, in addition to the general controls, specific controls that vary with the type of device. Class III devices require a Premarket Approval application (PMA), in addition to the general control.

General controls include e.g. device registration and listing, Premarket Notification 510(k), Good Manufacturing Practices, and others [21]. However, most of Class I and some of Class II devices are exempted from 510(k) requirements. [20]

The aim of the Premarket Notification is to compare a new medical product with one or more medical products that are already on the market. FDA then determine whether the devices are "substantially equivalent" or not [21].

Premarket Approval applies only for Class III devices and manufacturers of these devices have to prove, based on clinical data and scientific evidence, that their device is sufficiently safe. [22]

Regulations applied to medical applications

Compared with Europe, mHealth regulations in the US consider upcoming mobile technologies and stand-alone software used for health purposes in more detail.

To clarify the directives related to mobile medical apps, the FDA published the "Guidance for Industry and Food and Drug Administration Staff" [23] and updates this document regularly. The last version was issued in February 2015.

The regulatory status of a proposed product depends on its intended and indicated use. In addition, there are no flowcharts to aid a developer in the classification or regulation of their application. Instead, concrete examples of regulated applications and their features are listed within the Guidance [23] and sorted into 3 main categories of apps as a part of this Guidance (appendix A-C) [23] according to the FDA requirements. These are the "non-regulated" ones, those falling into "enforcement discretion", and those for which "regulatory oversight" is required. It is important to note that if an app falls within the scope of "enforcement discretion", it does not mean that such an app is not considered a medical device or does not need to be regulated. In this case, the FDA has the authority to decide, on a case-by-case basis, whether to place regulatory action on the product or not. However, at least for such medical apps that fall under "enforcement discretion", the FDA "*will not expect manufacturers to submit premarket review applications or to register and list their apps with the FDA*" [24].

The 2015 version of the Guidance [23], contains some noticeable changes when compared to the previous one [25], issued in 2013. The previous document dictates that mobile apps serving as an extension of a regulated medical device that "*display, store, or transfer medical device data in its original format*" are an issue for regulatory oversight. This means that if the app is used only as a display or storing place for medical data "in its original format", and does not control or alter the functions of the connected medical device, it is subject to Class I requirements, again which only require General Controls. However, in the 2015 Guidance, apps with this description are no longer mentioned within the category of "regulatory oversight". However, apps that meet the definition of Medical Device Data System (MDDS), which aim "*to transfer, store, convert format, and display medical device data in its original format from a medical device (as defined by MDDS regulation 880.6310 OUG)*" [23], are listed in the category of apps with "enforcement discretion". This category also applies to apps used for self-managing of diseases or conditions (e.g. cardiovascular disease, hypertension, diabetes or obesity) without providing any treatment, treatment suggestions or diagnosis, and, also, which enable patients to have easy access to their health information or interact with EHR. To simply remind patients to take their medication is possible, too. These apps are capable of allowing the patient to track their health information and share such data with their healthcare providers, without automatically recommending changes in their self-management or medication doses, etc. Under this classification, such apps are also allowed to perform simple and well-known calculations, e.g. Body Mass Index (BMI), mean blood pressure, and others [23][25]. Moreover, apart from the case of apps meeting the definition of an MDDS, "*mobile apps that allow a user to collect, log, track and trend data, such as blood glucose, blood pressure, heart rate, weight or other data from a device to eventually share with a heath care provider, or upload it to an online (cloud) database, personal or electronic health record*" [23] fall into "enforcement discretion", too.

To summarize, the FDA does not intend to strictly regulate apps for maintaining chronic health conditions that gather, store or share health information, as mentioned above, as long as they do not provide any treatment, diagnosis, or recommendations (e.g. in order to change prescribed medication). If an app did provide any of these, it would be a case for "regulatory oversight".

Apps considered to be regulated are, therefore, those that take the function of a medical device, e.g. using an integrated sensor (e.g. accelerometer, camera etc.) to measure physiological parameters for performing a treatment or diagnosis [23][25], or serving as the first display when collecting results of a measured value. This also applies to apps using an attachment for blood glucose measuring, which are classified as "Glucose test systems", for example the glucose meter iBGStar [26] or iHealth Align Glucometer [27]).

The impulse for lowering regulatory requirements for MDDS emerged from the growing need for inter-communication of several medical devices and health IT [28]. The MDDS were defined as Class III until 2011 and were afterward reclassified as Class I [28], yet still remained on the list of regulated systems (according to the guidance 2013 [25]). Gaining more experience with these systems, it has been demonstrated that "*MDDS devices, medical image storage devices, and medical image communication devices pose a low risk to the public*"[28]. Therefore, as it has already been mentioned above, with the arrival of the recent guidance 2015, apps being considered MDDS are under "enforcement discretion".

The FDA's "Product Code Classification Database" [29] is very useful source for developers who wish to determine whether their app should be regulated or not and, if so, which class the app falls under. One can search this database by accessing the official webpage of the FDA and search for devices similar to the one we need to classify, based on his/her inputs when filling a form on the front page of the database. Premarket notification summaries of already regulated medical devices are also accessible in official website. A particularly helpful part of these documents is a table illustrating which legally distributed and approved device is equivalent or most similar to the device being considered for approval, by displaying descriptions of existing apps with the ones needed to be approved.

It is also possible to contact the FDA Office of Compliance for determination of whether the app is a medical device or not. For classification and application decisions, the Office of Device Evaluation (ODE) is the authority which can be approached for these purposes. [30]

Steps for correct classification of the Diabetes Diary app

To determine if the Diabetes Diary app should be regulated by the FDA, and, if so, which class this app belongs to, we will compare our app with an existing one that has already been approved.

One of very few diabetes self-management apps which has received FDA clearance is the MySugr app. This app allows users to log their blood sugar values, insulin doses, meals (including the ability to take a picture of a food portion), activity and other notes [31]. It also enables the user to search in their data history, display data-analysis and graphical interpretations of the captured data, extract a printed version of report for a healthcare provider, set a blood sugar reminder, and share the information with other users, including family members. Apple Health integration and data synchronization with blood glucose meter are also possible [31]. In an interview of one of the co-founders, CEO, Frank Westermann, he declared that their app was classified as a Class I medical device in Europe and was registered with the FDA in US [32]. Here, he also mentions that "*this classification allows us to interpret treatment data and could mean that, for example, in the future we'd be able to communicate directly via a blood sugar measuring device*" [32].

We have observed that the features and purpose of the MySugr app are similar to the Diabetes Diary. Following the Guidance for mobile medical apps, we conclude that because the Diabetes Diary's purpose is to help patients with diabetes to self-manage their disease by enabling them to track, store, display and transfer medical data, in addition to enabling the individual to transfer blood glucose data from blood glucose meters, it would meet the definition of a Class I MDDS and fall under "enforcement discretion" [23].

The functionality of insulin dosage suggestions may, however, move the app into the scope of the "regulatory oversight" category, even though this tool is only based upon a simple search within the user's own history. Therefore, if the intended use is to recommend treatment, in this case medication dosage, it is indeed a case for regulatory oversight.

Discussion

It is evident that it is challenging to concretely define the boundaries between a "medical" and a "non-medical" mobile app, and to classify a medical device correctly based upon official documents.

Furthermore, the more functions the app has, the more complicated it is to make a clear decision. This is especially true if a developer decides, after receiving official approval, to further develop the app and add a function to adapt to market demands. It is not only necessary to evaluate each function separately when applying medical device regulations, but also to see the whole system and its impact on the final users and check it out when adding new functionalities.

Reading blood glucose values from an external blood glucose meter was one of the functions of the Diabetes Diary app, which made impact on how we examined the regulations. Whilst this case only deals with several finger-stick measurements captured during a day, the recent development of apps that display values from continuous glucose monitors (CGM) and share this data with other people, illustrate this foreseen challenge to both developers and authorities alike. Marketing of these apps have already been allowed by the FDA and classified as Class II, and are exempt from premarket submissions [33]. Such innovations represent a big step in diabetes self-management. Applications such as NightScout [34] or Dexcom´s app for Apple Watch [35], which allow remote monitoring of blood glucose readings using devices such as smartphones or smart watches [34], were struggling for regulatory approval. The FDA has finally approved the interoperability of Dexcom Share and Apple Watch, which should be available in US from April 2015 [36]. Thus, it is obvious that there will be more apps trying to share this type of data, which will impact their classification.

For both the EU Commission and FDA regulations, the more action performed on the data, the higher the probability of reaching the scope of medical device regulations.

Based on the directions mentioned above, developers of similar medical apps, usually serving as self-management systems, should be careful when specific alteration of captured data is performed, and/or when an app becomes a part of, or an accessory to, a regulated medical device.

Not only are added functions an issue, but the degree of sophistication and ability of singular functions, which blur the line between "simple" and "advanced". Different levels of complexity can be observed, for example, when implementing an insulin dosage calculator. Apps with this function can be

based on simple well-known calculations, where only a few parameters are needed, or more advanced calculations, where complex algorithms and more inputs are used. According to MEDDEV 2.1/6 [12] "insulin dosage planning stand-alone software" (such as bolus calculators) is clearly considered to be a medical device, and is moreover used as an example of Class IIb medical device when it influences a medical device of this Class. According to the FDA, mobile apps that perform simple calculations and that are used routinely in clinical practice are accepted to be under "enforcement discretion". However, the expression of "simple calculations" can mean different level of complexity to each individual. Nevertheless, if the intent of its use is a treatment recommendation, regulatory oversight is still required.

When searching for diabetes apps on iTunes or Google Play, there are several unregulated ones serving as an insulin dose calculator. These would, according to the directives, belong to the medical device descriptions (in both the US and the EU), whether this action was considered as a treatment recommendation. Although the developers often put warnings on their web page (if there exists any) about intended use of their app so that the product does not meet the definition of medical device, the potential risk of harm when using this app may not be sufficiently reduced by these announcements.

These examples illustrate additional concerns that we discovered during this process; who is authorized to determine what an "intended use" is for a device, i.e. individual users, developers, etc.? A product may be intended for use for one reason and effectively used for another purpose. Furthermore, based upon app descriptions on app stores or distributor websites, it can be unclear whether an app is reputable and who authorizes its use. The wording within official documents as well as advertised app descriptions can both be misleading to developers and users.

These apps displayed on Internet stores are often labelled as "medical", which may make somebody believe that it should be used for medical purposes [37]. Furthermore, there is often lack of information about whether the apps have been tested or not before being released to the market. Besides, developers often update their software based upon user or consumer desires, and not based upon medical necessity or medical regulation.

The purpose of the described regulations is not only to define and categorize a medical device, but also to ensure user´s safety and keep, or better, enhance the quality and usability of medical products. However, given the discussion presented, the evaluation and regulatory processes for the majority of the apps on the market still have many challenges regarding overall success of the rigorous application of the directives.

Conclusion

Rapid development of medical and health-related mobile apps has caught the attention of both EU and US regulatory institutions. Despite the fact that we have valid sources of information regarding related legislative issues, it is not easy for developers to interpret specific laws, directives and definitions, nor is their cooperation always enforceable, given the sheer volume of developers and apps. Therefore, the goal of this article was to provide simplified description of regulatory requirements related to mobile medical apps and also to highlight some serious issues the developers and regulatory bodies should keep in mind when inventing or designing a new product.

If a developer has some doubts about the correct classification of his/her product, or the app classified as a medical device or not, it is always better to consult the responsible organization.

Since the approaches to medical device classification and regulation of both the US and the EU systems are significantly different, it is difficult to directly compare them. As demonstrated, final steps of classification within the US system rely upon a comparison structure based upon apps which are already approved as medical devices. However, the EU system is based upon guidelines and defined rules illustrated through flow-charts which guide a developer's assessment. From a public perspective, identification of the correct classification of a regulated app often requires direct communication with its developer, because this information is not always publically available. This is especially the case for apps classified with respect to the EU regulations.

Although mobile medical apps are intended to help individuals improve their health and/or manage their disease, they all present different levels of potential risk of harm. Many of the apps that are currently available on the market and unregulated may present undetermined, or possibly higher, risk to the user, due to lack of understanding by the user or machine error.

While such classification processes present much additional work for app developers, these steps are essential to ensuring a device's quality, effectiveness, and above all, safety for end users.

Acknowledgement

The authors would like to thank the Norwegian Centre for Integrated Care and Telemedicine (NST) and the University of Tromsø for the support provided. The authors also thank Astrid Grøttland for her assistance in working on CE marking of the Diabetes Diary app. The first author is grateful to Jan Muzik for the opportunity to cooperate with NST.

References

[1] Wac K. Smartphone as a personal, pervasive health informatics services platform: literature review. Yearbook of medical informatics: Advances in an interdisciplinary science. 2012;7(1):83-93. ISSN 0943-4747.

[2] Klasnja P and Pratt W. Healthcare in the pocket: Mapping the space of mobile-phone health interventions. Journal of Biomedical Informatics. 2012, 45(1): 184-198. DOI: 10.1016/j.jbi.2011.08.017. ISSN 15320464. Available at: http://linkinghub.elsevier.com/retrieve/pii/S1532046411001444

[3] McGrath MJ, Scanaill CN. Sensor technologies: healthcare, wellness, and environmental applications. Apress. ISBN 978-1-4302-6014-1.

[4] Rigby M. Personal Health, Person-centred Health and Personalised Medicine - Concepts, Consumers, Confusion and Challenges in the Informatics World. Yearbook of medical informatics: Advances in an interdisciplinary science. 2012, (7(1): 7-15. ISSN 0943-4747.

[5] Holopainen A., Galbiati F and Voutilainen K. Use of Smart Phone Technologies to Offer Easy-to-Use and Cost-Effective Telemedicine Services. First International Conference on the Digital Society (ICDS'07). IEEE, 2007, p. 1-4. DOI: 10.1109/ICDS.2007.42. Available at:

http://ieeexplore.ieee.org/lpdocs/epic03/wrapper.htm?arnumber=4063766

[6] Silk A. Interoperability for Diabetes Diagnostic Devices and Diabetes Management Systems: Office of In Vitro Diagnostic Device Evaluation and Safety Center for Devices and Radiological Health/FDA. In: Public Workshop - Regulatory Science Considerations for Software Used in Diabetes Management [presentation]. November 13, 2014 [cit. 2015-04-13]. Available at: https://collaboration.fda.gov/p8yxaqookat/?launcher=false&fcsContent=true&pbMode=normal

[7] Brief Introduction of EU Council Directive 93/42/EEC: Medical Devices. Wellkang Tech Consulting [online]. 2009 [cit. 2015-04-23]. Available at: http://www.ce-marking.org/directive-9342eec-medical-devices.html

[8] Council Directive 93/42/EEC: concerning medical devices. 14 June 1993. Available at: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CONSLEG:1993L0042:20071011:en:PDF

[9] Guidelines relating to the application of: The Council Directive 90/385/EEC on Active Implantable Medical Devices; The Council Directive 93/42/EEC on Medical Devices. Definition of "medical devices"; Definition of "accessory"; Definition of "manufacturer". In: 1994. Availableat: http://ec.europa.eu/health/medical-devices/files/meddev/2_1-1___04-1994_en.pdf

[10] Changing the rules of health care: Mobile health and challenges for regulation. Aug 2014. Available at: http://www.aei.org/wp-content/uploads/2014/08/-fellaychanging-the-rules-of-health-care_100901289367.pdf

[11] How supportive is the regulatory framework for mobile health applications?. PwC: mHealth Insights. January 2013. Available at: http://www.pwc.com/gx/en/healthcare/mhealth/mhealth-insights/mhealth-insights-regulatory-frameworks-for-mobile-health-applications.jhtml

[12] MEDDEV 2.1/6. Guidelines on the Qualification and Classification of Stand Alone Software Used in Healthcare within the Regulatory Framework of Medical Devices. EU: EUROPEAN COMMISSION, Jan 2012. Available at: http://ec.europa.eu/health/medical-devices/files/meddev/2_1_6_ol_en.pdf

[13] Borderlines with medical devices: Guidance on legislation. MHRA: Regulating Medicines and Medical Devices. Feb 2014, s. 12. Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/284505/Borderlines_with_medical_devices.pdf

[14] MEDDEV 2. 4/1 Rev. 9. Medical Devices: Guidance document - Classification of medical devices: Guidelines relating to the application of the Council Directive 93/42/EEC on medical devices. European Commission, June 2010. Available at: http://ec.europa.eu/growth/sectors/medical-devices/documents/guidelines/files/meddev/2_4_1_rev_9_classification_en.pdf

[15] Skrøvseth SO, Årsand E, Godtliebsen F and Joakimsen RM. Data-Driven Personalized Feedback to Patients with Type 1 Diabetes: A Randomized Trial. Diabetes Technology & Therapeutics [online]. 2015 [cit. 2015-05-26]. DOI: 10.1089/dia.2014.0276.

[16] Ekker A and van Rest B. Infographic: Medical apps, is certification required?: Check whether your app requires CE marking. In: Nictiz: Betere zorg door betere informatie [online]. Nov 2013 [cit. 2015-03-20]. Available at: http://www.nictiz.nl/page/Publicaties?mod%5B360%5D%5Bi%5D=988

[17] NICTIZ. Centre of expertise for standardisation and eHealth: Providing guidance at the interface of healthcare and IT. Netherlands. Available at: http://www.nictiz.nl/module/360/1097/Corporate%20brochure%20Nictiz_EN.pdf

[18] Classify Your Medical Device. FDA: U.S. Food and Drug Administration [online]. July 2014 [cit. 2015-04-13]. Available at: http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/ClassifyYourDevice/default.htm

[19] Federal Food, Drug, and Cosmetic Act (FD&C Act). FDA: U.S. Food and Drug Administration [online]. March 2015 [cit. 2015-04-25]. Available at: http://www.fda.gov/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticActFDCAct/default.htm

[20] Understanding Medical Device Regulation for mHealth: A Guide for Mobile Operators GSMA. February 2012. Available at: http://www.gsma.com/connectedliving/wp-content/uploads/2012/03/gsmaunderstandingmedicaldeviceregulationformhealthreport1.pdf

[21] General Controls for Medical Devices. FDA: U.S. Food and Drug Administration [online]. June 2014 [cit. 2015-04-23]. Available at: http://www.fda.gov/medicaldevices/deviceregulationandguidance/overview/generalandspecialcontrols/ucm055910.htm

[22] Premarket Approval (PMA). U.S. Food and Drug Administration [online]. August 2014 [cit. 2015-04-25]. Available at: http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/PremarketApprovalPMA/default.htm

[23] Mobile Medical Applications: Guidance for Industry and Food and Drug Administration Staff. February 9, 2015. Available at: http://www.fda.gov/downloads/MedicalDevices/.../UCM263366.pdf

[24] Mobile Medical Applications. FDA: U.S. Food and Drug Administration [online]. April 2014 [cit. 2015-04-16]. Available at: http://www.fda.gov/medicaldevices/productsandmedicalprocedures/connectedhealth/mobilemedicalapplications/default.htm

[25] Mobile Medical Applications: Guidance for Industry and Food and Drug Administration Staff. February 9, 2013

[26] IBGStar® blood glucose meter. MyStar: Sanofi Daibetes [online]. 2014 [cit. 2015-04-13]. Available at: http://www.mystarsanofi.com/web/products/glucometers/ibgstar

[27] iHealth Align. iHealth [online]. 2015 [cit. 2015-04-13]. Available at: http://www.ihealthlabs.com/glucometer/ihealth-align/

[28] Medical Device Data Systems, Medical Image Storage Devices, and Medical Image Communications Devices: Guidance for Industry and Food and Drug Administration Staff. February 9, 2015. Available at: http://www.fda.gov/ucm/groups/fdagov-public/@fdagov-meddev-gen/documents/document/ucm401996.pdf

[29] Product Classification. FDA: U.S. Food and Drug Administration [online]. 2015 [cit. 2015-04-13]. Available at: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpcd/classification.cfm

[30] Device -- Not a Device. FDA. U.S. Food and Drug Administration [online]. Sept 2014 [cit. 2015-04-18]. Available at: http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/ClassifyYourDevice/ucm051521.htm

[31] MySugr [online]. [cit. 2015-03-19]. Available at: https://mysugr.com/

[32] Kuepper M. Startup of the Week – MySugr: the app that wants to make diabetes treatment "more fun". In: VentureVillage [online]. 13.9. 2013 [cit. 2015-03-19]. Available at: http://venturevillage.eu/startup-of-the-week-mysugr

[33] FDA permits marketing of first system of mobile medical apps for continuous glucose monitoring: Data-sharing capability allows caregivers to monitor patient's blood sugar levels remotely. In: FDA: U.S. Food and Drug Administration [online]. Jan 2015 [cit. 2015-04-13]. Available at: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm431385.htm

[34] Nightscout: We Are Not Waiting. NIGHTSCOUT PROJECT. [online]. 2015 [cit. 2015-04-25]. Available at: http://www.nightscout.info/

[35] Broussard M. Apple Watch Set to Include Third-Party Glucose Tracking App at Launch. In: MacRumors: news and rumors you care about [online]. Feb 2015 [cit. 2015-04-13]. Available at: http://www.macrumors.com/2015/02/09/apple-watch-dexcom-glucose-app/

[36] Dexcom Introduces Apps That Enable the First Ever Continuous Glucose Monitoring (CGM) on the Apple Watch™. In: Dexcom: One Step Ahead [online]. Apr 2015 [cit. 2015-04-13]. Available at: http://www.dexcom.com/news/dexcom-continuous-glucose-monitoring-cgm-apple-watch

[37] Eng DS and Lee JM. The Promise and Peril of Mobile Health Applications for Diabetes and Endocrinology. Pediatric Diabetes [online]. 2013, vol. 14, issue 4, p. 231-238 [cit. 2015-04-22]. DOI: 10.1111/pedi.12034.

Address for correspondence

Anna Holubová, Czech Technical University in Prague, Faculty of Biomedical Engineering, Sitna sq. 3105, 272 01 Kladno, Czech Republic

e-mail: holubann@fbmi.cvut.cz