The Regulation of Medical Device Apps

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Relevant Guidelines

- MEDDEV 2.1/6 “Guidelines on the Qualification and Classification of Stand Alone Software Used in Healthcare with the Regulatory Framework of Medical Devices”. To view please click here.
- MEDDEV. 2.7.1 Rev.3 “Clinical Evaluation: A Guide for Manufacturers and Notified Bodies”. To view please click here.
- EN ISO 13485:2012 "Medical devices - Quality management systems -- Requirements for regulatory purposes”. To view please click here.
- Mobile Medical Applications - Guidance for Industry and Food and Drug Administration Staff. To view please click here.
- EN IEC 62304:2006 "Medical device software - Software life cycle processes”. To view please click here.

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1 Purpose

This report explains the regulatory considerations that apply to mobile apps with medical applications (medical mobile apps) in the European Union (EU) and United States of America (USA). It sets out the circumstances when a medical mobile app is considered to be a medical device and the regulatory processes that apply to medical mobile apps that meet the regulatory definition of medical devices in these territories. Having explained the background to the regulation of medical mobile apps the report then provides answers to questions specifically posed by the University and WEAHSN in the briefing document that prompted the preparation of this report and questions raised after this report was initially issued.

2 Scope

This report is concerned with the relevancy of medical device regulations to mobile apps and does not deal with consumer protection, data privacy and other legislation that may apply. While the advice is particular to mobile medical apps it is also relevant to the regulation of other standalone software such as healthcare analytic, treatment planning and decision support software systems. The advice and guidance provided in this report is based on the latest guidance available from the regulatory authorities in these regions and where relevant published guidance by these authorities is referenced in the text. However, it is important to note that the regulations and the guidance that this report is based on is somewhat interpretative in nature and it is always advisable to confirm the regulation of any specific medical mobile app with the relevant regulatory authority. Such consultation is particularly advised for medical mobile apps as they represent a newly emerging technology for which the regulatory regime is still being clarified.
3 The Regulation of Medical Devices in Europe and the USA

In order to appreciate the regulatory considerations that apply to medical mobile apps in the EU and the USA it is first necessary to understand how medical devices are regulated in these territories.

3.1 Medical Device Regulation in Europe (CE Marking)

The regulation of medical devices in the EU is governed by the CE Marking process. When a medical device bears the CE Marking it means that it has been shown to meet requirements for safety and performance that have been agreed by the European Commission and published in one of the so called medical devices directives. Bearing the CE Marking means that the medical device can be freely traded (i.e. no barrier may be placed on its trade) throughout all of the European Union member states and the wider European Free Trade Area (EFTA). There are in fact three medical devices directives; the Medical Device Directive (MDD), the Active Implantable Device Directive (AIMDD) and the In-Vitro Diagnostic Directive (IVDD). The AIMDD is not dealt with in this report as it is not considered applicable to mobile medical apps. Each of these directives has been transposed into the national laws of each of the member states. It is therefore a legal requirement in each of these countries for any medical device to bear the CE Marking before it can be traded in that country. It is important to note that the medical devices directives and the associated national legislation only apply to a product when it meets the definition of a medical device as defined by the relevant directive. This is an important consideration for mobile medical apps and will be discussed in detail in section 4.1 later.

Once it has been established that a device meets the definition of a medical device then the manufacturer can undergo the conformity assessment procedure that demonstrates that the device in question does meet the requirements for safety and performance that is set forth in the relevant directive. The conformity assessment procedure that is to be followed is directed by the relevant directive and is determined by the way that the device is classified under that directive. For example the MDD recognises four device classifications; Class I, Class IIa, Class IIb and Class III, which have increasingly stringent conformity assessment procedures. The conformity assessment procedure for all classes, except devices in Class I, must be performed by a third party organisation referred to as a Notified Body. The conformity assessment procedure for Class I devices is actually performed by the manufacturer themselves unless the device has a measuring function when a Notified Body must assess...
the conformance of that measuring function. A Notified Body must also assess the conformity of Class I devices that are presented in a sterile condition but this is not relevant to mobile apps.

Notified Bodies are commercial organisations that are paid by the manufacturer to perform the assessment procedure. They are appointed by the organisation in a Member State that has the responsibility for regulating the requirements of the relevant medical devices directive in that Member State. These organisations are known as the Competent Authorities. For example the Medicines and Healthcare Products Regulatory Agency (http://www.mhra.gov.uk/) is the Competent Authority for the medical devices directives in the United Kingdom. The manufacturer of the device is free to choose any Notified Body even those that are not based in their own member state to perform the CE Marking assessment so long as the selected Notified Body has been designated to perform the required conformity assessment procedure.

The conformity assessment procedures require the manufacturer to compile a set of documentation known as “the technical file” that provides the evidence that the device in question fulfils the essential requirements for performance and safety that are set out in the directive. The conformity assessment procedure also involves the demonstration that there is a suitable quality management system in place to control in whole or in part the design, manufacture and final inspection of the device. As explained above unless a Class I medical device is involved, the assessment of the technical file and the quality management system must be performed by a Notified Body. When satisfied that the technical file provides the evidence that the device meets the essential requirements and the relevant quality management system elements are in place, the Notified Body may allow the CE Marking to be placed on the device. For Class I medical devices, this assessment is performed by the manufacturer themselves and they may apply the CE Marking to the device themselves. The manufacturer of the device must draw up a document known as “the declaration of conformity” before making the device available on the EU Market. Manufacturers of class I devices must also register the device with the competent authority in their own member state. This registration is performed by the Notified Body for other classes of device.

Once CE Marking has been obtained and the device has been released to the market the manufacturer is obliged to have procedures in place to monitor the performance of the device on the market (known as post market surveillance) and to identify and report incidents that involve the device in the death or serious deterioration in health of a patient or
other user of the device to the relevant competent authorities (known as regulatory vigilance). Notified Bodies must also monitor the conformance of the manufacturer after the device is released to the market. This is performed through periodic audits of the manufacturer’s quality management system in a process known as surveillance inspection. The CE Marking certificates issued by Notified Bodies also have expiry dates, typically three years. After the certificate expires, the CE Marking of the device is no longer valid and the manufacturer must apply to have the conformity assessment procedure done again in order to maintain the CE Marking. This is known as re-certification.

A more detailed description of the CE Marking process for a mobile medical device app is provided in section 4.1.

The CE Marking process for in-vitro diagnostic devices under the IVDD works in a similar manner to the MDD. However, it is only devices that diagnose the specific conditions that are listed in Annex II of that directive that must involve a Notified Body in the conformity assessment process. All other in-vitro diagnostic devices that do not diagnose the conditions listed in Annex II of the directive go through a self-assessment process that is performed by the manufacturer themselves. The exception being in-vitro diagnostic devices that are intended for self-testing by the patient which must involve a Notified Body in the assessment of the features related to self-testing.

3.1.1 The Recast of the Medical Devices Directives

The preceding discussion concerns the regulation of medical devices in Europe as it currently stands. However it is very important to note that these directives are currently undergoing revision with the intention that they will be recast as regulations rather than directives. The MDD will become the Medical Device Regulation and the IVDD will become the In Vitro Diagnostic Devices Regulation. As regulations, they will no longer need to be transposed into the national laws of the member states and they will be applied directly. It also means that there will be new more stringent requirements that medical devices must meet as part of the CE Marking process and after the device is released to market. Although the general nature of the CE Marking conformity assessment procedures will not change, the processes involved will be considerably more stringent with a higher burden of evidence required to demonstrate conformance to the regulation’s requirements. It also means that many device types will be reclassified so that they will be subject to a more stringent conformity assessment procedure. This is most relevant to in-vitro diagnostic devices under the IVDD.
because many of these types of devices that are currently self-assessed will require the involvement of a Notified Body in their CE Marking after the regulation comes into effect. It is anticipated that these regulations will come into effect in 2016. Anyone developing a medical device that is due for release after the regulation comes into effect needs to take account of the relevant regulation’s requirements. Even devices that are currently CE Marked or achieve CE Marking before these regulations come into effect will need to comply with the regulation for re-certification.

3.2 Medical Device Regulation in the USA

The sale of medical devices in the US is regulated by the US Food and Drug Administration (FDA), an agency of the US government. The FDA is responsible for enforcing medical device regulations that determine when a product is considered to be a medical device and the classification of that device. There are three classifications that may be assigned to medical devices under these regulations. Class 3 is assigned to devices that pose a high degree of risk in their application but this risk is justified by the benefit provided by the device. Class 3 is also automatically assigned to novel devices that are of a type FDA have not encountered before. Class 2 covers devices that are of a moderate level of risk and are a type of device that FDA has previous experience of. This covers the majority of devices on the market. Class 1 covers devices that involve very low levels of risk in their application or have been on the US Market for a very long time. The classification of the device determines the process by which the device is cleared for use on the US market by the FDA.

Class 1 devices are subject to a process referred to as pre-market notification. This involves providing notification to FDA of the intention to place the device on the market by registering details of the device and the manufacturer on a designated FDA data base. In addition, the device must be labelled in accordance with FDA’s regulation for device labelling. Labelling refers to the labels on the product, the user documentation that accompanies the product and any other document that provides direction on the use of the device e.g. product catalogues, web sites, marketing literature, advertisements.

Class 2 devices are subject to a pre-market notification process that involves submitting a notification document 510(k) to FDA. The purpose of the 510(k) is to provide evidence that the proposed device is substantially equivalent to a device that the FDA has already cleared to market, referred to as the predicate device. In order to demonstrate substantial equivalence, the proposed device must have the same intended use as the chosen...
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predicate device and if there are any differences in the technological characteristics of the
device, then the proposed device must not raise any new or additional efficacy or safety
concerns above those that are raised by the predicate device. The FDA reviews the 510(k)
and if they determine the proposed device to be substantially equivalent to the predicate
device they clear the device to the US market. This review by law is required to be
performed within 90 days but is usually extended beyond this time due to the pauses in the
review clock that occur as a result of the manufacturer responding to FDA questions and
requests for additional information. Once the device is cleared, the manufacturer must
comply with the registration and labelling requirements of the FDA before selling the device
in the US. In addition, the device must be manufactured in accordance with the FDA’s good
manufacturing practices for medical devices set out in the regulation 21 CFR 820. The
compliance of the manufacturing arrangements is not verified by FDA during the 510(k)
review process. However once the device has been cleared to market the FDA are entitled
to inspect these manufacturing arrangements for their compliance at any time.

Class 3 devices must be pre-approved by FDA before they can be placed on the US market
in a process known as pre-market approval (PMA). The PMA process involves the
manufacturer providing the evidence to FDA in a set of submission documents (PMA) that
the device is safe and effective in its own right and not by comparison to a predicate device.
This means that the device must be proven to not only achieve the intended use that is
claimed for it but that it does not cause any unnecessary harm to the patient or end user in
achieving that intended use. For this reason the PMA process relies heavily on the evidence
obtained from human clinical trials. It is also required for FDA to confirm that the
manufacturing arrangements for the device conform to 21 CFR 820 as part of the PMA
process by inspecting these arrangements. This is known as pre-approval inspection. This
makes the PMA process substantially longer and more onerous than the 510(k) process.
The PMA review time is 180 days which is usually considerably extended in view of the
questions that arise. PMA also costs about $260,000, whereas the 510(k) review costs about
$5,000, although reduced fees are available for small manufacturers.
4 The Regulation of Medical Mobile Apps

4.1 European Regulation of Medical Mobile Apps under the Medical Device Directive (MDD)

From the overview of the CE Marking process in section 3.1 it should be clear that a medical mobile app would only be subject to CE Marking if it meets the definition of a medical device under either the MDD or the IVDD. These directives define a medical device as:

- “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”.

This definition means that a mobile app can only be considered to be a medical device if its intended purpose is one of those set out above, i.e. diagnosis, prevention, monitoring, treatment or alleviation of disease, injury or handicap, investigation, replacement or modification of the anatomy or of a physiological process or the control of conception.

Another important definition under the directives is that of an accessory. An accessory is “an article which whilst not being a device is intended specifically by its manufacturer to be used together with a device to enable it to be used in accordance with the use of the device intended by the manufacturer of the device”. Accessories must also be CE Marked under the directive. The converse of this is that if a medical mobile app does not meet the definition of a medical device or of an accessory then it does not require CE Marking before it is placed on the market. In fact to CE Mark a medical mobile app that does not meet the definition of a medical device or an accessory is considered misplacement of the CE Marking and is not
allowed under the directives. In such circumstances the Competent Authority in the manufacturer’s member state must see that the CE marking is removed from the device.

When determining if a medical mobile app meets the definition of a medical device or accessory it is the intended purpose of the app that is considered. This intended purpose is defined as the “use for which the device is intended according to the data supplied by the manufacturer on the labelling, in the instructions and/or in promotional materials”. It is therefore the claims that the manufacturer makes about a medical mobile app either within the app itself (labelling), instructions for use provided with the App and in promotional materials (e.g. advertising, websites, brochures etc.), which are considered to determine whether an app is a medical device or not. It is important to be aware that if the intended purpose of the device evidently meets the definition of a medical device or an accessory, it will still be considered a medical device that must undergo CE Marking despite any disclaimers made by the manufacturer.

From a regulatory context medical mobile apps are considered to be standalone software. It was clarified in a recent amendment to the MDD that stand alone software can be considered a medical device in itself. To provide further clarification around this concept the European Commission issued a guidance document on the regulation of standalone software under the medical devices directives. Although written to consider standalone software in general when used in a healthcare setting this guidance document is of great relevance to mobile apps with medical features. It was this guidance that clarified that it is the intended purpose that determines if the app is to be considered a medical device or not. It also sets out, with illustrative examples, the qualification criteria that make stand-alone software a medical device. The following figure extracted from the guidance serves to illustrate the circumstances when stand-alone software such as a mobile app can and cannot be considered a medical device that is subject to CE Marking under the MDD.
Figure 1 Decision Flow Chart to determine if Stand Alone Software qualifies as a Medical Device

START

1. Is the software a computer program? (cf. ISO/IEC 2382-1)
   - No
   - Yes

2. Is the software incorporated in a medical device?
   - No
   - Yes

Stand-alone software

3. Is the software performing an action on data different from storage, archival, indexing, compression, communication or simple search?
   - No
   - Yes

4. Is the action for the benefit of individual patients?
   - No
   - Yes

Not a medical device

5. Is the action for the purposes defined in Art 1.2a of MDD?
   - No
   - Yes

Part of a medical device

6. Is it an accessory of a medical device?
   - No
   - Yes

Such as software driving, monitoring, performance of, or influencing performance of, or the use of a medical device

Covered by the medical device directives

Not covered by the medical device directives
The illustrative examples in the guidance clearly identify situations when stand-alone software such as mobile apps can be definitely considered to be medical devices and when they definitely cannot be medical devices. Under the former category, stand-alone software that is definitely considered to be medical devices are:

- **Software** that is intended to create or modify medical information where such modifications are made to facilitate the perceptual and/or interpretative tasks performed by healthcare professionals reviewing the medical information to make diagnostic or therapeutic decisions
- **Software** that is intended to be used for the benefit of individual patients by the evaluation of data related to that patient to support or influence the medical care provided to that particular patient

Under the category of stand-alone software that is not considered to be a medical device are:

- **Digital documents** including image files, DICOM files, digital ECG recordings, numerical results from tests and electronic health records
- **Software** that does not perform an action on data, or performs an action limited to storage, archival, communication, simple search functions or lossless compression (i.e. using a compression procedure that allows the exact reconstruction of the original data)
- **Software** that alters the representation of data for mere embellishment purposes and not to provide diagnostic interpretations of that data
- **Software** which, is not for the benefit of an individual patient such as software that aggregate population data, provide generic diagnostic or treatment pathways, scientific literature, medical atlases, models and templates and software for epidemiologic studies or registers
- **Software** intended for non-medical purposes such as invoicing or staff planning

The MHRA have recently issued their own guidance on the regulation of medical device standalone software (including apps). This guidance can be accessed at the following link:


This MHRA guidance has provided further clarification on the types of mobile apps that the MHRA consider should be regulated as medical devices. These include apps that monitor a patient and collects information that is entered by the user, measured by the app itself or collected by a point of care device if the output affects the medical treatment of an individual.
It also provides clarification on decision support software. Such software is not considered a medical device if it only provides information to enable a healthcare professional to make a clinical decision that is reliant on the professional knowledge of that professional. However it is considered a medical device if it performs a calculation or interprets or interpolates or otherwise manipulates the data to assist the healthcare professional make a clinical decision. Another important clarification is that software that carries out complex calculations that are intended to replace the clinician’s own calculations for one of the medical purposes defined by the relevant directive is also a medical device.

Once it is determined that a mobile app is a medical device under the MDD, it can then be classified to determine the conformity assessment procedure that is required for its CE Marking. Classification under the MDD is determined by classification rules set out in the directive. The most relevant rules to mobile apps are those which relate to active devices. Standalone software such as mobile app is considered to be an active device as is made clear by the EC guidance document discussed later. The relevant rules for active devices for mobile apps are:

- **Rule 9** which states that active therapeutic devices intended to administer or exchange energy are in Class IIa unless their characteristics are such that they may administer or exchange energy to or from the human body in a potentially hazardous way in which case they are in Class IIb. They may also be in Class IIb if they are intended to directly influence active therapeutic devices that are in Class IIb.
- **Rule 10** which states active devices intended for diagnosis are in Class IIa but only:
  - o if they are intended to supply energy which will be absorbed by the human body, except for devices used to illuminate the patient’s body, in the visible spectrum,
  - o if they are intended to image in vivo distribution of radiopharmaceuticals,
  - o if they are intended to allow direct diagnosis or monitoring of vital physiological processes. However if they are specifically intended for monitoring of vital physiological parameters, where the nature of variations is such that it could result in immediate danger to the patient, they are in Class IIb,
- **Rule 12**, which states that all other active devices not covered by the other rules are in Class I.

These rules show that a mobile app can potentially be classified as Class I, IIa or IIb. Classes IIa and IIb require the involvement of a Notified Body in the CE Marking process. The CE Marking process for Class I devices does not require the involvement of a Notified Body and is performed by the manufacturer of the device unless the device performs a
measuring function. When a Class I device includes a measuring function a Notified Body must be involved in the CE Marking process but only in relation to the measuring function.

The self-assessment process for Class I medical devices essentially involves the manufacture compiling the set of documents known as the technical file that demonstrates the device meets the requirements for performance and safety that are set out the directive. A critical essential requirement for a device that incorporates software or is software (as is the case of an app) is the requirement that it must be validated according to the state of the art taking into account the principles of development lifecycle, risk management, validation and verification. In practical terms this means that the following documents must be produced during the development of the app:

- A documented plan that covers the steps outlined below
- An initial risk analysis & evaluation that identifies and evaluates the risks associated with the software and identifies mitigation measures to address those risks that are evaluated to be unacceptable. Such risks must be addressed by eliminating them through the design of the app, by including alerts in the app and where necessary alerting the user to their presence
- A requirement specification document that states the design requirements that the app must meet including requirements related to the risk mitigation measures identified in the previous step
- A design specification document that states how the requirements are to be implemented into the programming of the app
- The coding of the app itself. It is important that this coding is led by the design specification and not vice versa. A CE Marking requirement that must be implemented is that the medical device features of the app must display the CE Mark but this must not appear on any non-medical features of the app
- A test plan(s) that states the test cases and acceptance criteria that verify that the app has been coded in a manner that meets the requirements of the design specification and can achieve the functionality stated in the requirement specification
- The executed test plan(s) that report the results of the test cases in the test plans and states whether the acceptance criteria of the test plan(s) has been met
- A final risk analysis & evaluation that re-evaluates the risks associated with the software after the risk mitigation measures have been implemented and verified
- A risk management report that states the residual risks (i.e. risks remaining after risk mitigations have been implemented) and acceptability of the overall risk of the App, verifies that each of the preceding steps have been performed and states how risks are
to be further evaluated during the post marketing surveillance phase (i.e. after the device has been launched to market)

In addition to the documentation described above the following documents would also be required to compile the technical file that is necessary for the self-assessed CE Marking process:

- A general description of the app
- A description of how the app works to achieve its intended medical purpose
- An essential requirements check list. This is a document that lists each of the essential requirements of the MDD and states how the device conforms to each requirement or why particular requirements are not applicable and makes reference to any standards that are applied to demonstrate conformance.
- A clinical evaluation. This is essentially a literature review that provides the supporting evidence based on scientific peer reviewed literature that the device is capable of achieving the medical purpose that is claimed for it. The guidance document MEDDEV 2.7.1 Rev.3 (to view please click here) has been issued by the EC to provide guidance on clinical evaluations and should be followed when compiling this literature review
- Screen shots of any features of the app that provide instructions for its use and copies of any documents that are supplied with the app to instruct its use
- Procedures to direct the means by which the manufacturer will review experience gained after the app is released to the market and implement any necessary corrective action (known as Post Market Surveillance) and to notify the Competent Authorities for medical devices in each member state (e.g. MHRA in the UK) of certain types of incidents involving the device (known as Regulatory Vigilance)
- A Declaration of Conformity, which is a signed declaration by an appropriately authorised authority of the manufacturer that the App has been demonstrated to conform to the essential requirements of the MDD and that this conformance has been demonstrated following the Annex VII process

As discussed in section 3.1 after compiling the technical file and signing the declaration of conformity the manufacturer of a Class I device must also register the device with the competent authority in their member state and maintain procedures for post market surveillance and regulatory vigilance.

The CE Marking process for Class IIa and Class IIb devices that could also be applicable to medical mobile apps also requires the manufacturer to compile a technical file and maintain post market surveillance and regulatory vigilance procedures. The main difference is that
these must be assessed by a Notified Body. In addition the Notified Body must also inspect the device itself and/or elements of the quality management system that the manufacturer has established to control the design, manufacture and final inspection of the device. The MDD allows a number of CE Marking procedures for Class IIa and IIb devices but due to the nature of mobile apps the only practical option involves the Notified Body inspecting the design, development and release of the mobile app and the quality management system that was used to control these activities. The international standard EN ISO 13485 (to view please [click here](#)) or quality management systems for medical devices is considered to be harmonised to the requirements of the MDD. For that reason the Notified Body will expect to perform its inspection of the quality management system against the requirements of this standard.

4.1.1 European Regulation of Medical Mobile Apps under the In Vitro Diagnostic Directive (IVDD)

It was discussed previously in this report that a mobile app that meets the definition of a medical device can be regulated by either the MDD or the IVDD. The MEDDEV 2.7.1 EC guidance referenced in the previous section clarifies that stand-alone software that fulfils the definition of a medical device and is intended to provide information derived from the in-vitro examination of a specimen derived from the human body is covered by the IVDD and therefore must be CE Marked under the provisions of that directive and not the MDD. It is further clarified that if the stand-alone software derives its information solely from an in-vitro medical device or a combination of in-vitro and medical devices then it is covered by the IVDD so long as the information is collected and analysed to serve a purpose covered by the definition of an in-vitro diagnostic device in the IVDD. The IVDD defines an in-vitro diagnostic device as:

- “any medical device which is a reagent, reagent product, calibrator, control material, kit, instrument, apparatus, equipment, or system, whether used alone or in combination, intended by the manufacturer to be used in vitro for the examination of specimens, including blood and tissue donations, derived from the human body, solely or principally for the purpose of providing information:
  - concerning a physiological or pathological state, or
  - concerning a congenital abnormality, or
  - to determine the safety and compatibility with potential recipients, or
However if the information is derived from medical devices only then it is a medical device covered by the MDD. These principles are depicted in the flow chart extracted from the EC guidance presented in Figure 2 below.
4.2 US Regulation of Medical Mobile Apps

FDA has issued their own guidance document on the subject of medical mobile apps (to view please click here). This clarifies the type of mobile apps that FDA intend to regulate as medical devices, those that they do not intend to regulate as medical devices and those that while meeting the definition of a medical device they will apply enforcement discretion to.

According to this guidance the categories of mobile apps that FDA intend to regulate as medical devices include:

- Mobile apps that are an extension of one or more medical devices by connecting to such device(s) for purposes of controlling the device(s) or displaying, storing, analysing, or transmitting patient-specific medical device data
- Mobile apps that transform the platform on which they are carried by use of attachments, display screens, or sensors or by including functionalities similar to those of currently regulated medical devices
- Mobile apps that perform patient-specific analysis and provide patient-specific diagnosis, or treatment recommendations

Any apps in these categories will be regulated as medical devices by FDA in accordance with the classification that is assigned to it as explained in section 3.2 of this report.

The categories of apps that FDA does not consider to be medical devices include:

- Mobile apps that are intended to provide access to electronic “copies” of medical textbooks or other reference materials with generic text search capabilities
- Mobile apps that are intended for health care providers to use as educational tools for medical training or to reinforce training previously received
- Mobile apps that are intended for general patient education and to facilitate patient access to commonly used reference information
- Mobile apps that automate general office operations in a health care setting and are not intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease
- Mobile apps that are generic aids or general purpose products

Finally the apps that FDA intends to exercise enforcement discretion are listed below. This means that such apps may or may not meet the definition of a medical device but in any case FDA does not intend to regulate their use. These include:
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- Mobile apps that are intended to help patients (users) self-manage their disease or conditions without providing specific treatment or treatment suggestions
- Mobile apps that provide patients with simple tools to organize and track their health information
- Mobile apps that provide easy access to information related to patients' health conditions or treatments
- Mobile apps that help patients document, show, or communicate potential medical conditions to health care providers
- Mobile apps that automate simple tasks for health care providers
- Mobile apps that enable patients or providers to interact with Electronic Health Records
5 Answers to Specific Questions

1). How can we tell whether the apps we are developing are likely to fall under MDD/IVDD? Is it possible to produce a questionnaire to guide decision making?

Guidance on when a mobile app is considered to be a medical device is in section 4.1 of this report. The key consideration in determining whether a mobile app is a medical device is if it meets the definition of a medical device under the MDD or the IVDD. To be a medical device it must have an intended purpose that is the diagnosis, prevention, monitoring, treatment or alleviation of disease, injury or handicap, investigation, replacement or modification of the anatomy or of a physiological process or the control of conception. It would also be regulated as a medical device if it was not a medical device but met the definition of an accessory to a medical device. In is an accessory when it is specifically intended to be used with a medical device to assist the medical device to achieve its intended purpose. The flow charts extracted from the EC guidance document provided in section 4.1 of this report can guide the decision making process to determine if a mobile app is a medical device and if it is a medical device if it is the MDD or the IVDD that applies. The following series of questions may also assist the decision making process:

- What is the purpose of the information that is provided by the app? →
  If it is intended to be used for one of the purposes defined by the MDD (i.e. diagnosis, prevention, monitoring, treatment or alleviation of disease or diagnosis, diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap or investigation, replacement or modification of the anatomy or of a physiological process or prevention, monitoring, treatment or alleviation of disease or control of conception) it may be a medical device if one or more of the other conditions explained below also apply. If the intended purpose is not covered by the MDD then it is not a medical device. It is important to note that the intent of the use is evaluated based on the use stated or implied by the manufacturer of the device regardless of any disclaimers made by the manufacturer.

- How does the information that the app provides relate to the source data? →
  If the app calculates, interprets, interpolates, enhances or otherwise manipulates the source data to provide its output information and this is used for a medical purpose defined by the MDD or the IVDD then it would be considered a medical device. However if the app does not meaningfully change the data (e.g. storage, archival, communication, ‘simple search’ or lossless compression) and is just used to communicate this information to the healthcare provider it is not a medical device.
This is because the healthcare provider is considered to be reliant on their own judgement of the source data to make their clinical decisions

- How much does the healthcare provider depend on the information provided by the app to make a diagnostic or therapeutic decision? → If the app performs a calculation, interpretation or other manipulation of data to provide the information that the healthcare provider then uses to make a clinical decision without reviewing the source data then the app is considered to have an influence on the clinical decision and for that reason is likely to be considered a medical device. Similarly if the app performs calculations that replace any calculations that the clinician would normally do before reaching a clinical decision it is also likely to be considered a medical device

- Who has access to the information provided by the app? → Is it just the healthcare provider or does the person that the information pertains to (the patient) also have access to this information. If the patient has access to the information could it influence any therapeutic measures that they would administer to themselves?

- Is the information provided intended to be used for the medical benefit of individuals? → If the information provided by the app is intended to be used for the evaluation of data to support or influence the medical care provided to an individual then it would be considered a medical device. But if the information relates to generic diagnostic or treatment pathways and not the diagnosis or treatment of a particular individual then it would not be considered a medical device

- What is the source of the data that the app calculates, interprets or otherwise manipulates to provide the information that influences clinical decisions? → If any of the data that the app manipulates to provide information influencing a clinical decision comes from an IVD Medical Device then it is subject to the IVDD and not the MDD

2). Is this likely to change soon?
As discussed in section 3.1.1 of this report the MDD and the IVDD are currently under revision and this will result in these directives been recast as regulations that are anticipated to come into effect possibly as early as 2016. However based on the wording of the draft regulations the considerations that are discussed in this report and summarised above as to when a mobile app is considered a medical device are not likely to change. The draft medical device regulation also does not change the classification rules that are applicable to mobile apps or the associated conformity assessment procedures that are discussed in section 4.1 of this report. However, these conformity assessment procedures are likely to be...
The Regulation of Medical Device Apps

more rigorously applied given the increased scrutiny that is implied by the draft regulations. The greatest change that can be anticipated is for those mobile apps that fall under the in vitro diagnostic devices regulation (IVDR). Under the regulation most mobile apps that would be self-assessed under the IVDD will require the intervention of a notified body. It is also likely that more clear guidance on the regulation of mobile apps will come from the European Commission and the competent authorities for medical device regulation in the member states as policies in this area are in an early stage of development.

3). Likewise FDA

FDA have issued clear guidance on when a mobile app is not considered a medical device, when a mobile app will be subject to FDA regulation of medical devices, and when a mobile app is considered to be a medical device but will not be subject to FDA medical device regulation. This FDA guidance is discussed in section 4.2 of this report.

4). What other legislation/ regulations/ standards should we be aware of (BS etc.)

Although outside the scope of this report there are European and national legislation on consumer protection and data privacy that are of obvious relevance to medical mobile apps. It is worth noting that the European Commission are currently formulating policies on these subjects with specific regards to their relevance to mobile apps. Public consultation on a green paper on mobile health is currently being sought and can be accessed at the following link:

The importance of harmonised standards in the CE Marking process is explained in section 4.1 of this report. A key standard in this regard is the EN ISO 13485 standard on quality management systems for medical devices discussed in section 4.1. It is also important to be aware of EN ISO14971v the harmonised standard on risk management for medical devices and EN IEC 62304vi the harmonised standard on software development lifecycle processes. A vital first step in the CE Marking of any medical mobile app is to conduct a search of the harmonised standards to identify those that are of relevance to the particular app. A list of the harmonised standards to the MDD can be accessed at the following link:
5). If we think an app will fall under MDD/IVDD/FDA then what strategies are available for us to circumnavigate this, if desired? E.g. Intended use statement perhaps with some examples.

As noted in the response to question 1 it is the intended use stated or implied by the manufacturer of the mobile app that determines if it is considered to be a medical device or not. This is the same for the MDD and the IVDD and the FDA. Under the European directives and FDA regulations the manufacturer of the mobile app is considered to be the entity that places it on the market regardless of how much that entity has been involved in the development of the app itself. It is also explained in this report that the intended use of the app will be determined by the intent of its use on the market regardless of any disclaimers made by the manufacturer. Therefore the only way to avoid being classed as a medical device is for its intended purpose to clearly not fall under the definition of a medical device under the MDD or IVVD in Europe or FDA regulation in the USA. This could be achieved by modifying the claims made for a mobile app from a medical purpose to a purpose that is not defined by the directives or regulation. For example a mobile app that interprets an image to make a medical diagnosis, which is a medical device, could be modified to a non‐medical device if it were modified so that it only communicated the image to a healthcare professional without an interpretation that would influence the clinical decisions made by that professional. Another example of this would be a mobile app that communicated a result from an in‐vitro diagnostic device with an accompanying interpretative diagnostic statement would be a medical device. However if it merely transferred the result without modification or any interpretation it would not be a medical device.

6). If we are clear that an app will fall under the directives and it is appropriate to proceed then what would we need to do differently during:

- **Design** → As explained in section 4.1 of this report the design of a medical mobile app is an essential element of the CE Marking process of the app. It is explained in that section that the documentation that comes out of the design process form key elements of the technical file that is required for CE Marking. The main difference between the design of medical mobile apps and non‐medical mobile apps is therefore the need to control and formally document the design

- **Coding / development** → There is no particular coding practice that is mandated for CE Marking and most techniques would be acceptable. However the key thing is that the coding must be led by the requirements and specifications and is not performed by the person(s) doing the coding making bespoke decisions. Part of the CE Marking process is
the demonstration that the coding of the app meets the specifications and the app meets the requirements. For that reason the testing of the app must be formally documented

- **Marketing** → It is essential that any marketing of the app is consistent with the intended use that it has obtained the CE Marking for. As explained previously the intended use of a medical mobile app is judged by the claims that are made for it either within the app itself (labelling), instructions for use provided with the app and in promotional materials that accompany it. If the marketing of the app makes claims that are not within the intended use that is covered by its CE Marking then the relevant authorities can demand it be withdrawn until the new claims are either withdrawn or appropriately CE Marked. It is the same situation with the US FDA. The FDA actively surveys the marketing of medical devices that they clear to market to ensure that they are not being marketed for unsupported claims

- **Sales or licensing** → As explained in this report a medical mobile app that is covered by the MDD or the IVDD cannot be placed on the market until the CE Marking has been obtained. Those mobile medical apps that can be CE Marked through self-assessment under the MDD or IVDD must also be registered with the competent authority in the manufacturer’s member state before they can be placed on the market in any of the EU member states. It is important to note that the CE Marking is required to place a medical device for its intended purpose on the EU Market even if it is offered free of charge. A mobile app that is regulated as a medical device in the USA discussed in the response to 2 above must be cleared by the FDA through the relevant FDA submission process (refer to section 3.2) before it can be made available in the USA

- **Post sales** → It is explained in sections 3.1 and 4.1 of this report that the manufacturer of a medical device is obliged to maintain procedures for post market surveillance and regulatory vigilance for so long as the device is placed on the European market. The US FDA has similar requirements. It is also important to note that any changes to the app that are made after it has been placed on the market must be identified, evaluated and controlled to ensure it maintains its intended use or that any new intended uses are subject to CE Marking or FDA submission as applicable. Documented records of this identification, evaluation and control must be maintained as they can be subject to inspection by Notified Bodies, European competent authorities and / or US FDA as relevant

- **Record keeping** → The technical file and other records generated during the CE Marking and post sales periods are required to be maintained for the lifetime that the medical mobile app is available to the market. These records must be appropriately
preserved and protected from unauthorised changes during this period whether they are held in paper or electronic format

7). How much is this likely to cost and what external help would be needed, at what cost and at what stage of development?

Where a Notified Body is involved in the CE Marking process the Notified Body charges for this service. This typically costs in the region of £5,000 to £10,000 for the initial CE Marking dependent on the conformity assessment procedure that is involved. There is then a further charge in the region of £3,000 to £8,000 per year for the continuing surveillance that is required to maintain the CE Marking. The fees associated with the various FDA submission processes are mentioned in section 4.2 of this report. Where self-assessed CE Marking is allowed, there are no Notified Body fees but there is the cost of registration with the relevant competent authority. Currently it costs £70 to register a medical device with the competent authority for the UK, the MHRA.

External help can be sought at each stage of the CE Marking process, starting with the determination of whether a mobile app qualifies as a medical device or not. It is recommended to seek external support at an early stage of the process as an experienced consultant can determine the optimum path to CE Marking. Experienced consultants are definitely advised when the developer of the mobile app has no previous experience of the CE Marking process. They can guide and assist the developer to produce the required technical file and other documentation at each stage of the design and development of the app and to prepare the procedures that direct post market surveillance and regulatory vigilance. When Notified Bodies are involved in the CE Marking process they can take a certain degree of assurance from the fact that an experienced consultant has been involved in the process. Similarly, the involvement of an experienced consultant is definitely advised for FDA clearance.

The cost of this external support will depend on the experience, knowledge, expertise and availability of the consultant. Engaging a highly experienced consultant should significantly reduce the time to market but this comes at a higher cost. The cost will also depend on the process that is involved (e.g. self-assessed or Notified Body assessed) and the extent to which the consultant is engaged in the process. Consultants can merely advise the documents that are to be produced or can actively participate in the process and produce the documents for the developer and assist them in dealing with the Notified Body and can provide every level of support in between. It is not possible to say how much this will cost but...
as a rough indication commercial rates for this kind of consultancy help range in the region of £500 to £1,500 per day depending on the experience of the consultant and their role.

8). **Any other relevant potential benefits, risks, costs and obligations?**
The benefit of obtaining the appropriate regulatory approval for a medical mobile app is that it should guarantee its acceptance by healthcare professionals and healthcare institutions. In Europe CE Marking is a vital precursor before a medical device can be used for its intended purpose. The same applies to FDA clearance for the use of a medical device in the USA. This is something that is likely to be increasingly enforced as the regulatory authorities in these territories are becomingly increasingly aware and concerned about the use of mobile apps for medical purposes. With this increasing regulatory scrutiny there is the increasing risk for any medical mobile app that does not have the appropriate regulatory approval that it will be ordered to be removed from the market by the relevant authority. In circumstances where a device produced in the UK is found not to carry the CE Marking when it is used for a medical purpose, the MHRA are obliged to ensure that the device is removed from the market.

While the regulatory approval processes involved are frequently used as a major justifier for the high cost of medical devices it is debateable if this will be the case with medical mobile apps. Mobile apps including those with medical purposes are typically made available free of charge or for nominal fees. It is unlikely that the public will pay a premium for these apps based on the costs of the regulatory approval processes as the costs of this process are not transparent where mobile apps are concerned. This will be one of the major challenges for the developers of medical mobile apps and the regulatory authorities for medical devices. There is the desire to promote the potential benefits of medical mobile apps but this must be balanced with the established processes to ensure that medical devices are safe and effective.

9). **Do you have useful contact details with the MHRA?**
Contact details for the Medical Devices Division of the MHRA can be found at the following link:

Enquiries related to proposed or existing medical mobile apps should initially be directed to the European & Regulatory Affairs contacts listed on that webpage.

10). What would be a ball park estimate of what it might actually cost us or an SME to develop a class 1 app? That is getting early input from a consultant on documentation (requirements and spec) then creation & maintenance of technical file etc.?

The cost of CE Marking a Class I device using a consultant's support is very difficult to estimate as it is subject to how much the company wants to use the consultant's support, the commercial rates charged by the consultant and how much internal resource the company is prepared to dedicate to the CE Marking process. A very ball park range would be a very minimum of £5,000 if the consultant was just to provide advice and little review support up to £20,000 if the consultant was to be actively involved in the process and prepare the majority of the technical file and associated procedures. The lower end of this scale would be based on a consultant charging at the lower end of the £500 to £1,500 per day. In terms of timing the technical file could be prepared in about a month in the latter scenario but could extend out to 3 to 6 months in the former scenario due to the unfamiliarity of the company with the CE Marking process and the implied inexperience of the consultant. In the author’s experience the former scenario typically ends up with the consultant getting more involved than originally intended or a more experienced hence more expensive consultant having to be called in to remediate the process.

In terms of internal resources, a company can typically support the CE Marking process with its existing resources but may want to consider hiring a documentation clerk due to the large amount of paperwork that is involved. A company may engage an experienced regulatory person to replace the consultancy help outlined above but this is considered an unlikely prospect for the typical app developer.

11). What are the responsibilities of the owner of the app in relation to post market surveillance? What would be a ball park estimate of how much this would cost to set up and maintain?

Post Market Surveillance (PMS) is an active process whereby the manufacturer of the app is expected to actively seek feedback on the product’s performance on the market rather than passively wait for such feedback to arrive. The manufacturer must consider all feedback (both passive and active) related to the app once it is made available to the market and also actively seek feedback on how it is performing on the market in terms of its medical device intended use and functionality. Passive forms of feedback include customer complaints, non-
conformances and deficiencies noted by the manufacturer themselves and public references to the app in media or social networking forums. Usage statistics can also be viewed as a form of passive feedback because it provides an indication of the market’s satisfaction with the app. Active feedback is when the manufacturer of the app directly asks users for their opinion on how it is performing in terms of its ability to fulfil its medical device function. The interactive nature of apps means that mechanisms to obtain such active feedback can be incorporated into the app itself. Other forms of active feedback that are commonly employed are user forums and surveys. The purpose of PMS is to use the active and passive feedback to review the performance of the app on the market in terms of its medical device functionality to instigate any necessary corrective actions necessary to resolve any deficiencies in that functionality. The PMS information is also reviewed to determine if any new risks have become apparent after the app has been released to the market that were not considered during the risk analysis and evaluation of the app that was performed during its development (refer to section 4.1). The PMS information must also be reviewed to determine if the app has been involved in incidents involving the potential or actual death or serious deterioration in the state of health of a patient due to a malfunction or deterioration in the performance of the app or any other technical or medical reason connected with the performance of the app that led or might lead to death or serious deterioration in the state of health that led to the app’s withdrawal from the market. Any such incidents must be reported to the relevant competent authorities for medical devices in the affected member states in a process known as regulatory vigilance.

The cost of setting PMS up is typically covered in the cost of setting up the technical file discussed in the response to the previous question. As explained in section 4.1 of this report the main requirement for PMS in the technical file is the establishment of a procedure that directs how this feedback is to be obtained and evaluated. Preparation of this procedure(s) is one of the key supports that an external consultant will provide during the preparation of the technical file. The cost of maintaining the PMS process involves reviewing and evaluating the feedback to determine if there are corrective actions required for the device and if any regulatory vigilance incidents have occurred. This would not typically be assigned to an external consultant and would be handled within the company, although a consultant may be consulted on an ad-hoc basis to confirm if particular incidents meet the regulatory vigilance reporting requirements. In which case the higher end of the consultant day rate quoted above would be expected to apply as it takes considerable experience to understand and interpret the issues that are involved. Due to its nature the internal resources required to
maintain the PMS process will increase the longer and more widely distributed the app is on
the market due to the increased feedback that is available for review.

12). Is the NHS app store (http://apps.nhs.uk/) any substitute for meeting one's
obligations under the MDD etc., even though the NHS reviews apps for clinical safety?
The NHS App store is not a substitute for any of the manufacturer's obligations under the
MDD. Demonstrating the conformance of a device to the essential requirements of the MDD
is entirely the responsibility of the manufacturer of the device including its clinical
evaluation. Under the MDD if an app qualifies as a medical device then it must have the CE
Marking before it can be made available to the market regardless of any other form of
evaluation it might undergo by a third party.