Essay 1- Software Engineering (CEN5035)

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Part (1): Heart Health notifications functionality introduced in the apple watch and iPhone can alert user about high and low heart rates as well as irregular heart rhythm by providing notifications. In order to use that functionality user should wear the apple watch and connect it with the iPhone. Once connected user can enable the heart health notifications in health application in iPhone to receive those notifications. Apple watch uses photoplethysmography to monitor users heart health, it consists of green LED lights photo sensors which can capture tachograms (plot of time and heartbeats) from the user's wrist every two to four hours by detecting volumetric changes in blood created by cardiac cycle in peripheral circulation. Tachograms are obtained only when the user is still and inactive. These tachograms are analyzed by the health system classification algorithms, if tachogram is found to be irregular then the frequency of tachogram snapshot is increased by the system. if five sequential tachograms out of six are found to be irregular within 48 hours period of time then it suggests that user is potentially suffering from atrial fibrillation (AFib), the Irregular Rhythm Notification Feature then notifies the user about the heart condition with an alert. If two consecutive tachograms are classified as normal by algorithm, system resets to take tachogram snapshot with normal frequency (two to four hours) and user is not notified.

AFib (Artial fibrillation) is a heart condition in which the upper chambers of heart beat irregular and out of sync manner with respect to the lower two chambers of the heart, this causes irregular and rapid heart beat which can cause complications such as strokes and heart failures in patients. The symptoms of Afib includes heart palpitations, shortness of breath and weakness.

Indication of use: The Heart health notification feature is for over the counter use with apple watch, the feature is intended to notify user about potential presence of Afib by detecting irregular heartbeat patterns, but it should not be used to diagnose the condition. It does not provide notifications continuously on every encounter of irregular heartbeat similarly if the notifications are absent it does not ensure that user can not have the AFib. This system cannot detect heart attacks. The apple watch system does not collect user health data when it is in close proximity of electromagnetic field. It should not be worn by user while going through a medical procedure also

it is not suitable for use by patients who are already diagnosed with Afib. The system is not intended to be used by users underage of 22 years.

Part (2): CDRH's role is to evaluate safety and effectiveness of the medical devices before and after they reach the market. According to CDRH's official guidelines in order to get a new medical device or product to the market and get CDRH approval for the medical devices there are five steps that has to be followed the first is establishing the product description and identifying the purpose which incorporates the intended use of device, duration of use and target population. Second step is to verify whether the product is a medical device, Third step is to identify the product class as I ,II and III(from CDRH class database) , fourth step is to develop scientific evidence to support the product's safety and effectiveness and the last step is to prepare premarket submission , each type has its own sets of processes, laws and regulations, review times and evidence burden. Premarket submission types are investigational device exemption (IDE), Premarket notification(510(k)), Premarket approval application (PMA), De Novo, Humanitarian device exemption.

Premarket Notification (510(k)) is a market application for low to moderate risk level medical devices, it applies to class I and class II type products. Premarket Notification application could be used if the medical devices show significant equivalence with already existing legally marketed device in terms of intended use and device features. Premarket approval application (PMA) is eligible for high risk devices and can be used in case of class III products. On the other hand, De Novo is the application type which could be used for a new novel device types which currently do not have any existing classification regulation, this application can create a new classification regulation according to the product.

The De Novo request submitted to the FDA by Donna-Bea Tillman clearly establishes product description and its intended purpose (to detect AFib in users and notify them) of the Heart health notification feature in apple watch. Apple watch with photoplethysmography sensors and Heart health notification feature qualifies as medical device according to definition of medical devices defined in section 201(h) of FD&C act. The application format used for marketing approvals from CDRH is De Novo which suggests that at the time when request was made classification of apple watch heart health notification feature could not be established, this suggests that at that

time there was no existing classification for similar marketed device. Hence De Novo Application format was used because it is used to request classification of new novel medical devices from CDRH.

In Angela Krueger's formal response to the De Novo request for classification of the “Irregular Rhythm Notification Feature”. It is mentioned that CDRH of the Food and Drug Administration (FDA) has completed the review of De Novo request for classification of the Irregular Rhythm Notification Feature under section 513(f)(2) of FD&C act which allows a person to request FDA to make a risk-based classification of the medical device under section 513(a)(1) of the Act without submitting a 510(k) first if device equivalence could not be established with a similar legally marketed device. After the application review it was concluded that Irregular rhythm notification feature should be classified as class II which signifies low to moderate risk medical device. The response letter explains that in order to classify the Irregular rhythm notification feature as class I or II, it was necessary to check that proposed class type incorporates sufficient regulatory controls and measures to ensure device effectiveness and safety for intended use. According to FDA class II special controls provide the safety assurance for the Irregular rhythm notification feature, hence it should be classified as class II. These special controls should be used as mitigation measures for the identified risks with the notification feature, these special controls are Clinical performance testing, Human factors testing, Software verification, validation, and hazard analysis, Non-clinical performance testing and Labeling. The letter mentions that all equivalent and similar medical devices of this generic type will be classified as Class II with generic name “photoplethysmograph analysis software for over-the-counter use”. The response letter explains that grant for De Novo request from FDA does not mean that device is compliant with all FD&C regulations and other federal agencies, the device must comply with all the rules of FD&C to be ready for marketing.

Premarket notifications are necessary in order to obtain assurance about the effectiveness and safety of the medical device. But under section 510(m) of FD&C act, it is stated that if FDA concludes that the premarket notification is not necessary to obtain safety assurance of the device then under section 510(k) of the FD&C act, FDA can exempt the class II devices from the premarket notification requirements. In the case of the Irregular Rhythm Notification Feature of apple app FDA concluded that premarket notification is necessary, and it is not exempt

from this requirement hence prior marketing of the device premarket notification has to be submitted containing information on the photoplethysmograph analysis software for over-the counter use. But the in the response letter Angela Krueger's stated that when the announcement notice of classification is published in federal register the device could be marketed immediately as mentioned in the De Novo request. These two statements are ambiguous and contradictory.

Part (3): According to FDA class II special controls provide the safety assurance for the Irregular rhythm notification feature, these special controls should be used as mitigation measures for the identified risks with the notification feature. these special controls are Clinical performance testing, Human factors testing, Software verification, validation, and hazard analysis, Non-clinical performance testing and Labeling.

Clinical performance testing: In order to benchmark the medical device in different scenarios clinical performance testing is done. Clinical performance testing is done in controlled environments where various parameters could be tweaked in order to assess the performance of the medical devices in different conditions. for example, testing the device on different groups of individuals with different age groups as well as different genders can benchmark the performance of the device against different age groups and gender.

Human factors testing: This testing is done in order to ensure that the user-device interaction is smooth. Human factors testing can identify the problems associated with device's usability. It can also be observed that whether the device is user friendly or not. human errors can also be analyzed.

Software verification, validation, and hazard analysis: Software verification is the process to check whether the design output of a particular software development phase meets all requirements of that phase. On the other hand, software validation is the process to check whether the final product meets the specification. Hazard analysis is used to assess risks associated with software system. These three pillars of software development assure that software is developed in right fashion, developed product meets all requirements and associated risks could be contemplated in advance. **FDA's software verification activities include** Software Testing**,** code and document inspections, various static and dynamic analyses, walkthroughs, and other techniques. **FDA's software validation principles include** documented software requirements specification, defect prevention in software, software validation should be planned effort, software validation should take place within an established

environment of a software development life cycle, software validation should make use of procedures, validation coverage, independence of review, flexibility and responsibility etc.

Non-clinical performance testing: This type of testing is performed either by a device manufacturer or third part testing facility. This incorporates all types of bench testing according to the device specifics.

Labeling: Labelling is the device manual which gives information regarding its hardware and operating system, device's functionality, input and output also the expected performance of the device in different environments especially best and worst case scenarios.

Identified Risks and Mitigation Measures for the Irregular Rhythm Notification Feature of apple watch:

Identified Risk (1): **Poor quality incoming PPG signal resulting in failure to detect irregular heart rhythms**

If poor quality PPG signals are fed to the system algorithm for detection of irregular heartbeats, the algorithm might misinterpret the results which could result in false positives and false negatives. As mitigating measures, in **clinical performance testing** the device sensors should be tested against external aggressor such as vibrations, hand and finger motion, Heat, cold, water, presence of electromagnetic field to bench mark the signal quality by the sensors in different conditions. The device sensors should be tested against individuals with different skin tones to check whether the sensors performance is uniform. **Human factor testing** should be done to check whether the participating individuals are following user guidelines before taking the measurements. Similarly **Labelling** should clearly mention dos and donts for the device so that users don't make mistakes and assumptions while using it.

Identified Risk (2): **Misinterpretation and/or over-reliance on device output**

Over reliance on device output might lead to either individuals not seeing a doctor despite having serious symptoms like fluttering sensation, dizziness and irregular pulse or if the device outputs are negative individuals might change their ongoing medication or stop it. As mitigating measures, **Human factor testing** could be used to study how the participating individuals in the study react when they receive a notification or when they do not receive any alert. This might give insights into how different people react to the notifications from the device. **Labelling** should state clearly how users should interpret the outputs and results obtained from the device.

Identified Risk (3): **False negative resulting in failure to detect irregular heart rhythms and delay of further evaluation or treatment**

If the system software fails to detect a positive case of AFib and classifies it as negative, then the user's life is at risk as he is not aware about his health condition. This raises questions on system's reliability. As mitigating measures **Software verification, validation, and hazard analysis** should be done carefully so that the system software performs as per its specification and is more reliable. During **Clinical performance testing** the device system could be tested against individuals who are already diagnosed with Irregular heartbeat in order to test the false negative rate. **Labelling** should guide the user to not rely on negative outputs from the device as the device does not guarantee the

Identified Risk (4): **False positive resulting in additional unnecessary medical procedures**

If the system software gives too may false positives, then the user might visit doctor for diagnose many times unnecessarily. This raises questions on system's reliability. As mitigating measures **Software verification, validation, and hazard analysis** should be done carefully so that the system software performs as per its specification and is more reliable. During **Clinical performance testing** the device system could be tested against individuals who are healthy and do not have any Afib in order to test the false positive rate. **nonclinical performance testing** can ensure whether the device system is performing as per its specifics. **Labelling** should guide the user to not rely heavily on positive outputs from the device as the device does not guarantee the diagnose of the health condition.

References:

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