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Mobile applications and compliancy: what you should know

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Skyping with somebody on the other side of the world via a smartphone, or watching movies on a tablet. What would our modern world be without the use of mobile devices? The mobile transformation of our society is irreversible. Not only for entertainment purposes, but also regarding the use of medical applications.

In the pharmaceutical industry for example, where people use mobile devices more and more in corporate processes and to exchange data with scientists, doctors, patients and participants in clinical tests. And what about wearables, like smartwatches, that are able to measure bodily functions in less than no time, and applications telling us when and how to take our medicines? The latest technologies enable the pharmaceutical and medical world to collect and process data faster, diagnose patients outside of traditional health care settings, stand closer to patients and help them manage their own health and wellness.

The expectation is that by 2018, fifty per cent of the more than 3.4 billion smartphone and tablet users worldwide will have downloaded a mobile health application, writes the International Society for Pharmaceutical Engineering. However, mobile devices and applications present a significant challenge to control. To guarantee the safety and reliability of these technologies, they must meet specific regulations and guidelines, especially when

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those applications may present a risk to users if they do not work as intended – as would be the case with the medical applications mentioned above. This compliancy of mobile applications is a relative new part of the validation process of organizations. How do companies in the pharmaceutical and medical sector guarantee the compliancy of their mobile devices and applications?

Quality by Design is engaged in the validation of computer systems, devices and applications on a daily basis, and lists the most important information and five tips for companies, based on our best practices.

Traditional computer systems versus mobile applications
As we all know, the medical and pharmaceutical world is subject to strict regulations and guidelines regarding the development, manufacturing and control of products, to guarantee that each product is safe and meets all demands. Take for instance the

Good Manufacturing Practice (GMP) which provides a detailed description of the way companies in the pharmaceutical, cosmetic or food industry should produce to guarantee the quality of their products. When organizations use mobile devices and applications in their processes, they also have to make sure these 'new technologies' are compliant with all regulations. And that is where the shoe pinches. Applications running on mobile devices require other legal guidelines, information security and privacy

What about the cloud?

We not only see an increase in the use of mobile applications, more and more companies switch from their own server rooms and data solutions to services of external providers. For example in the cloud, companies process and store their data in third-party data centres. Or they combine the cloud with mobile applications. In this case, data integrity is very important.

Companies need to realise that sharing information is much easier in the cloud. And that also goes for sensitive, confidential information. Do you want to destruct this kind of information? Take into account the possibility that your data is duplicated. One time, ten times, or maybe a hundred times. And those copies aren't so easy to destruct. Traditional validation of a flexible cloud environment may not be possible, so companies need to develop other quality and compliance practices to guarantee the quality and integrity of their cloud-hosted systems.

settings than our traditional computer systems. For example, when using a computerised system – 'a set of software and hardware components which together fulfil certain functionalities' – as part of a GMP regulated activity, European pharmaceutical companies can fall back on GMP Annex 11: Computerised Systems. And in the United States, part 11 of the Code of Federal Regulations (CFR) Title 21 (Food and Drugs) is applicable. But what about the regulations on mobile devices?

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At this moment there is no official legislation regarding the use of mobile applications, so we have to rely on guidelines. In 2013, the US Food and Drug Administration (FDA) issued final guidance for developers of mobile medical applications. This document functions as a guide for the industry to sketch a framework for future laws. The FDA focuses on applications that 'are intended to be used as an accessory to a regulated medical device' or 'transform a mobile platform into a regulated medical device'. In the former case, you can think of a doctor diagnosing a patient by analysing a medical image from a picture archiving and communication system. In the second case, a medical application on a smartphone may be used to detect abnormal hearth rhythms.

The FDA is not the only party to pay attention to the validation of medical devices and applications, European agencies also recognise the necessity of this modern compliancy issue. The European Medicinal Agency (EMA) for instance applies the general Medical Device Directive (93/42/EEC amended by 2007/47/EC) to mobile medical applications. The organization has set up a specific committee to evaluate all mobile applications.
When it comes to compliancy regulations for mobile devices and applications, we are on the right track, but the developments are still in their infancy. How do you guarantee that your organization is compliant with all current and future guidelines?

Quality by Design lists five important focus points

1. Keep updated on the latest technology trends
As stated earlier, the validation of mobile applications is a relative new aspect for pharmaceutical companies. An aspect that is emerging as well. That is why it is important to stick closely to recent developments by monitoring news items, statements, FDA announcements, et cetera. Only then a company will be able to manage and control the whole introduction of a mobile application, and to prevent potential risks.

But broader technological developments are also worth keeping an eye on. As a result of the digitalization of society and the rise of

Quality by Design takes care of your mobile application validation

Managing your pharmaceutical business is a full-time job and an adequate quality control process is time-consuming. As the expert in quality management, Quality by Design is happy to take care of the validation of your mobile devices and applications. With clients in the pharmaceutical, biotechnological, cosmetics and healthcare sector we are always up to date on the latest guidelines and legislations.

Supported by our validation experts you are able to bring new products onto the market without any worries, proving auditors that your applications and devices are compliant and safe. We know the mobile application process from A to Z. Together we create a Design History File, custom user requirements and the application of the ISO 13485 legislation. We design a custom risk analysis and risk reducing measures, and accomplish supplier audits. At the end of the project, Quality by Design verifies that the validation file is sound and verifiable. So you can sleep soundly.

the cloud and big data, subjects like data integrity and data mining – the process of discovering patterns in large data sets –receive more and more attention. Today, it is all about knowing where to store your data. Especially for the pharmaceutical industry it is important to guarantee and protect the accuracy and consistency of data. One important development regarding the storage of data has to do with the Safe Harbour Decision that was ruled invalid on October 6th, 2015. By declaring this data-sharing agreement – which made it possible for companies in the United States to prove they worked according to the privacy principles of the European Union – invalid, a vacuum arises. A lot of European companies doing business with US data centers don't have any official proof anymore that their data is safe there. Now they might have to find other ways to store data.

2. Formulate custom user requirements
When using computers or other systems for automated data processing in the pharmaceutical sector, it is important to validate systems and software. One important part of this validation is a document specification of the user requirements. According

User requirements may differ according to the respective mobile system or software, but there are some important points that can't be missing.

Ask yourself at least the following questions:

to the FDA, this document should define the 'intended use of the software or equipment and the extent to which the device manufacturer is dependent upon that software or equipment for production of a quality medical device'. As a user, you need to define the expected operating environment, and need to document requirements for system performance, quality, security, et cetera. You also need to identify any safety related functions or features and define objective criteria for determining acceptable performance. In short, you must ensure that the production and quality system software is validated according to a written procedure for the intended use. It needs to perform as intended on the respective application. Calling in the help of an expert in this situation is possible, but make sure that the user requirements for a mobile device or application are always formulated by you as an end user, because it is intended for your own use.

Mobile phone checklist

Synchronization, configuration and notifications
☐ Does the application need to synchronise?
☐ Do you want the application to generate notifications?
☐ Does the application need to make use of automatic updates?
☐ Is it important that the application depends on clock or calendar functions?
☐ Does the application require specific device configuration requirements?

Users
☐ Does the application run in the background, or do users need to open it before use?
☐ How does the user obtain the application?
☐ What happens when the user forgets to recharge his phone and the battery power fails?
☐ Are there important alarms the user should not disable?

Communication
☐ Does the application send emails or text messages?
☐ Are there specific browser requirements?
☐ Are there dependencies on communication like short range, Wi-Fi or cellular?

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Requirement Specifications	Risk Assessment		Verification Test Strategy
	Hazard	Risk	
Platform/HW (Technical)	Updated/new hardware	Compatibility issues due to variations in hardware	Product testing
Connectivity (Supplier)	No or poor 3G/4G network coverage	Interruption of transmission leading to data loss or corruption, performance problems	Connectegration testing, focussing on 'stress situations' • Connectivity • Interruptions • Memory/battery failure warnings
User Interface	User controlled configuration (user can adjust settings, uncontrolled downloads)	Misuse of the device, wrong user configuration	• Date/Time format • Portrait/Landscape • Training/Online Help
Regulatory & Legal	Inadequate access control	Access by unauthorized users (data integrity/data privacy issue)	• Virus protection • Fail safe security policy

Example of the different components of a risk analysis.

3. Develop and specify a custom risk analysis

During a risk analysis, you investigate all functionalities from a mobile application to make an inventory of everything that might go wrong. From serious risks to unlikely hazards, you document everything and define how to reduce risks. A thorough risk analysis is especially important for the pharmaceutical industry, as governmental bodies like the FDA and the European Medicines Agency pay a lot of attention to risk. Because you cannot test each and every aspect of a product, it is important to make sure that you cover the critical aspects, patient safety, data integrity, product quality and compliancy to legislations.

A risk analysis may consist of a requirement specification, an

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assessment of estimated hazards and risk, and a verification test strategy to reduce risks as much as possible. An example:

After you perform a risk analysis, there are additional risk reducing measures to take. Try to test your mobile applications as much as possible, implement extra technological features, and coach and train end users that are about to use a specific mobile application. Although humans are always the weakest link in this kind of processes, you can make them aware of certain risks, like phishing, lending out devices to other people or certain applications which can't be used together on the same platform.

4. Collaborate with reliable third parties

It is not always the pharmaceutical company that develops a mobile application. Often, companies cooperate with specific developers specialised in the development of applications for mobile devices. This could be classic developers specialised in pharmaceutical computer systems but delivering applications

Classical developers versus pharmaceutical software specialists

Quality by Design does not develop applications, we help our customers to validate them for their intended use. We cooperate with both clients and their application developers to guarantee proper validation of devices and applications. Looking to develop a pharmaceutical or medical application? Ask yourself one important question, do you choose a classic software developer, specialised in pharmaceutical computer systems but also offering development of applications? Or do you prefer a 'normal' application developer, with none or minimal experience in the pharmaceutical sector?

One disadvantage of traditional application developers is that the companies are often big and complex, while dedicated mobile application developers are able to work more flexible. The problem with this last party: they start immediately and are already half way there when they realise the physical and financial efforts to comply with legislations. Make sure you prepare thoroughly from the beginning and inform your mobile application developer on every important quality and compliance aspect. No matter which one you choose, Quality by Design acts as a mediator and bridges the gap between your company and your developer.

as well. Or you can choose a specialised application developer with or without pharmaceutical knowledge (see box 2 for a more detailed distinction). Whatever party you choose, it is important to guarantee that third parties are compliant and aware of relevant legislations and guidelines. One way to accomplish this is by

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performing a supplier audit for your third party. During an audit you search for weaknesses in the party's different processes, including the development of mobile applications.
Another focus point is to make sure your Service Level Agreement (SLA) covers all requirements. The purpose of an SLA is to ensure mutual understanding of responsibilities between two parties. This way you regulate the processes around software devices and applications and ensure that applications comply with all regulatory requirements and quality policies. Want to formulate an SLA?

Here are some examples of possible topics[1]:

- Change control
- Application/infrastructure
- Security provisioning
- Incident/problem management
- Backup and recovery
- Disaster recovery
- Business continuity
- Performance monitoring
- Training
- Record retention
- Archiving/retrieval

[1] www.cbinet.com/sites/default/files/files/Session%202_pres(1).pdf

5. Create a sound and verifiable validation file

Last but not least, one of the most important things is to create a sound and verifiable validation file. This is the ultimate proof that an application is built according to quality principles. Validation means you are able to demonstrate how you've managed the process. That's why the validation file needs to comply to certain criteria, in case it needs to be consulted. With an accurate validation file, you show both the governance, auditors, partners and customers that your application is truly validated.
How do companies ensure that their validation file is right? Make sure you have access to a thorough methodology to validate computer systems. ISPE's GAMP5® guide offers a good framework to validate your computer systems. It reflects current regulatory expectations and good practices, to provide you with an interpretation of regulatory standards. This way you improve compliance, quality and efficiency while reducing costs.

About Quality by Design
Quality by Design delivers consultancy services to companies in the pharmaceutical, bio technical and cosmetics industry. With its years of experience, QbD helps these companies set up and improve quality assurance, and with an optimal validation of products and processes. To do so, QbD employs forty specialists in the field of validation, technology transmission and quality control.

The renowned company operates mainly in the Netherlands and in Belgium, and works for small and innovative companies as well as influential and worldwide organizations. QbD's clients include Alcon, DSM, Genzyme, Heel Belgium, Janssen Pharmaceutica, Labo Wolfs, MSD, Multipharma, Pfizer, Pronails, UZA and Wase Werkplaats. For more information, please visit www.qbd.eu.