Developing a guide to regulations for the Medical Device Industry

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Abstract

All Medical devices are required to go through regulatory processes before they can be put on the market. The regulatory processes differ depending on what market is the aim. To release medical devices within the European Economic Area (EEA) the devices need to have a CE marking affixed. To release within the United States approval or clearance from the Federal Food and Drug Administration (FDA) is needed. Regulations and requirements for both these markets differ depending on device types and risks that may be associated with the device.

The biggest problem with regulations is the big amount of information and how it is presented. The regulatory processes are based on a vast number of regulations and requirements, many times with cross references that lead to confusion. Especially for smaller companies, where no specific person is assigned to these types of tasks, the processes can be overwhelming and create aversion. Gathering information regarding the regulations and the approval process of a specific product type is hard and can be very time consuming.

The Sister Kenny Research Center (SKRC) has a new medical device ready for commercialization, meaning it needs to go through the regulatory processes. The SKRC have ever gone through any regulatory process before, which creates problems since the processes are complex. They experience problems due to lack of knowledge and understanding of the regulatory processes, as well as finding and interpreting information.

The purpose for this thesis is to create understanding of the current problems in working with the regulatory processes for the American and the European market, and to create a way to help the SKRC go through these processes. The questions interesting in this thesis are: How do regulations pose a problem for release of medical devices, for small companies? How can this problem be aided?

To assist the SKRC a guidebook to the regulatory processes has been created. The guidebook has been viewed as a product, and to develop it different product development tools and techniques have been used. The guidebook gives an overall understanding of the regulatory processes, instructions on tasks and references to where more information can be found. Presenting the different regulations in an understandable way in the guidebook will make the regulatory processes more graspable and help the SKRC release their devices to market.

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Sammanfattning

All medicinteknisk utrustning behöver gå igenom regulatoriska processer innan de får lanseras på marknaden. De regulatoriska processerna varierar beroende på vilken marknad produkten skall släppas på. När man lanserar inom europeiska ekonomiska samarbetsområdet (EES) måste produkten bära en CE-märkning. För lansering I USA måste produkten godkännas av the Federal Food and Drug Administration (FDA). Regleringarna och kraven för dessa marknader skiljer sig dessutom beroende på typ av produkt samt vilka risker som är associerade med produkten.

Det största problemet med de regulatoriska processerna är den omfattande mängden information som finns tillhanda och hur den presenteras. Processerna baseras på flertalet regler och krav med interna referenser som leder till förvirring. För små företag, där det oftast inte finns en specifik person anställd för att hantera dessa ärenden, upplevs detta ofta väldigt överväldigande. Att samla in all information om de regulatoriska processerna för en specifik produkt kan vara väldigt svårt och tidskrävande.

Sister Kenny Research Center (SKRC) har en ny medicinteknisk produkt som är redo kommersialisering och behöver därför gå igenom dessa processer. SKRC har inte gått processerna tidigare vilket skapar problem då erfarenhet inom det regulatoriska området och dess processer saknas.

Syftet med detta arbete är att skapa en bättre förståelse för de befintliga problemen med regleringsprocesserna för både den den amerikanska och den europeiska marknaden. Syftet är även att skapa ett hjälpmedel för SKRC att ta sig igenom processen. De frågeställningarna som är intressanta för detta projekt är: på vilket sätt är de regulatoriska processerna ett problem vid lansering av medicinteknisk utrustning för små företag? Hur kan detta problem underlättas?

För att hjälpa SKRC så har en guidebok om de regulatoriska processerna skapats. Denna guidebok har tagits fram med hjälp av olika produktframtagningsverktyg och metoder. Guideboken ger en övergripande insikt i processerna, instruktioner för olika delsteg och referenser till var läsaren kan hitta mer information inom området. Att informationen här presenteras på ett förståligt sätt gör att den blir lättare att hantera och hjälper SKRC att få ut sin produkt på marknaden.

Contents

1. Introduction

This chapter provides an introduction to the SKRC and the challenges they experienced with the regulatory approval processes of medical devices. The chapter also presents a brief description of the regulatory processes for medical devices in the United States and in Europe.

The Sister Kenny Research Center (SKRC) is the research arm of the Sister Kenny Rehabilitation Institute. It opened its facility at the Abbot Northwestern Hospital Campus in 2007 (SKRC, 2001). The SKRC works with innovation and development of Medical devices intended to use in rehabilitation. The research center has few fulltime employees and a lot of work is done with the help of volunteers, students and part-time researchers. As a result, during the development of a medical device many different people may be involved. One of their products, the Walkasins™ is far along in the development process, meaning it has reached its commercialization phase, and alongside with that the need for regulatory procedures has emerged. The research center has not been working with regulatory approval processes before and has no designated personnel to handle the process.

It is important for SKRC to have a strong synergy with the business world, to be able to turn research into usable medical devices and patient outcome (SKRC, 2001). The SKRC partly works with research activities and partly as a medical device incubator supporting companies making new medical devices for rehabilitation. The purpose of this is to involve Sister Kenny Clinicians in creating technologies as well as supporting companies that wish to test their technologies and ideas by taking advantage of the Research Centers infrastructure (Parmar, 2011). The research center can help build value and handle risk in the early stages of start-up companies as well as provide a connection with the clinical world (Schwartz, 2012). At the same time the SKRC get a chance to work with inventors. This idea is meant to allow small start-up companies to build value and assess risks before contacting investors (Parmar, 2011).

All medical devices go through an elaborate regulatory process before it can be introduced and sold on the market. For The European Economic Area (EEA) and the American, the regulations and requirements differ. For both markets regulations also differ, depending on the device type and the risk that may be associated with the use of the device. The CE-marking is a mark mandatory for all medical devices to be sold within the EEA. For the American market the Federal Food and Drug Administration, shortened FDA, is the authority that control and ensure the regulations and requirements for medical devices are met.

The regulatory system for medical devices in the United States is complex and stringent (Maisel, 2004). Smaller companies will often need expert help to be able to understand and go through this process (FDA, 2009). To be able to release a product on the market within the EEA is overall considered quicker and easier compared to the American market (Cohen & Billingsley, 2011).

Alongside with meeting applicable requirements, the manufacturer of medical devices must develop and maintain a quality control system. This is required for devices to be sold both in the United States. and in the EEA. The requirements on the quality control system from the two markets differ a bit in detail, but they largely cover the same areas and they do not contradict each other. This means that one well developed quality control system can meet requirements for both markets.

2. Problem description

This chapter presents and discusses the problem definition of this master thesis as well as the projects demarcations. Furthermore this chapter defines the aims and purposes of the project.

The regulatory approval process for medical devices is vast and in many cases creates a lot of work, confusion and frustration for companies developing medical devices. In the case of SKRC, innovation, research and product development is mainly performed in the hospital, by many different actors, such as students, volunteers, physicians, researchers and engineers. Most of these people are neither educated nor interested in quality control systems, regulatory aspects and the administrative work for getting a device approved. There is no natural way to start working with the regulatory aspects and its heavy administrative load. Making healthcare personnel, volunteers and students work with too much documentation and administration is likely to scare them of and worst case scenario inhibits innovation. For a new device, for example the Walkasins™ which is ready for commercialization, there is a lot of administrative work to be done, just to establish the correct documentation. As a consequence there is risks that some features need to be reworked since they may not meet the requirements of regulations or the quality system. The less the regulatory aspects are synchronized with the product development the bigger the burden of working with regulations may become, and more non-value added time will be spent. This ultimately increases time to market, which SKRC wants to be as short and simple as possible.

SKRC have not been through this process before which means they do not have any experience or templates to use. This creates problems since the processes are very vast. The main problem, described by the managements of SKRC, was the lack of knowledge and understanding of the regulatory processes. They also experience problems with finding and interpreting the information. Since one of their products has reached a phase where consideration of regulations has become important, the SKRC initiated this project to help them move forward.

2.1 Purpose

The purpose with this thesis is to investigate how the regulatory poses a problem for small medical device companies. The aim is to find a solution to the existing problems and help the SKRC in their work with regulations for the Walkasins™, as well as in general.

The questions interesting for this thesis are: How do regulations pose a problem for release of medical devices for small companies? How can this problem be minimized?

2.2 Demarcations

This thesis covers the medical device regulations for the American and the European market. The regulations concerning medical devices are many and cover a broad spectrum of different device types. This research focuses on device types likely to be developed within SKRC, which are rehabilitation devices. These are generally low to medium risk devices.

Furthermore it has been assumed that a quality control system is already in place at the manufacturers, as well as at the research center. The different regulations covering quality control aspects are explained, but how to create, implement and work with quality control is outside the scope of this project.

3. Literature review

The literature review includes descriptions and explanations to the regulatory approval processes in Europe and America. This Chapter also presents background information about the SKRC, RxFunction and the Walkasins. Furthermore this chapter gives an understanding on how the regulatory approval processes affect the industry.

In healthcare, the role of medical devices is essential and quality and effectiveness of healthcare can be significantly improved by the diversity and innovativeness of this sector (European Commission, 2010). Patient care increasingly depends on the use of medical devices and today some form of medical device is used on almost every patient (Maisel, 2004). Medical devices range from basic equipment, such as syringes, needles and blood pressure measuring devices, to more advanced equipment such as anesthetic equipment, surgical instruments, catheters and MRI scanners (Jeffreys, 2001).

Even though medical devices bring a lot of positive effects to healthcare, faulty or incorrect devices can have serious negative consequences on healthcare. Malfunctions, misbranding or other faults may create a dangerous situation for patients and other users, deteriorating health or even causing death. To avoid this, regulating medical devices has become essential. This means public health can be protected and users can be confident that the devices on the market are safe, effective and high-quality (FDA, 2009)

3.1 The European Economic Area – CE-marking

A medical device is defined within the EEA as an instrument, apparatus, appliance, software, material or other article including its necessary and intended software. The medical device is used alone or in combination, intended by the manufacturer, for human beings. A medical device does not achieve its principal intended action by pharmacological, immunological or metabolic means, but may be assisted in its function by these means ((MDD 93/42/EEC, 1993), Article 1).

All medical devices need a CE-marking to be released within the European Economic Area. The affixed CE-marking ensures that the product meets the European Union's safety, health and environmental protection requirements (European Commission, 2010). By affixing the CE-marking the manufacturer declares on his sole responsibility that the product meets all demands and requirements that EU has set for medical devices and that EU-directives are followed. This means that the manufacturer has verified that the product complies with all essential requirements laid down in the applicable directive and, if stated in the directive, had it examined by an independent conformity assessment body. The EU does not have a government agency responsible for regulations of medical devices (O'leary, 2010). Instead products are more self-regulated and the manufacturer is responsible for assessing the products conformity to the applicable legislations and directives (Jeffreys, 2001).

There are three legislations for regulating medical devices in the European Union. The legislation relevant for this project is the "major Medical Devices Directive" also called MDD or 93/42/EEC. This directive covers all medical devices, except *in vitro* diagnostics devices and active implantable devices.

3.1.1 6 steps to CE-marking

An overview of the CE-marking process can be presented in the following 6 steps.

1. Identify Directive

The first step in the CE-marking process is to find what directive is applicable for the device in question. This means verifying that your product falls within the definition of the directive. For major Medical Devices Directive the definition is stated in Article 1 in the MDD (European Commission, 2010).

2. Verify Requirements

Once the correct directive is identified the requirements need to be identified and met. All medical devices regulated by the MDD need to meet the essential requirements stated in the directive. Compliance with these directives must be demonstrated by a clinical investigation in accordance with the MDD (European Commission, 2010).

3. Classification and need for notified body

Medical devices shall be placed into class I, IIa, IIb or III. Classification of medical devices corresponds to the level of potential risk coupled with the use of the device (European Commission, 2010). Some risks can be acceptable, providing that they are outweighed by patient benefits (O'leary, 2010).The Classification is performed by the manufacturer itself with the help of 18 rules within of the MDD (European Commission, 2010); (O'leary, 2010). For device that can be classified according to different rules, the highest possible class applies.

For class I Devices the manufacturer may use a self-certification system where they are allowed to affix the CE-marking (Jeffreys, 2001). For high-risk devices, i.e. class II and class III, notified or conformity assessment bodies are required for assessment (European Commission, 2010); (Jeffreys, 2001).

4. Conformity Assessment

The conformity assessment is the method used by the manufacturer to demonstrate that their device comply with the requirements of the MDD. The devices classification determines what conformity assessment route to follow in order to affix the CE-marking on the medical device (European Commission, 2010). There are different conformity assessment procedures which consist of the application of one or more of the Annexes in the MDD Directive (MDD 93/42/EEC, 1993) Article 11); (European Commission, 2010).

5. Technical Documentation

The manufacturer is responsible to establish and maintain technical documentation. The technical documentation must enable assessment of conformity with the applicable requirements of the directive (European Commission, 2010).

6. Affix the CE-marking

When all necessary steps have been successfully completed the CE-marking must be affixed to the medical device. The mark is required to be placed visibly and legibly on the product. The CE-marking must have the correct form, given by the European commission, described in the MDD (MDD 93/42/EEC, 1993) Article 17); (European Commission, 2010). This is shown in Figure 1.

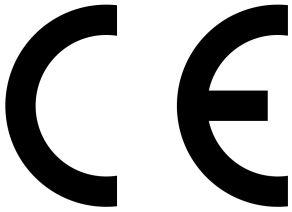

Figure 1. CE-marking. (European Commission, 2013)

3.1.2 After market release

The manufacturer must establish and maintain a systematic procedure to review experience gained from devices in the post-production phase. Post-market surveillance does not only have regulatory importance, but is also considered as good business practice. ((Jeffreys, 2001); ((MDD 93/42/EEC, 1993) Annex I).

There is never 100% guarantee that a product bearing the CE-marking is safe, due to counterfeiting and misuse of the mark. However the manufacturer of a product with an affixed CE-marking assumes full responsibility for its compliance with all applicable requirements in EU legislation. The consequences for counterfeiting of the CE-marking vary according to the member states' national administrative, civil and criminal laws (European Commission, 2010). Economic operators may be liable to a fine and in some cases imprisonment depending on the seriousness of the crime. Also products with faulty CE-marking may be recalled from the market (European Commission, 2010).

3.2 The American Market – FDA

A medical device is defined by the US congress as an instrument intended for use in diagnosis, cure, treatment or prevention of disease. A medical device, according to the definition, does not achieve any of its purposes through chemical action on or within the body (Maisel, 2004). FDA was given the authority to regulate medical devices from Congress 28 May, 1976. In the beginning the law only applied for drugs. This meant that a lot of medical devices had been released to market without FDA-approval before 1976 (Zuckerman, Brown, & Nissen, 2011)

The FDA is the agency responsible regulations and control in a number of different product areas. The agency operates within seven different centers covering all regulated products. The Center for Devices and Radiological Health (CDRH) is responsible for ensuring safety, effectiveness and quality on medical devices, as well as safety of radiation-emitting electronic products (FDA, 2009).

The FDA regulations are designed to prevent, or at least minimize health risks and to ensure shields from a large number of public health hazards. Similar to the European market the regulations for medical devices for the American market differ depending on the type of device risks that may be connected to it. A device is classified I-III and then goes through the appropriate process for that class. The FDA makes the decision whether or not to accept the device for market release. This Decision is based, among other things, upon the demonstrated safety and effectiveness of the device. Safety in this context means that the devices benefits exceed its risks. Effectiveness means the device reliably performs the function which it is intended to perform (Maisel, 2004).

Regulations in the United States is mainly codified in the Code of Federal regulations title 21 (21 CFR) and the Federal Food and Cosmetic Act chapter V (FD&C Chapter V). Medical devices are reviewed and regulated by the FDA by using mainly two alternative regulatory standards, depending on perceived risk. These are Premarket Notification, 510(k) or Premarket Approval, PMA. The 510(k) submission can be *cleared*, whilst the PMA submission can be *approved*. The 510(k) is the dominant regulatory process used for low- and intermediate-risk medical devices. Only 1% of all medical devices go through the more extensive PMA-process, created for high-risk devices (Zuckerman, Brown, & Nissen, 2011); (Trautman, 2011).

3.2.1 Classification

During classification the device is analyzed and its risk level is determined. Depending on the level of risk that may be associated with the device it is assigned to one of three defined classes.

- Class I: Lowest risk
- Class II: Intermediate risk
- Class III: Greatest potential risk. Implantable or life-sustaining devices.

Classifications of devices are performed by finding a predicate; a device already legally marketed with substantial equivalence to the new device. If no predicate is found, or if it is unclear how to classify a device, a written request, called a 513(g) respecting the class or applicable requirements may be submitted to the FDA (21 CFR part 860, 2013). Class I devices are subject only to general controls. Class II devices will be subject to general controls as well as special controls. Most class II devices are subject to Premarket Notification, meaning a 510(k)-submission is required. Class III devices will be subject to general controls as well as premarket approval (PMA). (Zuckerman, Brown, & Nissen, 2011); (21 CFR part 860, 2013); (Mansfield, O'leary, & Gutman, 2005)

3.2.2 General and special controls

The general controls are requirements that must be fulfilled to ensure safety and effectiveness. (Mansfield, O'leary, & Gutman, 2005). The general controls are described in FD&C Act Chapter V and they cover (FDA, 2013):

- Adulterated drugs and devices
- Labeling of devices
- Registration of producers
- Banned Devices
- Notifications and other remedies
- Records and reports on devices
- Control of devices intended for human use

For class II devices general controls are not sufficient to ensure safety and effectiveness. For some class II devices a special controls document is defined. These special controls are enumerated existing methods required to provide insurance of safety and effectiveness. These methods are usually device specific and include guidance documents with performance specifications and standards, labeling recommendations and post market surveillance (Mansfield, O'leary, & Gutman, 2005). If a special control document is established for the device type, this explains what the 510(k) submission shall include.

For Class III medical devices general and special controls are not sufficient to provide assurance of safety and effectiveness, due to the level of risk involved with these devices (and). These devises need to go through the more extensive Premarket Approval (PMA). (Mansfield, O'leary, & Gutman, 2005); (Zuckerman, Brown, & Nissen, 2011); (FDA, 2012)

3.2.3 Premarket Notification: 510(k)

The 510(k) process is based on the existence of a predicate, a similar device that has already been approved and marketed. There is no 510(k) form, but the requirements of a 510(k) is described within the Code of Federal Regulations (FDA). (Zuckerman, Brown, & Nissen, 2011); (FDA, 2010). In proving the new medical device is substantially equal to a device already approved a less burdensome path to getting FDA approval is possible (Zuckerman, Brown, & Nissen, 2011); (Maisel, 2004). Similarities with the predicate device need to concern both intended use and technical characteristics of the devices. (Maisel, 2004).

3.2.4 Premarket Approval PMA

The PMA application is the most stringent type of device marketing application required by the FDA (FDA, 2012). This process is an approval pathway for medical devices that are class III (Zuckerman, Brown, & Nissen, 2011); (FDA, 2012). A device that requires PMA approval needs to have documentation that ensures safety and effectiveness for its intended uses on its own merits. Comparison with other devices is not interesting in the PMA approval process, since it is usually not sufficient (Mansfield, O'leary, & Gutman, 2005).

3.2.5 After market release

After FDA approval post-market evaluation is used to identify potentially serious device malfunctions. The primary method is the spontaneous reporting system which depends on a passive reporting system where patients and healthcare providers report adverse and rare serious events (Maisel, 2004). Each manufacturer is responsible to report events and malfunctions that may have caused or is potential to cause serious injury or death, however they are not required to actively seek out problems and malfunctions (Maisel, 2004); (FDA, 2013).

If regulations are violated recurrently or if they cause serious health threats the FDA may seize the medical device or injunctions may be issued. If a reasonable probability of serious harm exists mandatory recalls and premarket approval suspension or withdrawal may be used. In rare cases even criminal prosecution may be considered (Maisel, 2004).

3.3 Quality Management

A quality control system is important for all companies. Working with quality control will decrease the costs of errors and rework, meaning savings can be made (Donovan, 2006). Quality control also increases profit as well as keeps the customers satisfied. A large number of different quality control tools exist. A good way to start working with quality control is to stepwise implement the quality control tools that are appropriate for the business in question. The continuous work with quality control should include reviews where measurements and controls are performed regularly to evaluate if and how quality objectives are met and if the strategic plans are followed (Summers, 2009).

3.3.1 Quality requirements in the EEA

Quality control is a part of the conformity assessment pathways for class II devices and higher for the EEA. The manufacturer must ensure application of an approved quality system of the products concerned. It is presumed that quality systems that implement relevant harmonized standards conform to the requirements. The quality control requirements are covered in the annexes for conformity assessments ((MDD 93/42/EEC, 1993) Annex I).

3.3.2 Quality requirements in the US

Similar to the EEA manufacturers of medical devices are required by the FDA to develop and maintain a quality management system to help ensure safety and effectiveness. The quality system need to correspond to the risk and complexity of the device manufactured as well as the size and complexity of the organization. For FDA regulated products the quality system need to correspond to current Good Manufacturing Practices (cGMP) which is codified in the Code of Federal Regulations (Trautman, 2011); (FDA, 2011); (21 CFR part 820, 2013).

3.4 Regulations and Industry

As mentioned before the regulatory approval system in the US is very stringent and complex (Maisel, 2004). The FDA's responsibilities are defined in around 200 laws and resulting requirements cover hundreds of pages in the Code of Federal Regulation. Dealing with regulations of medical devices can be time-consuming and frustrating and in many cases expert help is likely to be needed (FDA, 2009). In 2002-2003 the average time for initial PMA application submission to a final decision is 8,5 months. In the same period the average time for initial 510(k) application submission to a final decision is about 3 months (Mansfield, O'leary, & Gutman, 2005).

To protect the public from all potentially harmful products would require a very cautious and thorough the approval process. It is crucial to have adequate controls to ensure the product is safe and effective, to minimize health risks and risks of injuries. On the other hand, making valuable new technology available to the public, to improve health or save lives, argues for a speedy process (Deyo, 2004); (Maisel, 2004). There are opinions among many manufacturers that the regulatory process for the American Market is too slow and that it kills people waiting for new cures. Some argue that the slow process is due to "careless scientific reasoning" and "bureaucratic incompetence". There is a source of tension within the agency due to the pressure for speedy approvals. The pressure to increase the pace of approvals creates attrition on the medical officers within the FDA. Employee burnouts are now judged to further threaten the speed of the approval processes (Deyo, 2004).

The regulatory processes of medical devices in Europe are commonly viewed as easier to manage. The regulations in Europe follow "the new approach" policy of the European commission. This approach means more self-regulations and the EU does not have a government agency equivalent to the FDA (Jeffreys, 2001); (O'leary, 2010). Within the EEA the reasoning is that if a device, in spite of limited declared performances, is able to save even one life, it must be made available to doctors. Doctors should decide whether or not a device is suitable (Pirovano, 1998). To be able to release a medical device on the market may not be as hard in the EEA as it is in the US, since it depends on self-regulation. However, wanting to go properly through the process is still hard and there are massive amounts of reading to do. The Medical Device Directive is very extensive and it contains a lot of different parts and chapters. Within the different parts there are a lot of internal references which

at times lead you in circles. There are also many involved parties, which may be confusing. Furthermore the regulations, for both the EEA and the US, are changed and updated continuously making regulatory work even more difficult.

3.5 Product development

Product development tools and methods are required to effectively identify the nature of projects and concretize what and how the product should handle the different requests. Six basic actions take place for almost all design problem-solving processes. These actions are (Ullman, 2003):

1. Establishing the customer and/or user needs and defining the problem
2. Planning how to solve the problem
3. Understanding the problem
4. Generating solutions
5. Evaluating alternatives
6. Deciding on acceptable solutions

The use of these actions varies based on product and industry. A generic phase based pathway can be considered showing the steps that every product more or less needs to go through (Ullman, 2003):

Figure 2. Five product development phases (Ullman, 2003)

These phases cover the whole product life cycle and consist of different required actions or tasks. Before moving on to the next phase the current phase faces a need to be refined, approved or cancelled. Hasting a phase results in a product with poor design quality. The different phases are described below.

Project Definition and Planning

This phase covers the forming of a project team, allocation of the company's resources of money, equipment and such necessary to accomplish the project. Combined with a task definition this constructs the framework for the project. This step needs to be well thought through to ensure a solid foundation for the rest of the project. When planning a project the following five steps need to be taken (Ullman, 2003):

1. Identify the tasks
2. State the objective for each task
3. Estimate the personnel, time and other resources needed to meet the objective
4. Develop a sequence for the tasks
5. Estimate the product development costs

Specification Definition

With the purpose of defining aspects such as the customer and the customer's requirements the information needs to be collected and analyzed efficiently.

Information gathering from the customers can be made in a lot of different ways. To do it efficiently, user integrations are almost mandatory. Gathering information is an be performed through interviews and meetings with customers and end-users. Interviews can be done with three major structural methods, Non-structural, Semi-structural or structural. Non-structural resembles a dialog or discussion where the participants are able to very freely speak about the subject in hand. A structural interview leaves the interviewees with limitations to express aspects that the interviewers are not looking for. This makes it very effective when it comes to gathering and managing larger quantities of information. Semi-structural is a mix of the two above mentioned methods where the interviewer have some questions that needs answering but still leaves the interviewee with low limitations to express his or hers thoughts. This minimizes the possibility to accidently influence the customer too much with the product development team's line of thoughts regarding the product (Lund, 2009); (Stickdorn & Schneider, 2011).

Conceptual Design

When the project-foundation is well defined the concept generating work can begin. Different tools for generating and evaluating the product are needed to get effective functional models and prototypes (Ullman, 2003). Brainstorming sessions is very commonly used for concept generation. This is a good way for groups to quick and easy generate ideas and illustrate them to each other. During brainstorming, negativity is strongly discouraged, making brainstorming a purely creative tool that helps the project group to get a broad perspective on the task and a wide variety of solutions. Some ideas might seem impossible or unrealistic initially but might contribute to the final concept later on.

Product Development

When ideas and concepts have been generated and evaluated, it is time to start developing the actual product. All too often the earlier phases get rushed and the product development phase begins without a properly defined work process, which leads to poor design practice and a low-quality product. Performance, cost and manufacturing all need to be considered before going to the production phase. As this phase prolong, new improvement and feature that did not exist in the original product might arise (Ullman, 2003).

Product Support

This phase is an after-market phase and it is important that the manufacturer provide support to insure a good quality for the end users. This does not necessarily mean end user support; it could also be vender support. In some cases this phase also involve retirement of the product (Ullman, 2003).

3.5.1 Quality Function Deployment - QFD

A method that is very commonly used in product development, as a phase overlapping tool and to get a good overview on the whole project is the Quality Function Deployment matrix, QFD for short (Ullman, 2003). The QFD is a powerful tool that is designed to translate customer needs into measurable technical solutions. This gives the developer objective feedback on whether the product meets the customers' expectations and requests. In other words, the QFD helps the developers to easy overview the whole development phases from customer identification to prototype assuring that crucial aspects don not get lost along the way. To be able to utilize the QFD, the targeted customer and their requests must first be identified. Identifying customers segments is vital to the project because it helps sorting out what kind of information is required in the product as well as it

helps distinguish the language and terminology. These customers or personas rule out the areas and aspects of the product that are less relevant as well as help determine which areas are more relevant (Stickdorn & Schneider, 2011).

Within the QFD the customers' requests are defined as customer values which are non-technically specified attributes that the customer may express directly or indirectly. Non-technically specified means that the value is not a specific technical solution, instead it is defined as a function. If the value is defined to specific, it will hinder the open mind and limit the variations of solutions of the developers throughout the process, especially during brainstorming. A QFD have many uses and users and can consist of more elements and matrixes depending on the nature and purpose of the product (Ullman, 2003), (Modular Management, 2011).

A part of the QFD is the relationships matrix which shows connections between specific customer values and corresponding products properties. To create this matrix first off the relations are identified and visualized and then the information is inserted. When in the actual matrix, the different relations are weighted. The weighting shows how strong the relationship between the customer value and the product properties is. By doing the relationship matrix, an easy overviewed illustration is created that tells what to focus on and when (Ullman, 2003). Design Property Matrix (DPM) is another part of the QFD and shows relations between product properties and technical solutions. Technical solutions are hand-on elements of the final product that are measurable and easy to work towards when creating the product.

4. Project context: Sister Kenny Research Center

This chapter gives background information on the Institute and the research center where the case study has been conducted. It also briefly explains the current management structure of the research center.

4.1 Sister Kenny Rehabilitation Institute

Elisabeth Kenny was a nurse and served for the Australian army for 31 years. During most part of her career she was treating the sick in the bush lands of Australia. In 1940 Sister Kenny traveled to The Unites States and in 1942 the Sister Kenny Institute was established in Minneapolis, Minnesota (Allina Health, 2013).

The sister Kenny rehabilitation institute work with technologies and therapies that help patients rebuild their lives after physical and medical challenges (Allina Health, 2013). The Sister Kenny Rehabilitation Institute has a legacy of innovative rehabilitation research that springs from Sister Elisabeth Kenny Challenging the prevailing medical treatments for paralytic polio (SKRC, 2001). The Rehabilitation Institute strives to include advanced technology in the patient care to be able to help patients get back to their lives in the best way (Lund, 2009).

4.2 The Research Center

The Sister Kenny Research Center, SKRC in short, works with patient-focused research to develop new rehabilitation technologies (Allina Health, 2013). SKRC serves as a learning laboratory for innovations in rehabilitative care and treatment as well as provide support to clinicians with research and innovation interests (Lund, 2009). The SKRC focuses on low-risk technologies, meaning class I-II devices. The goal for technologies to be commercialized is to keep them simple and inexpensive. This means not applying for more than a 510(k) and the corresponding for the European market. They envision a fairly short path to market (Parmar, 2011).

4.3 RxFunction and the Walkasins™

The SKRC has taken equity in a company that is based on the technology created by the SKRC director Lars Oddsson. The company is called RxFunction and its technology is the Walkasins™. The Walkasins™ help improve the balance of people to reduce the risk of falling and was developed by Dr. Lars Oddsson et. al. at Boston University's NeuroMuscular Research Center. A CEO has been hired to build the company and commercialize the product and to see it through the regulatory processes (Parmar, 2011). The main objective for RxFunction is to turn the vibrotactile research into a commercial product. To achieve this, the company has focused its efforts on managing the design and system performance design in accordance with regulatory guidelines (Leach, 2013).

The Walkasins™ are a gait and balance augmentation system in the form of a wearable device (Leach, 2013). The device is a sensory prosthesis which senses the users balance and gives gentle vibratory cues that help the user walk with greater stability. The vibrations give the user a new sense of balance to improve stability for safer walking and standing (RxFunction, Inc., 2011).

5. Methods

Developing this product focuses on the first three steps of the design process described in the theory chapter. The following chapter describes which methods and tools used to achieve this and how they were adapted in this specific project.

5.1 Conducting literature review

Research has been made in literature to learn more about the different procedures and aspects of the regulatory processes, both for the European market and the American. The main part of this research has consisted in finding and reading the different regulatory documents for the two markets, as well as different guidelines presented by the European Commission and the FDA. For the European Economic Area the research has been done with the Medical Device Directives (MDD) Directive 93/42/EEC on Medical Devices, and its Annexes, as well as guidance documents and FAQ from the European Commission. For the American market this means the Code of Federal Regulations, Title 21, the Federal Food, Drug, and Cosmetic act (FD&C) chapter V, as well as guidance documents from the FDA. Alongside with this research different articles and guides from other sources have been used, to create a wider understanding. Following this research a study of the Sister Kenny Research Center has been made. This study covers history, operations, research activities and structure, all to create a better understanding, to be able to develop the best solution possible.

5.2 Product development

After background information had been gathered the next step, in the project definition and planning phase, was to define the actual problem and decide on which tasks need to be performed to solve the problem. The problem in this project is defined as a need to create better understanding of the regulatory processes and make them more graspable. To accomplish this, a regulatory guidebook is the product that will be developed within this project. Product development tools have been used and a number of tasks were defined. These tasks and what tools where used is described below.

5.2.1 Initial brainstorm

To get started with the specification definition phase, a cluster based mind map brainstorming session was performed. The brainstorm was made up with many smaller brainstorming topics on different clusters. This made it massive but still comprehensive with a good base for the project framework. The brainstorming was performed after the main literature study, with its information in mind. The goal with this mapping was to, with a wide perspective, visualize the possible or likely components of the guidebook, as well as help the project to find common grounds for the development team to continue work from. The brainstorm rules were simple: with the use of Post-its, different thoughts about the guidebook, subjective and/or objective, where put on a wall in categorized clusters. These clusters were made up as the session progressed with the only preference being that they revolved around the guidebook. Seven main clusters were identified, which are presented below.

Users

This cluster identifies all possible users of the guidebook. They vary widely from expected high frequents user such as the management of SKRC to the less likely such as Physical Therapists (PT's).

Required actions

This cluster contains the major required actions throughout the regulatory process regardless of classification as long as it is in the reasonable product range for SKRC.

Required documents

These are the documents that are considered mandatory for every regulatory application. Some of them are an actual document that needs to be submitted and some are documentation that needs to be available within the company for future inspections.

Presentation

These are aspects about how the guidance should or could be presented. The cluster contains visual tools and illustrations as well as subjective context, for example how fun it is to read or the difficulty level of the language.

How do we get feedback?

Since this product is the first of its kind at SKRC, getting feedback will be crucial otherwise the guidebook might end up being useless. Having a relevant feedback plan is there for important. In this cluster different feedback channels are presented**.** Both initial feedback from the customer for outlining the project frame as well as final feedback and testing for the next generation product was considered.

How do we use the guidebook?

This cluster consists of different ways that the guidebook can possibly be used. This plays a major role in defining the purpose of the guidebook and what to fulfill. All of the aspects cannot be fulfilled since that would make the guidebook to voluminous. But having all possible usages defined helps minimizing the risk of missing the important ones.

What's in it?

The thoughts in this cluster are mainly related to the purpose of the guidebook and general presentation methods considered when creating it. It also includes most of "must haves". Even if some of these might be considered obvious, it is important to define them so that they are not forgotten.

5.2.2 QFD

After the initial brainstorming, a QFD was initiated. The QFD was created in steps with the initial task is to identify different customer segments. Since the product targets a small customer group at SKRC, identification of the customer was done through interviews, meetings, observations and in collaboration with the customer. The interviews were conducted as non- to semi-structural interviews, allowing the interviewee to speak very freely about their visions regarding the product. Three general customers or user segments were identified. These segments represent the most likely users that will use the guidebook. The identified customer segments represent different business field with different values. The information from meetings and interviews was also used to define customer values.

After the customers and customer values had been defined a survey was performed. In this survey different customers at SKRC rated the defined customer values using a scale from 1 to 12 where 1 meant least important and 12 most important. The purpose of this was to create understanding of which of the defined customer values where most important. The customer values were then

translated into product properties with the help of fishbone diagrams. Connections between customer values and the product properties where weighted in a relationship matrix. The strength of the relationships was divided into 4 levels. A strong relation was shown with a solid black dot, a medium relation with a half filled dot, a weak relation with a white dot and a non-existing relationship was illustrated with a blank cell.

With the specification definition phase finished, the conceptual design phase could be initiated. With the customer values and product properties and their relations identified a second brainstorming session was performed. The purpose of the second brainstorming was to identify suitable technical solutions. These solutions are elements of the final product that are to be included or should serve as a guideline for the product property.

With our project the Design Property Matrix, DPM, is the final element. The DPM is also a form of relationship matrix but instead of showing a relation between customer value and product property the DPM shows whether or not a relationship exists between a product property and a technical solution. By showing the relations, the DPM works both as a guidance tool and an evaluation tool.

6. Results

The different product development tasks generated a number of results. These results and analysis of them created the base on which the guidebook was created. This chapter presents the different partial results leading to the guidebook.

The results from the initial brainstorm are presented in Appendix 1. The brainstorming session made it possible to start working with the QFD. First of all the customer segments were identified.

6.1 The customer

The identified customer segments are described below:

Project leaders and management at SKRC

This user is well educated, and has expertise in medical science. This customer is also used to working in projects. The user has an academic background and the ability to process a lot of information. For this user it is very important that the product is accurate, reliable, has a high level of usability and is trustworthy. Appearances in the form of presentation and illustrations are of less importance.

Smaller companies/start ups

This user is likely to have a more business-oriented background. The user is also well educated, but less aware of the medical devices industry and the requirements in it. For this user the regulatory aspects are more difficult to grasp meaning usability and presentation is very important. Since these start-ups most likely will work in some proximity or correlation to the management at the SKRC, one can assume that some guidance and help will be provided from SKRC.

Researchers/engineers/product developers

These users are probably the least frequent users but they are also the widest group. These are the different people involved in product development, students, researcher, healthcare personnel, and engineers, which have different levels of education. These users may or may not be directly involved in the regulatory stages of development projects. However some understanding of regulatory aspects and quality control is necessary to at least be able to understand what kind of work that is required eventually before market release and understanding how their documentation in earlier stages might be of use.

After analyzing the information gathered, through meetings and interviews with the SKRC customer values were identified. The customer values are listed in Table 1.

Table 1. Customer Values

Costumer Values, The product should:
Be easy to use and understand
Help me understand the regulatory processes
Help me get through the regulatory processes
Be fun and inspiring
Easy to manage
Updated and reliable
Give an overview of the regulatory processes over time
Refer to and help me find more information if I want to
Make the use of consultants more effective
Shall help cut the time to market
Identify what is appropriate to do in-house and not
Be relevant for our range of products
Help me understand and use a quality control system
Tell me what documents are required and when

The result from the survey where translated into averages for the different customer segments and then inserted into the QFD in the matrix between the customer values and the users segment, shown in appendix 2. The most important customer values for the different segments are highlighted with red in the QFD.

6.2 Product properties

The different Product properties are listed in Table 2.

Table 2. Product Properties

Product Properties
Easy Overview
Illustrative
Assistance
Quality Guidance
Chronology
Understandable Language
Process understanding
Purpose
Professional
Reduce waste
Instructions for use
Accurate information

6.3 Relationship matrix

The relationship matrix was filled out as shown in appendix 2. The relationship matrix gives a good overview of the existing relations as well as the strength of the relation. This helps keeping track of the customer values throughout the process and also helps the evaluation on how to fulfill the customer values.

The result of the survey together with the relationship matrix gives a strong indication on which product properties are most important to work with in the creation of the guide. The product properties that have relationships with the most import customer values are the ones that should get the most attention.

6.4 Second brainstorm storming, Technical solutions

The second brainstorming session was performed to identify suitable technical solutions. The technical solutions are shown in Table 3.

Table 3. Technical solutions

Technical Solutions
Chapters
Timeline
Vocabulary
Table of contents
Models
Color
Chart
Picture
Right amount of info
Task/responsibility
References
Document Handling
Step-by-step
Testing
Explanation
Professional language
Right level of language
Accessible format
Recommendations
Journal
Instructions
Quality Requirements

6.5 Design Property Matrix – DPM

The DPM is this projects final element of the QFD. The DPM shows what shall be achieved with each "technical solution", as well as serves to make sure that the correct product property is achieved with the help of the accurate technical solution. The DMP is a part of the QFD shown in appendix 2.

6.6 Conclusions of the QFD

For management the most important product property is *accurate info* followed by "*assistance*" and "*purpose*". For researchers the most important property is "*illustrative*" followed by "*assistance*". Finally for start-ups the most important is "*assistance*" followed by "*waste reduction*". The conclusions made from this are that the product properties most important, which technical solutions needs the most attention is:

- Assistance
- Accurate info
- Illustrative

Assistance is in top two for product properties for all the customer segments, meaning this is the utter most important. *Assistance* is also the widest property, with a lot of technical solutions and connections to it. The technical solutions to mainly focus on according to this analysis are the ones connected to these three most important properties.

7. The regulatory guidebook

This chapter presents and explains the final product created in this project. It gives information on the final format and contents of the regulatory guidebook and presents its images and illustrations.

The guidebook shall make the regulations more understandable, and is to be used as a tool to help projects at SKRC with the regulatory process throughout the product development. This has been the main focus when developing the product, both in literature review and in creation of the guidebook. To accomplish this emphasis on the right areas was crucial. Emphasis was made on ensuring correct and accurate information about the regulations. Limited to what is interesting for Sister Kenny Research Center and their product scope. The guidebook is not meant to be read from cover to cover making the reader an expert in regulations. Instead it is meant to give an overview, show what is needed in different stages and where more information can be found.

7.1 Contents

The guidebook contains 18 chapters that are created as modules. The first chapter of the guidebook is an introduction. This chapter starts with explaining some background around regulations, and why they are needed. This is important, since it explains the purpose of regulations to the reader. The introduction also provides recommendations on how to use, manage and update the guidebook. The other chapters of the guidebook do not have to be read from the beginning till the end, instead they should be used as they are coinciding with the process. The introduction chapter ends with recommendations to sign up for newsletters from both the FDA and the EC. In this way changes in regulation, which happen all the time, will be notified, and the guidebook can be updated continuously by the research center. After the introduction there is a regulatory glossary, presented in appendix 3. This is meant to give understanding of the different terms and expressions used in regulations, and to create a common vocabulary for the users.

The glossary is followed by three different flow charts. The first two are pathway maps for the regulatory processes in the US and the EEA (see Figure 2 and Figure 3). These maps present the different steps that are included in the different regulatory processes. The illustrations are meant to give an overview and understanding of the regulatory processes. The headlines in the illustrations are all represented by chapters in the guidebook that give more detailed information of the different steps. This structure makes it easy to know what to read and when.

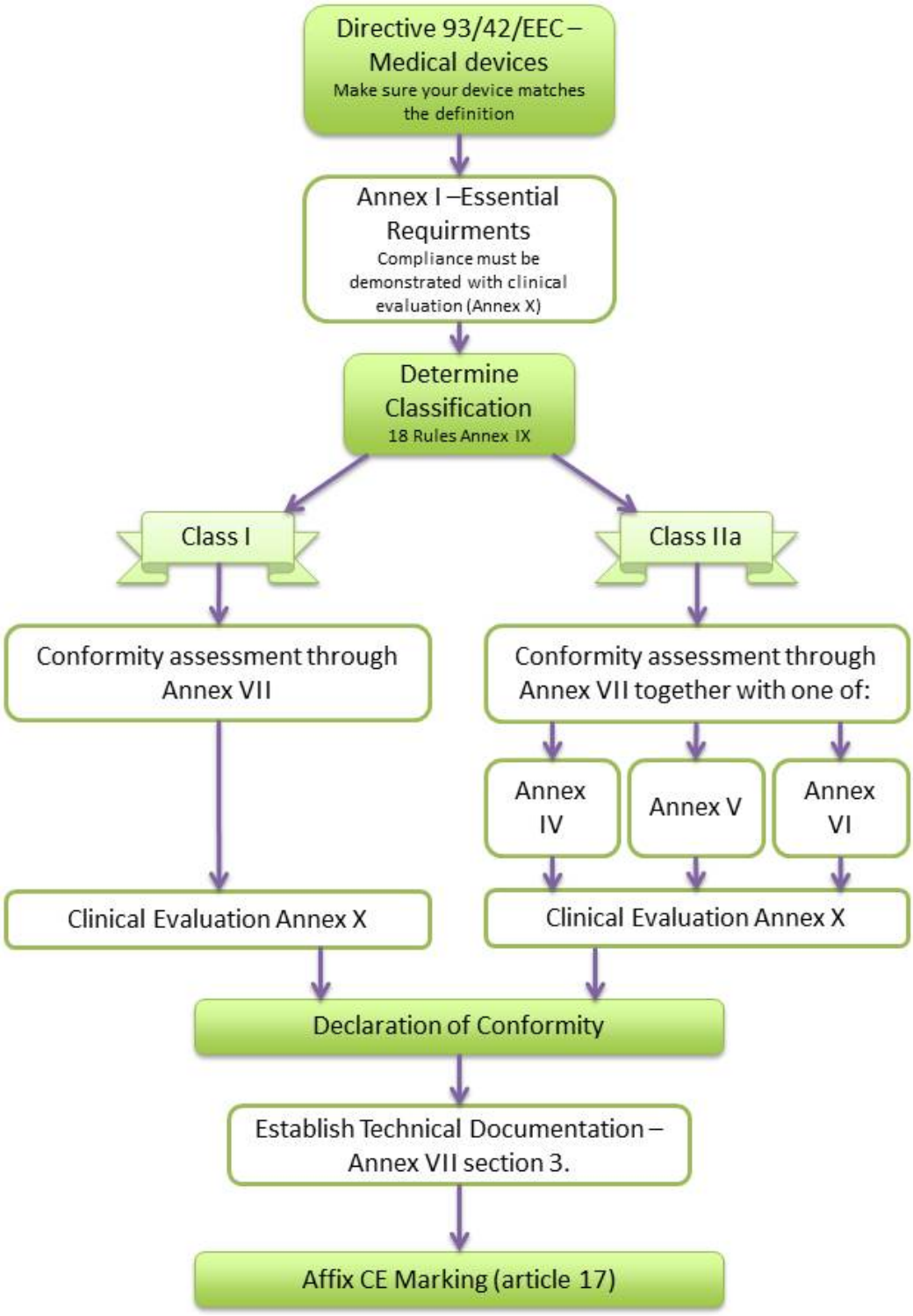

Figure 2. Regulatory path for CE-marking

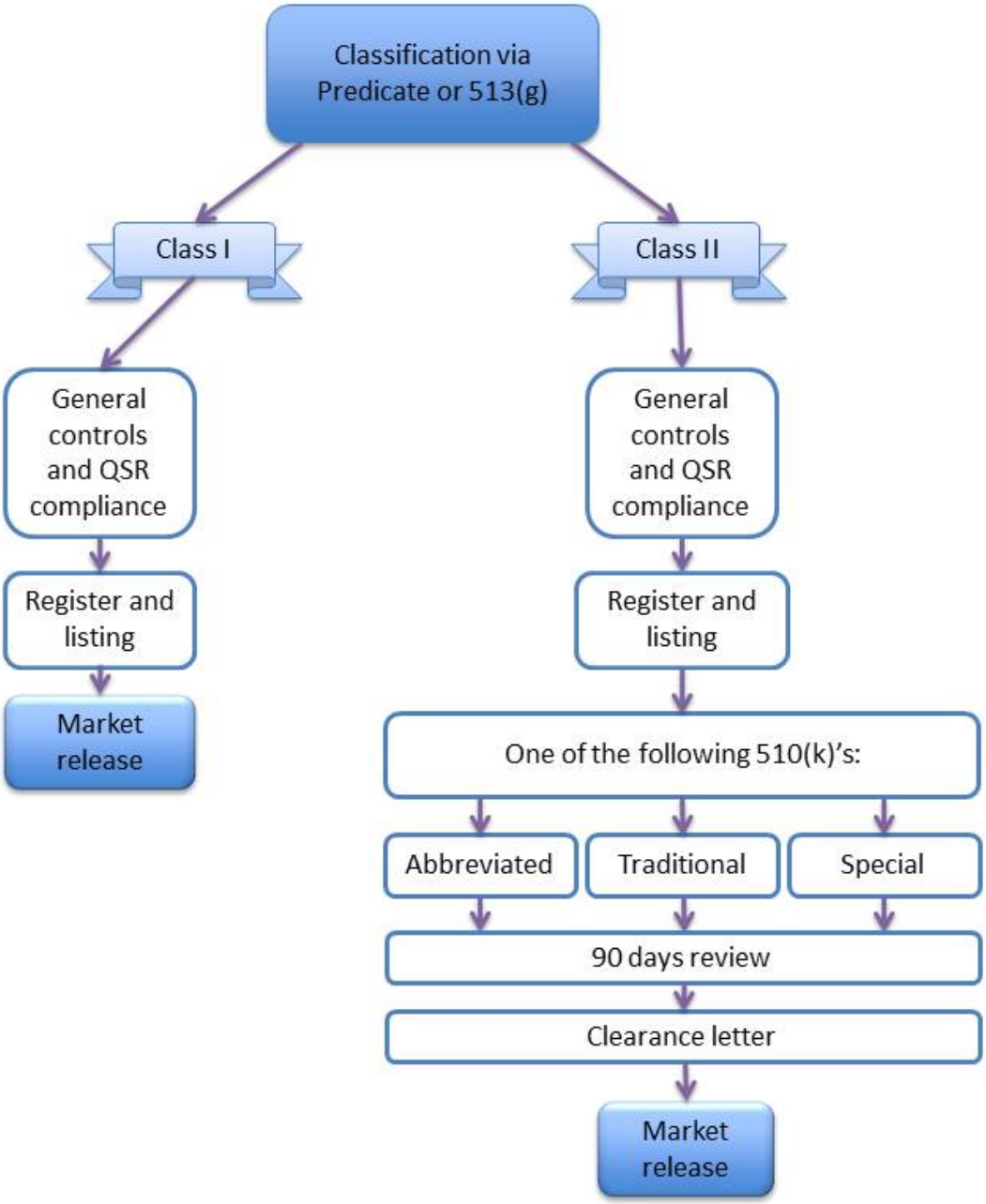

Figure 3. Regulatory path for FDA clearance/approval

With the different steps presented in these pictures the reader will be able to recognize where they are in the process, and how to proceed. To further help the overview the next picture presented in the guidebook is a regulatory timeline, where both the FDA and the CE-marking processes are shown (Figure 4).

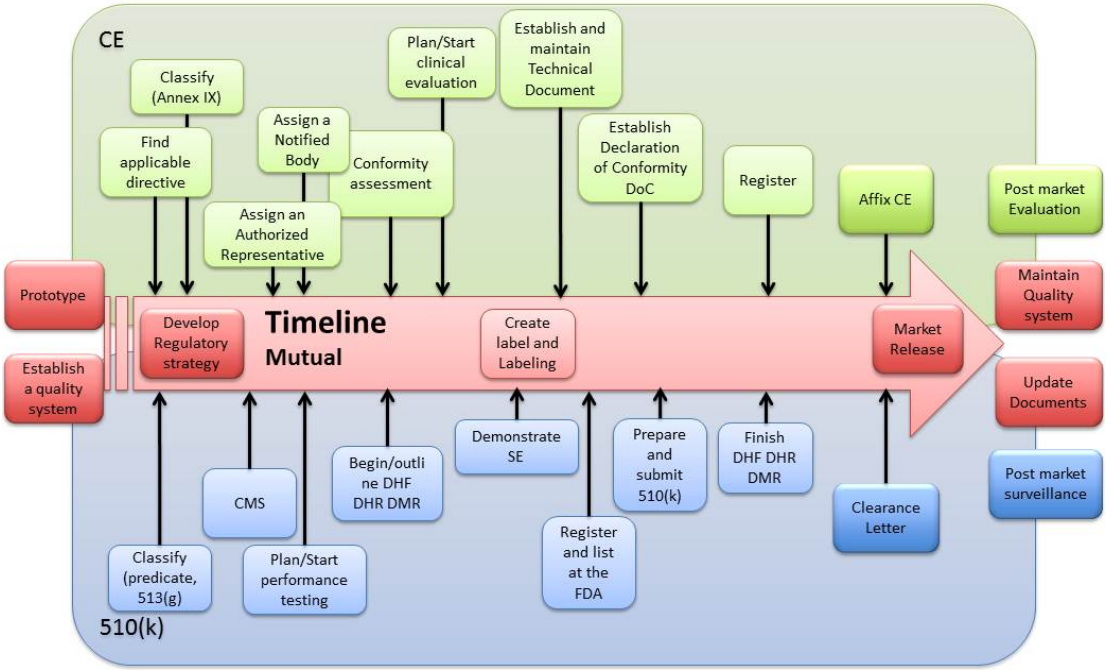

Figure 4. Regulatory timeline

To have both processes presented in one picture gives a better understanding of how they work, how they differ and what they have in common. This is another helpful tool in working with the regulatory processes and it was requested early on from the SKRC.

In creating the guidebook the result from the QFD was used. Emphasis was at make the guidebook illustrative and ensuring that it contains accurate information. *Assistance* was the most important property to the users. It means the technical solutions that are connected to *Assistance* in the DPM shall be focused on in the guidebook. These technical solutions are: *right amount of info, tasks/responsibility, references, Doc. Handling, step-by-step,* and *testing*.

To ensure the guidebook contains the right amount of information only information deemed to be interesting for the SKRC product scope has been included. Instead of giving full insight in all regulations the book covers a generalization of the process, adapted to a limited amount of product types. These limitations mean, among other things, that invasive devices, sterile devises and dental devices are excluded. Where information is presented there is always a reference to where the information is gathered. Wherever something has been excluded, this is also mentioned, so that the reader is always aware of the generalizations and limitations of the guidebook. If more information concerning something is required, it will be easy to know where to find it, even if it is not in the guidebook. Having the right information along with understanding of the regulatory processes and its tasks will help the reader to create and define different responsibilities and tasks.

Within the regulatory processes, as well as quality management, there are a lot of documents required. Therefore there is a separate chapter covering document handling in the guidebook. This chapter names the documents required for the two markets, and gives references on how to create them. Some documentation is required for both the CE-marking and the FDA. These documents may

be have different names but contain the same information. To clarify and help the reader, the document chapter includes a checklist, in the form of a table that covers all documentation required, and what files should be a part of it.

Another property of the three most important was *Accurate info*. This property is connected to the technical solutions: *right amount of info*, *references* and *instructions*. With this in mind the different chapters was created to contain information as well as instructions, concerning the different steps to take through the regulatory processes. Instructions are presented both as text and pictures and cover both regulatory actions and how to find more information.

Illustrative was another property that was important, according to the QFD. The technical solutions connected to this property are: *timeline, color, chart, picture*. These technical solutions are incorporated in the guidebook in many ways. The illustrative pathway maps as well as the combined timeline described earlier are examples of this. These illustrations are also connected to the technical solution *step-by-step*, connected to *assistance*. Furthermore the entire guidebook is color-coded. Chapters and information about the CE-marking is marked with green. Information concerning the American market is blue and chapters concerning both, that are more general, are marked with red. The color-coding cover headlines and references, and all chapters are color marked in the top right corner. This helps the reader quickly find what they are looking for. Examples of these color-coding are presented in Figure 5 as well as in Figures 2-4.

Figure 5. Color coding in the guidebook

To make the guidebook easy to use and understand and instructive, as well as illustrative, some instructions have been presented as pictures. An example how to create a label that follows the regulatory requirements is shown in Figure 6.

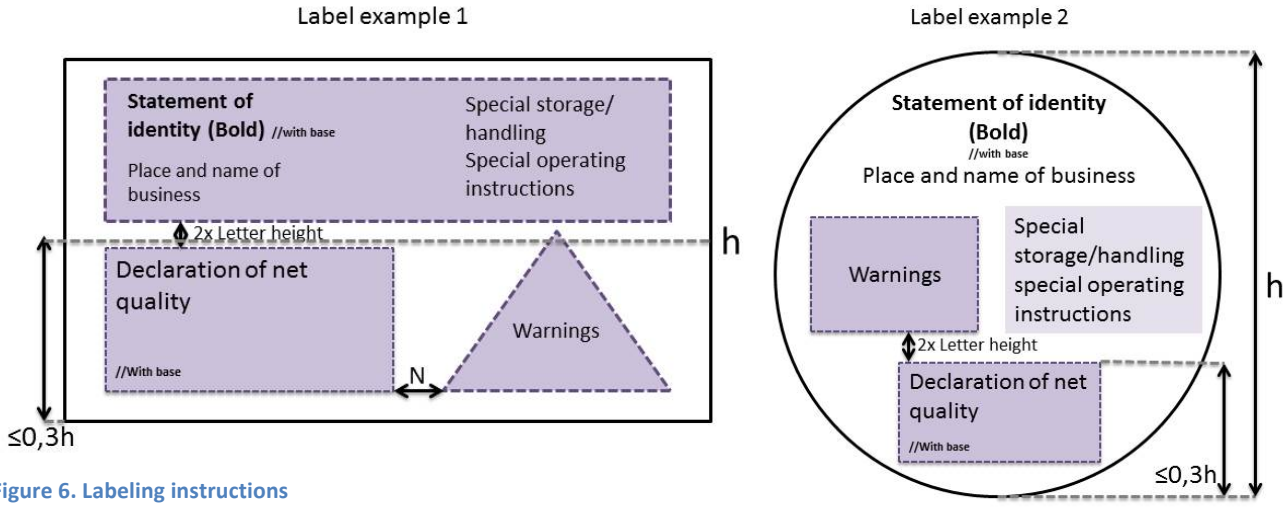

Figure 6. Labeling instructions

Labeling for over the counter devices need to follow a large quantity of requirements. To make it understandable the information and instructions in this chapter was complemented with pictures illustrating the different requirements.Figure 6

7.2 Easy to manage

Since there will be no one specific at SKRC assigned to work with regulation it is important that the guidebook is easy to manage, not adding more work, but easing the processes. This was kept in mind through the entire creation of the guidebook. The complete guidebook contains 18 chapters structured as different modules. The chapters are separate digital files, and they were also presented as a printed version in a binder. The different chapters are built as modules, mainly to ease the management and auditing of the guidebook. When regulations have changed in some area, it is sufficient to update the specific chapter instead of managing the entire guidebook. All chapters contain the date of latest review presented in the bottom right corner. Changing the date of latest review makes the user confident in the material and that it is updated. To further ease management of the guidebook all programs used to create it are standard programs that most people have access to and are capable of handling. The programs are Microsoft Word and Microsoft PowerPoint.

8. Discussion

The regulatory guidebook need to cover different types of product and it needs to be accessible for different type of users. Furthermore a guidebook is not a typical product since it has few measurable features making. The discussion covers problems encountered during product development. It also gives suggestions for future improvements of the guidebook.

8.1 Difficulties and limitations

A very early problem during the development process was to figure out how to organize the information so that the user can navigate in the documents and find the information. Depending on which development phase the specific device is in and who the reader is, the focus may vary greatly. Covering all different angles with one guidebook is challenging and requires a lot from the presentation. Throughout the development process it became clear that the final product probably would become a fundamental for future developments. Early the decision on making the product a guidebook rather than any other guide device was made. This was because it needed to be accessible, easy to manage, and in a familiar format. With that decision made, other difficulties remain; a guidebook is not a typical product when it comes to product development. There are not a lot of measurable features to verify the product and the results. Most of the tools used for product development are based on exact results and validations. This meant the methods needed to be tweaked, to fit this product. Technical solutions for instance, instead of being a measurable validation whether the goal has been met, was used as a guiding tool to make sure that we focus on the right aspects at the right section of the texts. Every product and industry is unique which in turn puts unique requirements on the different available methods and tools. Therefore the tools and methods need to be tweaked accordingly to ensure a good usability in the information gained from them. There is no right answer to which tools that should be used or not so the developing team needs to choose based on experience and anticipations making sure that there is a vision and goal with the method. We choose the QFD as our main tool knowing that it is a powerful tool with great overview making it reliable to fall back on. Also it is a tool we felt comfortable with making the tool more effective.

An aspect that was more time-consuming than expected was the problem definition, customer identification and with that, customer values. SKRC did not really know what they wanted from this project, except help with regulations. The SKRC themselves was not entirely sure what development phase they were in or where the actual problem was. This made the project move back and forth in the beginning, trying to figure everything out which was very time consuming. More time and emphasis should have been spent on discussing and defining the actual problem and its causes, before starting product development.

This project has mainly evolved around the regulatory processes in theory. The initial thought was to work with the theory parallel to working with the test case, the Walkasins™. This however proved difficult, since the main object of the project was to create a tool or a guide to working with regulations. Creating this guidebook demanded good understanding of the regulations and the procedures, which was fulfilled by reading and researching within the regulations. The guidebook was supposed to work for all of SKRC's product range, meaning a general approach was needed. Also, putting a specific device through the appropriate regulatory processes is time consuming, and its timeframe exceeded the amount of time we had at the SKRC. The consequences of the above mentioned issues are that the guidebook is mostly based upon theory around the regulations, and

not on actual use for a product. It consists of different regulations and requirements that are likely apply to SKRC's product range as well as references to all interesting regulations and rules. Furthermore illustrations and checklists have been made to ease planning, overview, documentation and document handling. Since the guidebook has not been applied on an actual case yet, it is hard to imagine which difficulties the user may face, what the actual timeframes are and exactly what needs to be performed, especially since regulations are very device dependent.

The guide-book in its current state is still a major help for SKRC. It can be used as a tool to get better understanding of the regulatory processes and help in where to look for more information. It is a summary and a tool to be used to help clarify the regulation and gather all relevant information in one place. It gives an overview of the regulatory process for the two markets and by doing so it supports innovation by keeping projects on track. The SKRC expressed a feeling of hopelessness toward what initially feels as an overwhelming task of the regulation process. By providing an overview of the processes at this stage, they have gotten help in starting to organize and create a strategy to how they should approach the regulatory process.

8.2 Future work

It is very difficult to create an accurate guide for a product without actually taking a product through out the whole process, since regulations differ with every different device. Therefore the information and material in the guide-book is generalized, and meant to serve as a helpful tool for all different product types at the Sister Kenny Research Center. Some parts of the chapters are probably in need of a rewrite, as is often necessary when it comes to early versions of papers. Going through the regulatory processes in theory is likely to not always meet the actual processes in practice. It would be advantageous to use the guide-book for a product step by step and update it with a trial and error mentality making sure that each chapter fills its purpose.

To have had access to an actual SKRC related product already approved by the FDA and granted a CE-marking, would have been very helpful in creating the guidebook. This would give a greater insight in which documents that are needed, what kind of tests that need to be performed and what needs to be proved. That would result in a greater understanding in the specific cases that is the product range for SKRC, and would make it easier to do a more specific guideline with more detailed information, and the generalizations made would be more accurate. This kind of approach was not possible for us because SKRC have never gotten all the way to market with a product. Eventually when the Walkasins™ get approved, a new project with those applications and the guide-book as a foundation will most likely generate a very effective, informative and adapted guide-book. So even though it is in need of a trail run, the guide-book that we created will serve the company well as a foundation for future editions or versions.

Another work for the future could be to create a stronger connection between the guidebook and the innovation handbook. This would connect the regulatory process even more to product development and innovation. Since the SKRC already have a positive relationship to the innovation handbook and a well-defined habit of using it, this would also help make the guidebook and regulations more accepted.

Discussions may be made whether a "book" actually is the best format to guide the users throughout the regulatory process. Like mentioned earlier the reader's interest and reason for reading it may vary greatly and some bits and pieces might be more or less interesting. Having one text to fulfill and

answer an in depth readers every question that and at the same time is not too overwhelming for someone doing a preparatory light read is challenging. In the future, having one text is probably not the answer but rather trying to have different levels of information depending on the information required. If that is the case, having a different presentation form, like a hyperlinked document or other digital presentation platform might be more efficient.

9. Conclusion

The regulatory approval processes are difficult in many ways. This chapter describes conclusions that can be made on why this causes a problem for small companies, such as SKRC. The chapter also presents ideas on how to minimize these problems.

Medical devices cover a very wide variety of products and there is, for many, an overwhelming amount of information in these regulations. That makes finding the relevant information hard and also knowing if the information you actually have found is the right one. Furthermore regulations change all the time making it hard to keep track of the latest guidelines and regulation procedures unless you are a full time regulatory expert. A conclusion that can be made is that presentation is the overall biggest problem with regulation of medical devices. It is difficult to know what to look for and where. Developing better and more accessible guidance documents is one way of minimizing this problem.

For the personnel at the Sister Kenny Research Center the regulatory process for medical devices is unknown territory. Their biggest problem is their lack of experience in this area, meaning they have little to none knowledge about how to get a device through a regulatory process. During the project observations fear and aversion related to regulations have been made at the SKRC. The existing quality control system at SKRC is based on documentation and approval, following a number of standards and requirements. Having to document and approve every action is in many ways not suitable for this small research center with limited number of employees. It seems unnecessary to document and approve actions that only concern yourself. This may also create an aversion to develop and make changes, since that would create a demand for a lot of paper work that may feel excessive. The reason for this aversion stems from lack of understanding of the purpose of quality work. If there is no sense of purpose, creating these documents will seem unnecessary and stupid. There is also fear and aversion towards the actual regulatory processes. When scratching the surface of these processes even more questions arises understanding the processes is very time consuming. The reason for this is mainly the way regulations are presented and made available. The big amount of available information makes it hard to find which regulations apply to a specific device, and when you do there are many exemptions. Furthermore the regulations are written in a very formal and juridical language that is difficult to grasp for the unaccustomed. Within the texts there are references to other texts and paragraphs, and the same document may have different titles. All of this combined makes is very hard to create overview and understanding.

To solve this problem and reduce the existing aversion of regulations guidance documents and simplified instructions could be a solution. There are guidance documents on both the FDA and the EC webpage which may help. These are however somewhat hard to find and in many cases too simplified and even substandard. Especially the FDA has problems here since many of the links to guidance are broken, and their webpage is hard to navigate. Presenting the regulations in an understandable way and with a clear purpose would facilitate a lot of the work with regulations. Checklists, step by step pathways, illustrations and helpful tips would help even further. In this project a guide-book has been created with that exact purpose, to help create an overview and make regulations more understandable. This guidebook covers products that are likely to be developed at the SKRC, and it is simplified and adapted to their business.

The elusive and demanding regulatory processes may be an obstacle that actually hinders innovation. The easiest way to get a medical device approved for sale in the US is to find a product that is similar, a predicate, and follow the exact same regulatory route. If no predicate can be found, or if the difference between the new device and its predicate is significant, the regulatory process will be a lot harder to get through. This could have the effect that new devices are modified to be more similar to an already existing device, with the loss of new and innovative solutions. The results of this can be that devices and solutions that could revolutionize the industry could be lost, and never reach the market, simply because regulations are perceived as to massive. This risk is even bigger for the American market than the EEA, which is more based upon self-regulations. However for both markets, the more complex the device is, the more rigorous the regulations are, so there will always be risk of innovation and development being deselected over a faster route to market. To avoid this it is crucial to make the regulations more graspable. Regulations still need to exist, to protect the health and safety of the user, but in making them more understandable and graspable they may be used more efficiently and a lot of the problems with regulations could be minimized.

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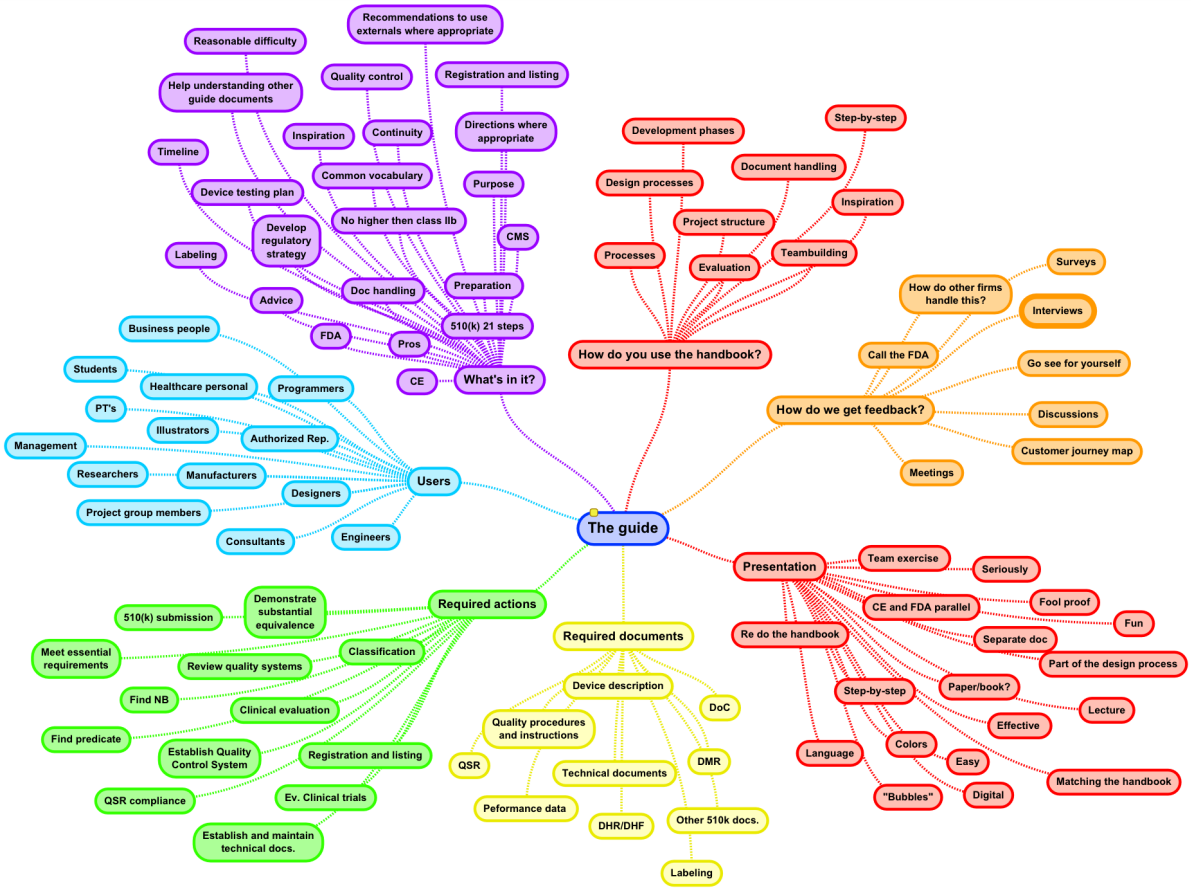
Appendix 1: Initial brainstorming

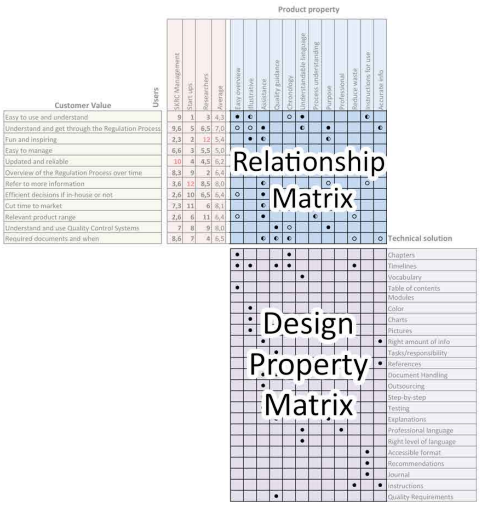


Appendix 2: QFD

Customer Value / Users	SKRC Management	Start ups	Researchers	Average	Easy overview	Illustrative	Assistance	Quality guidance	Chronology	Understandable language	Process understanding	Purpose	Professional	Reduce waste	Instructions for use	Accurate info
	Product property															
Easy to use and understand	**9**	**1**	**3**	4,3	●	◐			○	●					◐	
Understand and get through the Regulation Process	**9,6**	**5**	**6,5**	7,0	○	○	●			◐		●				◐
Fun and inspiring	**2,3**	**2**	**12**	5,4		●	◐					◐				
Easy to manage	**6,6**	**3**	**5,5**	5,0	◐										●	
Updated and reliable	**10**	**4**	**4,5**	6,2									◐			●
Overview of the Regulation Process over time	**8,3**	**9**	**2**	6,4	○		◐		●							
Refer to more information	**3,6**	**12**	**8,5**	8,0			◐					○			○	
Efficient decisions if in-house or not	**2,6**	**10**	**6,5**	6,4	○		●				●			○		
Cut time to market	**7,3**	**11**	**6**	8,1			◐		◐					●		
Relevant product range	**2,6**	**6**	**11**	6,4	○		●				◐			○		
Understand and use Quality Control Systems	**7**	**8**	**9**	8,0				●	○			●				
Required documents and when	**8,6**	**7**	**4**	6,5			◐	◐	◐					○		○

Technical solution

●				●							Chapters
●	●		●	●					●		Timelines
					●						Vocabulary
●											Table of contents
											Modules
	●										Color
	●										Charts
	●										Pictures
		●								●	Right amount of info
		●	●								Tasks/responsibility
		●						●		●	References
		●	●								Document Handling
		●									Outsourcing
		●									Step-by-step
		●									Testing
			●				●				Explanations
					●			●			Professional language
					●						Right level of language
									●		Accessible format
									●		Recommendations
									●		Journal
									●	●	Instructions
			●								Quality Requirements



Appendix 3: Guidebook glossary

Definitions, glossary and abbreviations

To help understanding and create a mutual language, a glossary with abbreviations and definitions is given below.

General

- **Classification:** All medical devices are divided into classes according to the level of potential risk involved with its intended use. For U.S the classes are I, II, and III and for the EEA they are I, IIa, IIb and III.
- **Design input:** Physical and performance requirement that are used as a basis for device design.
- **Design output:** Results of a design effort at each design phase and at the end of the total design effort. Finished design output consists of the device, its packaging and labeling and the device master record.
- **Design review**: Documented and systematic examination of a design. Evaluates adequacy of the design requirements and evaluates capability of the design to meet the requirements.
- **Duration of use**: The duration for which the product achieves its intended purpose.
- **Establish**: Define, document and implement.
- **Establishment**: Any place of business under one management at one general physical location where a device is manufactured, assembled or otherwise processed.
- **Implantable device**: A device intended to be totally introduced into the human body or to replace an epithelial surface or surface of the eye and intended to remain in place after the procedure.
- **Intended use**: The use for which the device is intended according to the labeling, the instructions and/or in promotions. The data is provided by the manufacturer.
- **Invasive devices**: A device which in whole or part penetrates the body, through a body orifice or the surface of the body.
- **Label:** Generally the part of the display that is attached to the device itself.
- **Labeling:** The label together with descriptive and informational literature that accompany the device.
- **Manufacturer**: The natural or legal person that has responsibility for the design, manufacture, packaging and labeling of a device before it is placed on the market in their name. The word applies to any person, who designs, manufactures, fabricates, assembles or processes a finished device.
- **Product**: Components, manufacturing materials, in-process devices, finished devices and returned devices.
- **Quality policy**: The overall intentions and directions of an organization with respect to quality.
- **Quality System**: Organizational structure, responsibilities, procedures, processes and resources for implementing quality management.
- **Validation**: Confirmation by examination and provision of objective evidence that specified requirements can be consistently fulfilled. “Did I make the right product?”

- **Verification**: Confirmation by examination and provision of objective evidence that specified requirements has been fulfilled. “Did I make the product right?”
- **Human factors**: Application of knowledge about human capabilities and limitations to design and development.
- **Usability**: Characteristics of the user interface that establishes effectiveness, efficiency, ease of user learning and user satisfaction.

The EEA

- **CE-marking:** The declaration that a product meets applicable requirements. The marking is required for sale in the EEA.
- **Custom made device:** A device specifically made with a qualified medical practitioner’s written prescription intended for the sole use of a particular patient.
- **Devices with measuring functions**: A device intended to measure quantitatively a physiological or anatomical parameter or a quantity characteristic of energy or substance delivered or removed from the human body.
- **DoC:** Declaration of Conformity**.** A document indicating that the device meets all necessary requirements.
- **EEA:** The European Economic Area, the EU countries plus Iceland, Liechtenstein and Norway.
- **Medical Device Directory (MDD) 93/42/EEC:** The directive for regulation of medical devices, except implantable and in vitro diagnostics devices.
- **Medical Device**: An instrument, apparatus, appliance, software material or other article used for human beings. It is used for diagnosis, prevention, monitoring, treatment or alleviation of disease, injury or handicap, or for investigation, replacement or modification of anatomy or physiological process, or control of conception. Its principal intended actions is not achieved by pharmacological, immunological or metabolic means, but may be assisted by these means.
- **Single use device:** A device intended to be used for only one single patient.

U.S. Market

- **21 CFR**: Code of Federal Regulations title 21. The different parts cover regulations.
- **510(k):** A premarket notification submitted to the FDA.
- **Active device**: Any medical device depending on a source of electricity or other power (not directly generated by the human body or gravity), which acts by converting this energy.
- **CDRH:** The Center for Devices and Radiological Health, one of the FDAs seven different centers for regulation. CDRH is responsible for ensuring safety, effectiveness and quality on medical devices, as well as safety of radiation-emitting electronic products.
- **Clinical trials:** Required for PMA. Trials that are intended to reflect the performance of a device in routine clinical practice.
- **CMS:** The Center for Medicare and Medicaid Services. Administrator of Medicare, Medicaid, the State Children’s Health Insurance Program and the Clinical Laboratory Improvement Amendments.
- **Design History File (DHF):** Compilation of records, which describes the design history of a finished device.
- **Device History Record (DHR):** Compilation of records for the production history of the finished device.

- **Device Master Record (DMR)**: Compilation of records containing the procedures and specifications for a finished device.
- **Effective device:** The device reliably does what it is intended to do.
- **Established name**: Official name designated by the FDA or the official title of an official compendium where the device is an article recognized. If neither clause of these cases apply, then any common or usual name of such device. *FD&C V §352(e).*
- **FD&C Act Chapter V**: Federal Food, Drug, and Cosmetic Act chapter V: Drugs and Devices. Often referred to as "the act".
- **FDA:** The U.S. Food and Drug Administration, the Agency responsible for regulation of medical devices for the U.S. market.
- **Medical Device:** an instrument intended for use in diagnosis, cure, treatment or prevention of disease that doesn't achieve its primary purpose through chemical action on or within the body.
- **PMA:** Premarket Approval. The most rigorous regulatory path where safety and effectiveness need to be demonstrated on the devices own merits.
- **Predicate:** A Device that has already been approved and marketed. Proving substantial equivalence to a predicate is a path to FDA clearance.
- **QSR**: Quality system Record. Shall be maintained by each manufacturer and include documentation and procedures of quality activities.
- **QSR**: Quality system regulations. The requirements to be met for quality control, regulated in 21 CFR 820.
- **Safe device:** The devices benefits exceed its risks.
- **Sponsor:** A person who initiates a clinical investigation, but do not conduct the investigation. A person other than an individual (e.g. corporation or agency) that uses one or more of its employees to conduct a clinical investigation it has initiated.
- **Substantial Equivalence:** similarities exist in both intended use and technical characteristics. The substantially equal device is at least as safe and effective as the predicate.