A Comprehensive Review of the Food and Drug Administration, the 510(k) Application Process, and FDA Certification for a Diagnostic Device

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Introduction

Ebola is a rare and deadly disease caused by infection with a strain of the Ebola virus. The year 2014 saw the largest Ebola epidemic in history, affecting multiple countries in West Africa.[1] One of the many problems with this disease is the difficulty and time constraints associated with its diagnosis. Diagnostic tools are a huge portion of the medical device industry which is regulated by the US Food & Drug Administration. In the peak of this epidemic, the FDA realized this need for better diagnostic tools and approved (for emergency use only) 8 different in-vitro diagnostic devices throughout the years 2014 and 2015.[2] This is an amazing example of the FDA's ability to react quickly to a real world issue and to improve the care of those affected by this outbreak; although, this is not usually the experience that most companies have with the FDA. In a debate in 2013, Scott Gottlieb, M.D. and Peter Huber argued that the FDA's caution is hazardous to the public's health because they are preventing innovation. Jerry Avorn, M.D. and David R. Challoner, M.D. argued against this motion and although they lost the debate, it is still a highly controversial topic.[3] This highly debated topic may be due to the conflicting self-proclaimed goals of the FDA. In short, the FDA's role is to protect the public health from harmful foods, drugs, biologics, medical devices, electronics, cosmetics, and tobacco products; although, its role also includes advancing the public health by helping to speed product innovations.[4] In summary, they want to protect public health while also helping to speed product innovations, and unfortunately these two goals don't always cooperate.

The company G-Force CRC LLC is currently experiencing this dichotomy right now as they begin to approach FDA approval. G-Force CRC LLC is a small medical device company headquartered in San Diego, CA. The owner of the company, Dr. Ian Purcell, is an Otoneurologist apart of Alvarado Hospital. His medical practice mainly deals with patients who have balance disorders and therefore the devices that he has developed over the last 6+ years are primarily used to assist in the diagnosis of those balance disorders. G-Force CRC LLC was officially created in the summer of 2013 around these medical devices and is very close to turning in its first 510(k) application to the FDA.

The review below was written due to the difficulties that many companies and individuals encounter in approaching the "FDA clearance/approval" process. The goal of the review will be to give a detailed account of the process that G-Force CRC LLC has gone through to date. It will detail the research and writing associated with a traditional 510(k) application, the current status of that application, what I personally learned throughout this process, some of the challenges I encountered, and the next steps for the company.

Methods

The Business

The summer of 2012 I began working for Dr. Purcell in his medical practice in San Diego. At the time, I was interested in becoming a PA and was therefore gaining experience in the workplace. As I spent my summer scribing for Dr. Purcell, he began to share more and more about his medical devices. By the beginning of the summer of 2013, Dr. Purcell and I began to brainstorm about this great endeavor of receiving "FDA clearance". The first thing we decided was necessary was to create a company around the medical devices because at that point Dr. Purcell had just been in the "design-tinkering" phase; although he did have an associate in China that was helping him to manufacture prototypes. That summer, I created 3 different companies around the 3 different medical devices. According to the CalGold website, a surgical and medical instruments manufacturer business has a series of responsibilities attached to doing business in San Diego, CA.[5] The most important of these being: a business license, an employer identification number (EIN), a seller's permit, and finally the company names. Obtaining a business license is done at the city level; obtaining a seller's permit is done at the state level; and obtaining an EIN is done at the federal level because it is through the IRS. As of today, there is just one company that oversees the 3 different medical device products and its name is G-Force CRC LLC. To date, the company has an EIN number and business license, but not its seller's permit.

As mentioned earlier, Dr. Purcell was developing three different medical devices. My first summer of research was spent researching the regulatory details for all three of these devices; although two years later I am now only focused on two of those three devices. The other device is still going through significant design iterations and are therefore not ready to make regulatory considerations other than for design. For this reason, the remainder of this review will focus on the regulatory considerations that G-Force CRC LLC made in context of one of their devices, the "DizzyDoc System" which is the mobile diagnostic unit used for consumers. Although, as you will see, both of the 510(k) applications will be available in the appendices at the end of the document.

The Research

After finishing the necessary research relating to the administration of the business I was able to turn my focus to the regulatory portion. When I first arrived on the FDA's website, it was overwhelming. There were 9 available tabs to click on, 8 other subsections below that from which to choose a link, as well as news, updates, and even link to FDA's social media sites. Although, for me, only a few of these tabs/links were relevant. The FDA regulates foods, drugs, medical devices, radiation-emitting products, biologics, veterinary products, cosmetics, and tobacco products, but obviously, the medical devices tab was the only relevant tab to my research. Additionally, the right side of the website featured 5 links titled, "For Consumers", "For Patients", "For Health

Professionals", "For Scientists and Researchers", and "For Industry". This was another great place to start in my initial research because after clicking on one of these links I was able to narrow it down further by choosing a product line (i.e. "Industry (Medical Devices)").

After a few hours of research I discovered that for our medical devices (non-combination products, with no biologic or drug component), the Center for Devices and Radiological Health (CDRH) was the main entity within the FDA with which we were bound to interact with. I also discovered that all medical devices are classified and regulated according to their level of risk. Class I is the lowest level of risk, followed by Class II and Class III. In order to determine the classification that the DizzyDoc System would be regulated through, I referenced the device classification panels. There were 19 different classification panels organized by medical specialty to choose from, but the most relevant of these was "Ophthalmic Part 886." After clicking on part 886, I was led to a long list of ophthalmic devices. On this list, was a device entitle "Eye Movement Monitor" which was a sufficiently close enough description of our device. From here, I learned that any and all eye movement monitor devices are regulated as class II devices. After learning the classification of the device it was important to determine the submission pathway to go down. Since it was going to be regulated as a class II device, it was likely not going to be exempt from a 510(k) application, but it also likely did not require a full PMA application, especially considering it was not an implantable or life saving device. This led me to investigate whether this device could be 510(k) exempt by inspecting the list of 510(k) class II devices on the FDA website. Unfortunately, our device was not present on this list which lead me to click on the "How to Prepare a Traditional 510(k)" link.[6]

<u>510(k) Application</u>

In December 2014, there were a total of 2 PMA approvals. In stark contrast, there were 316 510(k) clearances in December 2014.[2] What this suggests is that receiving FDA clearance with a 510(k) application is a significantly easier process when compared to receiving FDA approval with a PMA application. What this does not mean is that it is easy to receive FDA clearance with a 510(k) application. It is still a very complicated and involved process; although, as it was stated earlier, hopefully this review will sufficiently summarize and outline the process so that it is much more understandable. A 510(k) application has approximately 20 main components that breakdown in the following way:

1) Medical Device User Fee Cover Sheet
2) CDRH Premarket Review Submission Cover Sheet
3) 510(k) Cover Letter
4) Indications for Use Statement
5) 510(k) Statement or Summary
6) Truthful and Accuracy Statement

7) Class III Summary and Certification
8) Financial Certifications or Disclosure Statement
9) Declarations of Conformity and Summary Reports
10) Executive Summary
11) Device Description
12) Substantial Equivalence Discussion
13) Proposed Labeling
14) Sterilization and Shelf Life
15) Biocompatibility
16) Software
17) Electromagnetic Compatibility and Electrical Safety
18) Performance Testing (Bench)
19) Performance Testing (Animal)
20) Performance Testing (Clinical)
21) Any other relevant information (risk analysis, verification, validation, etc.)[6]

The subsequent paragraphs below will give a brief overview of each section of the 510(k) application.

The Medical Device User Fee Cover Sheet is a short 1 page form that the FDA uses to scan the pertinent information related to the product. This form includes the following: Company name and contact information, the type of premarket application, a small business qualification statement, an establishment registration fee statement, and a user fee exemptions statement. The information that you will need to know before filing this form out is relatively minimal but still very important. The main two pieces of information you will need to know about is 1) whether or not your business qualifies as a "small business" and 2) the type of premarket application you will be pursing. For US based business', if your business (and its affiliates) had gross receipts or sales of no more than $100 million for the most recent tax year then you will be eligible to apply to qualify as a small business. The main benefit of qualifying as a small business relates to the major decrease in user application fees. For example, the cost of a PMA application for a small business is $62,724 whereas the cost of a PMA application for a standard business is $250,895.[6] The second important piece of information that you will need to know is the type of premarket application you will be turning in. There are 9 different application types and 2 different centers to apply to not including supplemental application types; although as mentioned before, this document will be focusing on a traditional 510(k) application. An example cover sheet can be referenced in Appendix A.

The CDRH Premarket Review Submission Cover Sheet form is similar to the Medical Device User Fee Cover Sheet. It contains some basic contact information and the type of submission. Additionally, this form requires the "predicate device" information, the original product classification, manufacturing information and a list of the standards utilized to design, prototype and manufacture this device. The predicate

device information is arguably the most important part of the entire 510(k) application. The devices that you reference in this section determines the device to which yours will be compared. Product K-numbers are referenced here. Additionally, the device product code will be required later in the document. This information will determine the section of the Code of Federal Regulations that your device will be held to as well as the classification panel through which your device will be reviewed. Manufacturing contact information including a Facility Establishment Identifier (FEI) number is required. On the last page of this document is a form that allows you to list all of the standard that your company followed throughout the design, prototyping and manufacturing process.[6] An example standard document that can be listed in this section that is also very applicable to medical device design and manufacturing is ISO 10993. ISO 10993 is titled "Biological Evaluation of Medical Devices" and there are approximately twenty sections detailing the requirements regarding everything from animal welfare requirements in animal testing to immunotoxicology testing and everything in between. Be sure to reference this document throughout the process of bringing a product to market. An example cover sheet can be referenced in Appendix B.

The 510(k) cover letter is another very important summary document that the FDA reads in order to understand the overall function and desired usage of your device. There are three main parts of the cover letter including: administrative information, the basis for submission, and a comprehensive summary table. The FDA recommends that the following information be included in the administrative information section: type of 510(k) submission, your device type by its common name, 510(k) submitter, the contact information of one point person, your preference for preferred confidentiality, your recommended classification regulation and class, the panel and product code, and lastly any FDA documentation numbers associated with prior formal correspondence.[2] Be sure to check out the "Classify Your Medical Device" link on the FDA website. Next, the explanation and basis for submitting the 510(k) is required. An example of an appropriate basis would be as follows: new device, modification of a legally marketed device that would not otherwise qualify for a Special 510(k), new indications for use, new device design, a submission for a reprocessed, single use, disposable device, or an exempt device which exceeds the limitations for exemption. Lastly, a summary table should be included. An example table from the FDA website is shown below.[2]

Table I –Design and Use of the Device

Question	**YES**	**NO**
Is the device intended for prescription use (21 CFR 801 Subpart D)?#		
Is the device intended for over-the-counter use (21 CFR 807 Subpart C)?#		
Does the device contain components derived from a tissue or other biologic source?		
Is the device provided sterile?		

Is the device intended for single use?		
Is the device a reprocessed single use device?		
If yes, does this device type require reprocessed validation data?		
Does the device contain a drug?		
Does the device contain a biologic?		
Does the device use software?		
Does the submission include clinical information?		
Is the device implanted?		

#A device may be intended for both prescription and over-the-counter use. If so, the answer to both of these questions is yes.[2]

The indications for use statement is a simple document but an important one. This statement needs to be as similar as possible to the predicate device indications for use. The indications for use statement is used to document and guide the type of user the device is for. For example, the indications for use statement should document whether it is for prescription use or over-the-counter use. It should also document any and all populations the devices should be excluded from. An example Indications for Use Statement can be found in Appendix C.

The 510(k) application requires either a 510(k) summary or a 510(k) statement. A 510(k) summary is a summary of information upon which you based your claim of substantial equivalence. The 510(k) statement is a certification that the 510(k) owner will provide safety and effectiveness information supporting the FDA finding of substantial equivalence to any person within 30 days of a written request.[2] A 510(k) summary will be evaluated with the following checklist, so be sure to make sure all aspects are included.

Table II – Requirements Checklist of a 510(k) Summary

[ ]	The summary should be in a separate section of the submission. It should begin on a new page and end on a page not shared with any other part of the 510(k) submission. It is clearly identified as "510(k) Summary" as required by section 807.92(c).
[ ]	The summary contains on the first page, preferably on your letterhead paper, the 510(k) owner's name, address, phone and fax numbers, name of contact person, and date the summary was prepared [807.92(a)(1)].
[ ]	The summary includes the name of the device, including the trade or proprietary name, if applicable, the common or usual name, and the classification name, if known [807.92(a)(2)]. Example: 1. Trade name - DRAG@N LATEX EXAMINATION GLOVES 2. Common name - exam gloves 3. Classification name - patient examination glove (21 CFR 880.6250, Product Code FMC)
[ ]	The summary identifies the legally marketed device to which your firm is claiming equivalence [807.92(a)(3)].

[ ]	The summary includes a description of the device such as might be found in the labeling or promotional material for the device, including an explanation of how the device functions, the scientific concepts that form the basis for the device, and the significant physical and performance characteristics of the device, such as device design, material used, and physical properties; [807.92(a)(4)].
[ ]	The summary provides the intended use of the device including a general description of the diseases or conditions that the device will diagnose, treat, prevent, cure, or mitigate, including a description, where appropriate, of the patient population for which the device is intended. If the indication statements are different from those of the predicate device, the 510(k) summary shall contain an explanation as to why the differences are not critical to the intended therapeutic, diagnostic, prosthetic, or surgical use of the device, and why the differences do not affect the safety and effectiveness of the device when used as labeled [807.92(a)(5)].
[ ]	The 510(k) summary contains a summary of the technological characteristics of your device compared to the predicate device. If the device has the same technological characteristics (i.e., design, material, chemical composition, energy source) as the predicate device, a summary of the technological characteristics of the new device in comparison to those of the predicate device should be included. If your device has different technological characteristics from the predicate device, provide a summary of **how** the technological characteristics of your device compare to the predicate device. [807.92(a)(6)]
[ ]	If the determination of substantial equivalence is also based on an assessment of non-clinical performance data, the summary includes a brief discussion of the nonclinical tests submitted, referenced, or relied on in the premarket notification submission for a determination of substantial equivalence and how their results support a determination of substantial equivalence [807.92(b)(1)].
[ ]	If the determination of substantial equivalence is also based on an assessment of clinical performance data, the summary includes a brief discussion of clinical tests submitted, referenced, or relied on in the premarket notification submission for a determination of substantial equivalence and how their results support a determination of substantial equivalence. This discussion shall include, where applicable, a description of the subjects upon whom the device was tested, a discussion of the safety or effectiveness data obtained from the testing, with specific reference to adverse effects and complications, and any other information from the clinical testing relevant to a determination of substantial equivalence [807.92(b)(2)]. Please note: Clinical data is not needed for most devices cleared by the 510(k) process.
[ ]	The summary includes the conclusions drawn from the nonclinical and clinical tests (discussed above) that demonstrate that the device is as safe, as effective, and performs as well as or better than the predicate device . 807.92(b)(3)
[ ]	The summary includes any other information reasonably deemed necessary by FDA. Such requests will be made directly to the applicant by FDA or the requirements will be published in guidance documents. Additional information requested by FDA during review of the 510(k) may include additional safety and effectiveness information which may necessitate an update of your summary if requested by FDA. 807.92(d)
[ ]	Please make sure you have included all of the information listed above and verify that the following criteria have been met. 1. The summary includes only information that is also covered in the body of the 510(k). 2. The summary does not contain any puffery or unsubstantiated labeling claims. 3. The summary does not contain any raw data, i.e., contains only summary data. 4. The summary does not contain any trade secret or confidential commercial information. 5. The summary does not contain any patient identification information.

If you elect to prepare a signed 510(k) statement, anyone may request a copy of the 510(k) from the applicant of record.[2] The following is a copy of the example statement, although it can also be found in Appendix D.

"I certify that, in my capacity as (the position held in company by person required to submit the premarket notification, preferably the official correspondent) of (company name), I will make available all information included in this premarket notification on safety and effectiveness within 30 days of request by any person if the device described in the premarket notification submission is determined to be substantially equivalent. The information I agree to make available will be a duplicate of the premarket notification submission, including any adverse safety and effectiveness information, but excluding all patient identifiers, and trade secret and confidential commercial information, as defined in 21 CFR 20.61."[6]

The Truthful and Accuracy Statement is simply a form that holds the owner of the 510(k) responsible for everything enclosed in the application. It verifies the truthfulness and the accuracy of all enclosed information. An example statement is included below and in Appendix E:

"I certify that, in my capacity as (the position held in company) of (company name), I believe to the best of my knowledge, that all data and information submitted in the premarket notification are truthful and accurate and that no material fact has been omitted."[6]

The Class III Summary and Certification document is also a simple form that holds the owner of the 510(k) responsible for researching all the possible sources of safety and efficacy problems with their product. An example statement is included below and in Appendix F:

"I certify that, in my capacity as (the position held in company) of (company name) that I have conducted a reasonable search of all information known or otherwise available about the types and causes of safety and/or effectiveness problems that have been reported for the (device name). I further certify that I am aware of the types of problems to which the (device name) is susceptible and that, to the best of my knowledge, the following summary of the types and causes of safety and/or effectiveness problems about the (device name) is complete and accurate." (Attach the summary of problem data, bibliography or other citations upon which the summary is based.)[6]

The Financial Certifications or Disclosure Statement forms document that there were no financial arrangements made between the sponsor and the clinical investigators. This kind of an arrangement would obviously skew the results of the

clinical study and therefore inaccurately represent the safety and efficacy of the medical device. Example forms can be found in Appendix G.

The Declarations of Conformity and Summary Reports section is only important for sponsors that want to apply for an Abbreviated 510(k). This is where they tell the FDA what standards and summary reports were meticulously followed in the design and manufacturing of their device.

The Executive Summary portion of the 510(k) is the first real summary and full description of the device. It should include the following: concise description of the device (including the indications for use and technology discussion), a device comparison table to the main predicate device, and a summary of any of the performance testing executed.

The Device Description section, as the title suggests, is a very in depth description of the device and all of its components. Some of the important portions of this section include: device description, performance specifications, design requirements, models for the device, diagrams, dimensions, tolerances, schematics, as well as a full list of the materials of the portions of the device that come in contact with the patient.

The Substantial Equivalence Discussion is very important. It is where you make your case in convincing the FDA that you are sufficiently similar to a predicate device and therefore should not have to go through significantly more testing and verification steps. The important parts to focus on when comparing your device to the predicate device are as follows: indications for use, technology details, performance specifications, testing similarities. When writing this section and when determining your predicate device, please consult the figure to the right. For further background refer to Blue Book Memorandum K86-3.

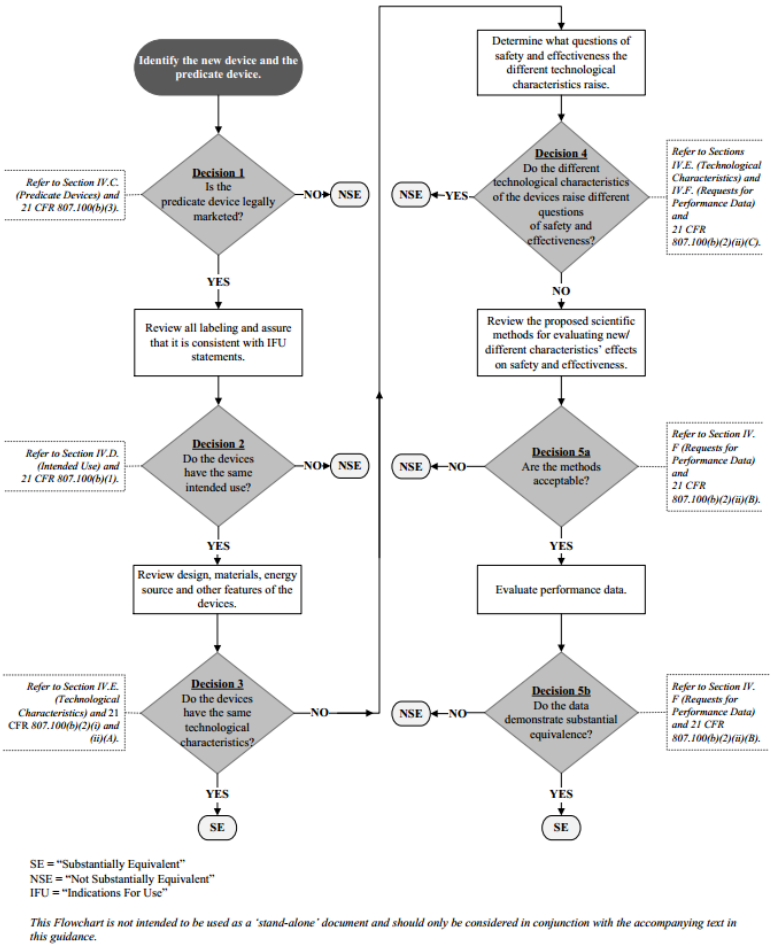

Figure 1 Substantial Equivalence Decision Flow Chart. This flow chart is not only what application reviewers use to review the similarities of a product and its predicate device, but it is also a useful tool for companies when identifying a predicate and comparing the two devices.[8]

The Proposed Labeling section is used to document the labeling on any of the documentation associated with the device. This includes the labeling on the actual device, the labeling on any and all of its packaging, instructions for use, and any patient forms. There is a very thorough guidance document to reference for any and all questions regarding labeling. This document is titled “Device Labeling Guidance #G91-1 (blue book memo).” Appendix H will show example logos created in Adobe Illustrator.

The Sterilization and Shelf Life section is where you would document all sterilization techniques and their details. For example, if your product comes in a sterile package and was sterilized with Ethylene Oxide gas, you would need to detail the specifics on how you sterilized and packaged the device to meet standards (SAL: $1x10^{-6}$). You would also need to document that EtO sterilization often leaves behind toxic residues and detail the effects that that might have on the use of your product. Similarly, if your product has a shelf life either in relation to the sterility or not, you would document that in this section. Luckily, our device is not a sterilized device, nor does it have a shelf life which makes this section irrelevant to our application; although if you need further clarifications refer to the “Updated 510(k) Sterility Review Guidance K90-1; Final Guidance for Industry and FDA.”

The Biocompatibility section of the 510(k) application is a section that will apply to basically all medical devices. This section details the biocompatibility of your device if it comes into direct or indirect contact with patients. This section is well characterized by a guidance document called ISO 10993. Additionally, the FDA created a guidance document of their own to assist companies in meeting the standards detailed in ISO 10993 entitled **“**Blue Book Memo, G95-1, Use of International Standard ISO-10993, and Biological Evaluation of Medical Devices Part 1: Evaluation and Testing.” The main testing documented in these guidance documents are represented in the table below. Additionally, it should be stated that if your device is made of the exact material and manufactured in the exact same way as your predicate device, no testing needs to be done.

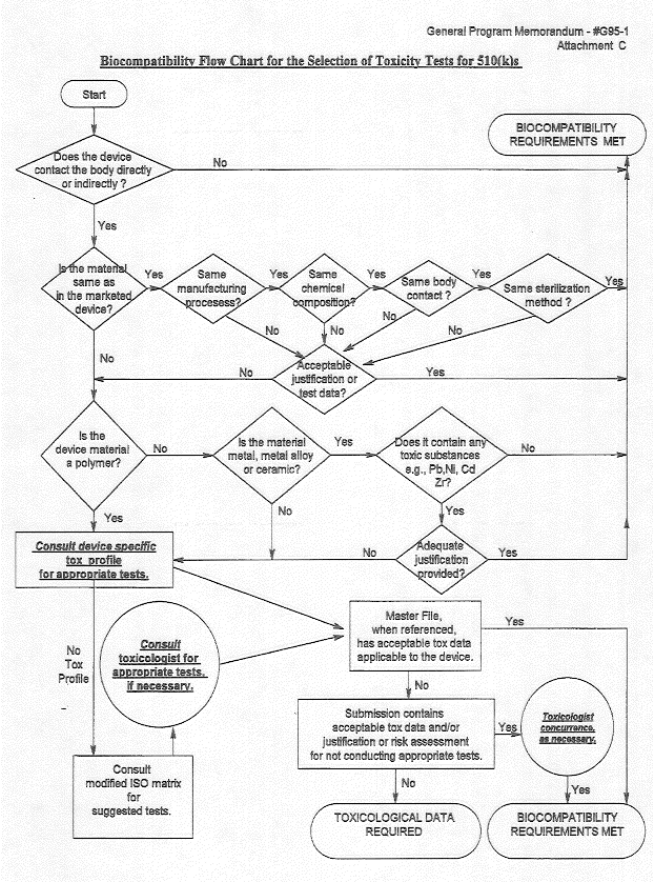

Figure 2 Biocompatibility Flow Chart. This flow chart assists companies in identifying the necessary toxicity tests needed, especially in context of the predicate device.

Table III – Determination of Biocompatibility Testing Required

Device Categories			Initial Evaluation								Supplemental Evaluation	
	Body Contact	Contact Duration	Cytotoxicity	Sensitization	Irritation or intracutaneous reactivity	Systemic toxicity (acute)/pyrogenicity	Subchronic toxicity	Genotoxicity	Implantation	Hemocompatibility	Chronic toxicity	Carcinogenicity
Surface Devices	Skin	A	●	●	●							
		B	●	●	●							
		C	●	●	●							
	Mucosal Membrane	A	●	●	●							
		B	●	●	●	0	0		0			
		C	●	●	●	0	●	●	0		0	
	Breached/compromised surface	A	●	●	●	0						
		B	●	●	●	0	0		0			
		C	●	●	●	0	●	●	0		0	
External Communicating Devices	Blood Path indirect	A	●	●	●	●				●		
		B	●	●	●	●	0			●		
		C	●	●	0	●	●	●	0	●	●	●
	Tissue/bone dentin communicating	A	●	●	●	0						
		B	●	●	0	0	0	●	●			
		C	●	●	0	0	0	●	●		0	●
	Circulating blood	A	●	●	●	●		0		●		
		B	●	●	●	●	0	●	0	●		
		C	●	●	●	●	●	●	0	●	●	●
Implant Device	Bone/tissue	A	●	●	●	0						
		B	●	●	0	0	0	●	●			
		C	●	●	0	0	0	●	●		●	●
	Blood	A	●	●	●	●			●	●		
		B	●	●	●	●	0	●	●	●		
		C	●	●	●	●	●	●	●	●	●	●

● = ISO Evaluation Tests for Consideration 0 = Additional Tests which may be applicable[6]

The Software section is relatively self-explanatory, in that it is a full description of the software used in the device system and its associated risks. The amount of documentation required in this section is broken down by the level of concern associated with the device.[6] For example, the software associated with a defibrillator device has a high level of concern because a malfunction in the software of the device could result in major injury and/or death of the patient. Luckily, our device is classified as a minor level of concern and therefore the kind of documentation necessary for our device is minimal. It includes descriptions, risk analysis, etc. If you desire to understand further the documentation required for your device refer to the document entitled “Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices.”

The Electromagnetic Compatibility and Electrical Safety section documents the safety associated with any medical device that has an electronic component. You are required to

document the emissions associated with the device as well as the immunity the device has towards the emissions of other devices. There is even further documentation required if the device design results in patient contact with any electrical powered device, which luckily our device design does not. For this section, follow “IEC 60601-1- 2 Medical Electrical Equipment -- Part 1: General Requirements for Safety; Electromagnetic Compatibility -- Requirements and Tests.”[6]

The remaining sections are where any bench, animal, or clinical testing is included. For all of these, the FDA asks that you include the following broad descriptions: a list of all tests conducted, describe each test protocol, summarize the results, describe your analysis, and discuss your conclusions. More specifically, the FDA asks for the following: objective of each test, test articles used in test, test methods and procedures, study endpoint, predetermined pass/fail criteria, and summary tables.

Outside Assistance

Over the last two years of working on this project, I have sought help and assistance in a few different specific ways. First off, as I began working on the 510(k) application, I began thinking, “If only I had an example 510(k) application to reference.” I had questions about formatting, the type of language to use, and specific details in each section. Luckily, the FDA requires any previously approved or cleared device to publish either their 510(k) Summary, or if the company used a 510(k) statement in their application, then they are required to send their entire 510(k) application upon request from another company. This resource was extremely helpful as I was writing up our own 510(k) application. A copy of this document will be included in Appendix I.

Additionally, as Dr. Purcell and I considered whether we would need to do significant levels of testing (including bench, animal, and clinical) we began seeking outside help. Neither Dr. Purcell nor I had experience with doing testing that complied with standards documents or Institutional Review Boards (i.e. ISO 10993, IACUC, etc.) which led us to researching a company that we could outsource this kind of work to. I asked my professor Dr. Michael Whitt, who I knew had had a significant amount of industry experience, and luckily he was able to direct us to a friend’s company called Syprosoft Engineering. This company is based out of Irvine, CA and their scope found on their website is as follows: “As an extension of your engineering department, we provide the critical skills and expertise at the right time to help you meet your product development goals.”[7] Some of the services they offer are as follows: documentation, verification and validation, regulatory filings, technology assessments. This company was exactly what we were looking for. Currently, we have had email communication, one conference call, and we are likely going to set up a “capabilities presentation” where we will learn more in depth what their company can offer us. Hopefully, this partnership will expedite our application process.

Another source of outside assistance that we sought was for our labeling. Once again, neither Dr. Purcell nor I had any graphic design experience and so I asked one of

my graphic design friends to make a logo for us. Marissa Varni created a logo for the company name at the time which was “Novertigo LLC.” Unfortunately, since creating the logo we decided to change names to “G-Force CRC LLC.” The work she did can be referenced in Appendix H.

Lastly, in the summer of 2013 I was able to take a trip to China with Dr. Purcell to visit the manufacturing plants and research groups assisting him in the creation of his devices. We visited three different Chinese cities where we had a myriad of meeting and brainstorming sessions. It truly was the trip of a lifetime. In Xian, we were able to meet with the manufacturing factory manager and his associates. At this meeting I was able to give a presentation (that was translated into Mandarin) about an overview of the FDA including the way that they regulate medical devices and how they should go about meeting standards at their factory. In Lanzhou, we were able to meet with a group of students and professors that were assisting Dr. Purcell in the software development and user-interface for all three devices. In this meeting Dr. Purcell and I were able to work with the team troubleshooting the software while also giving input on how we’d like to see the software improved or optimized. Lastly, in Beijing, Dr. Purcell and I met with a group of Chinese businessmen as well as head person at the Chinese equivalent of the American Medical Association. In this meeting, we were able to present about the disease that these devices are aimed to diagnose as well as the potential benefits of bring these devices to market in China. The experience that I gained while in China was priceless when it comes to field experience in project engineering and in bringing a product to market. I was able to see the many different sides of this process including, research and development, manufacturing, regulatory, and even the business marketing. The information that I gained through the many different meeting and conversations while in China gave me significantly better idea concerning the scope of the project and the device specifics. For example, I was able to ask specific questions to the engineering students about the software used in their system so that I could more accurately write about it in the 510(k) application under the Software section.

Figure 3 Pictures from China. a) This is a picture of me troubleshooting the software with the students and professors at LanZhou University b) This is a picture of me giving an FDA presentation at the factory in Xian c) This is a picture of Dr. Purcell and I observing the chair prototype.

Results

The entire 510(k) application can be found in Appendix J (DizzyDoc System) and Appendix K (ER Goggles) as well as photos of the DizzyDoc System device in Appendix L. As you will see when referencing these appendices, the applications are not completed; although, they is still being worked on and will hopefully be completed by the end of this year. Additionally, Appendix M shows an expected timeline once the application has been submitted and Appendix N is the actual checklist that all FDA reviewers use to review 510(k) applications.

Discussion/Conclusion

This two year process involving research, document writing, conference calls, copious amounts of emailing, and trips to china was a long process and it was absolutely priceless experience. There were many things that I learned about myself, about engineering, and about the FDA that I am incredibly thankful to have learned. Additionally, there were many challenges that I faced throughout this process that have caused this endeavor to be longer one than I had originally planned. With this in mind, it is still an ongoing venture that will hopefully be concluding soon. In this section I will give a summary of what I learned, all of the challenges and limitations that I faced, as well as give a preview of what lies ahead for the company.

This project has taught me so much. Possibly the most important lessons I learned were about myself. When Dr. Purcell approached me with the idea of heading up the regulatory division of his device endeavors I was excited but also very nervous about what that entailed. I had never dealt with regulatory responsibilities nor had I learned anything about it in school except for a few basic facts about the FDA. And further, not only was I lacking in experience and knowledge but I was essentially the only person responsible for the project. This meant that I had no one to rely on and if anything went wrong, the burden was entirely on me. Overall, as I mentioned earlier, this process was overwhelming, but it was also an amazing experience because I learned that I was capable of doing it. This might sound insignificant but what I learned was profound. I learned that I was capable of researching and tackling a complex problem through perseverance and patience. I learned that I could be self-motivated to an extreme if necessary and I have talked about this example in many job interviews. Another very important thing that I learned about myself was that confidence can go a long way in industry. While in China I was easily the youngest person in the room throughout the trip. There were many business and engineering meeting where it was likely that I had the lowest amount of industry experience; although with that said, I was also likely the most knowledgeable person in the room considering FDA certification. In that environment, I was tempted to shy away from being an authoritative voice; nevertheless, as the trip progressed i gained more and more confidence to the point

where I was making presentation in front of a room of engineers and businessmen and felt confident enough to state what I knew to be fact and field questions with poise and certainty. It is important for me to note that without having done the extensive research that I did before the trip, speaking with the confidence that I did would not have been a wise thing to do; but, because I had done my research and felt confident in my presentation I was able to command authority without hesitation from the audience. These two profound qualities that I learned about myself will forever benefit my future professional ventures.

Alternatively, I also learned a lot that will be helpful in industry later. For one, I have a very good handle on the overall structure and function of the FDA. For future engineering jobs, especially in R&D, this background knowledge will likely be extremely important and appreciate by my fellow employees. Additionally, I also feel that I have a very strong grasp on the 510(k) application process including all of its details and the guidance documents that are in place to help companies write the document and adhere to the standards required by the FDA. This will also likely be helpful knowledge to have for future engineering efforts. One thing that I did not expect to learn about as I started doing research was the details of and importance of having a company and business plan around a medical invention. I not only learned about the details of starting a business, but I also realized that without a company, business plan, and set of investors, getting a start-up through the FDA is near impossible. Overall, the largest lesson I learned was a simple one. It is not an easy task to bring a device to market, no matter how revolutionary or amazing it is. With this lesson in mind, and the knowledge that you can learn from your mistakes, there were a number of challenges and limitations that I encountered throughout this process that I will thankfully be able to avoid in the future if another regulatory opportunity presents itself.

The first challenge I encountered on the job is obvious, a lack of knowledge and background experience. As I detailed in the introduction, the FDA website is overwhelming. Its vast network of links and tabs were over stimulating as I began my research especially considering my lack of exposure to it. As time went on, I learned to navigate the website much more successfully; although unfortunately, it did presumably elongate the amount of time it took to start the document writing process. Something that further elongated this process was the fact that I was still in school while pursuing this. I was a full-time student who had a part time job and volunteered a significant number of hours a week. I had a limited amount of time to devote to continued research and document writing which significantly elongated this process. The last, and possibly most significant, retardant to the swiftness of the application process was the lack of money and investors. To start, Dr. Purcell did not have a significant amount of available resources to outsource any of this regulatory work. This is a limitation that we are currently facing with Syprosoft. We have a desire to outsource some of the work, but do not have the capital to do so. Additionally, we have no investors. We have essentially no

one backing our product which means our only source of cash flow is from Dr. Purcell. This is a challenge that we hope to address in the very near future.

As you will see when referencing the 510(k) application in the appendix, there are unfinished sections. This is mostly due to a confusion on what is required in that section. For example, we are not entirely sure what needs to be included in the Labeling section. I know that a company logo as well as any warning labeling should be documented in this section but we are unsure if they need the information in a format to show the positioning of the logo/warnings/etc. on the product's box. This was a challenge that I faced in the actual application documentation. Additionally, you will notice a lack of documentation detailing the testing that the device has been put through because I am confused about the extent of testing that the FDA requires of 510(k) applications. From the research I have done both through the FDA website and through interviewing professionals/professors I have gotten a mixed set of answers. Some say that clinical data is absolutely necessary even if it is a 510(k) application. Others say that you just need to do some simple toxicity testing while animal and clinical testing are unnecessary. This confusion has led to a lack of attention given to this section of the application which is apparent in the fact that there are no details documented.

The 510(k) application is in process and I have hopes to finish it by the end of 2015. The two most important next steps that I think the company should take are to investigate acquiring investors and to begin conversations about how Syprosoft can assist in bring these devices to market. Ideally, Syprosoft will give a capabilities presentation soon which will be followed by writing up a contract detailing the partnership that will proceed. As for investors, I am going to reach out to Dr. Whitt again because he mentioned a few weeks ago that he has a group of investors that are always interested in "the next new thing." Hopefully, we will be able to gain investors and therefore financial backing which will allow us to finance the partnership with Syprosoft. The future of this company is very bright, in my opinion, if we can do this.

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