Engineered Success: The Engineer's Contributions to FDA Medical Device Commercialization

By Russ King

www.methodsense.com | 919.313.3960

Engineered Success: The Engineer's Contributions to FDA Medical Device Market Commercialization

By: Russ King, President, MethodSense, Inc.

In 2012, the Bureau of Labor Statistics (BLS) reported there were 19,400 biomedical engineering jobs in the United States with a projected growth of 27% (much faster than the average) from 2012 to 2022. Considering the additional support from electrical, mechanical, clinical, manufacturing, human factor and software engineers, these statistics seem to underestimate the number of engineers contributing to the $110 billion US medical device industry. With the strong growth in IVD innovation, the introduction of 3D printing, the wireless revolution creating healthcare delivery platforms, and other technology-centric trends, the medical device industry should sustain the demand for qualified engineers for some time to come.

The contributions engineers make to this industry are both critical and substantial. Medical devices must be designed to satisfy their intended use. Some medical devices are simple enough – or the appropriate tools are sufficiently accessible to non-engineers – that a professional engineer may not be necessary for their design. However, a medical device always requires some level of engineering, and the bulk of medical devices require the skills of a professional engineer to ensure they safely and effectively fulfill their approved intended use.

Without a doubt, the engineer is critical to fulfilling the regulatory requirements of a medical device company. Sadly, there is often a lack of gratitude toward the engineer when it comes to recognizing their role in regulatory compliance and public safety.

In what follows, we outline an FDA regulatory pathway a medical device might follow on its road to commercialization in the United States… but with a slightly different twist. We recognize FDA medical device approval pathways represent a well-worn and oft-told story, which we freshen by identifying contributions engineers make along the way. We will share some anecdotes regarding how we have seen commercialization journeys made both easier – and more difficult – based upon the engineer's role in the process. Our hope is that these anecdotes will serve as tips for both personal and commercial success.

Preparing for and Anticipating the FDA Approval Process

One of the most common questions we hear from emerging medical device companies is, "When should we begin preparing for the FDA?" The answer is, "As soon as possible." Emerging companies often devote their time, energy and treasure to product development driving toward the completion of their pre-clinical program or a final prototype.

It is not uncommon for licensees, acquirers and investors to express interest in a deal with early stage companies and products. Moreover, the value of that deal can be enhanced or diminished depending on the condition of correct and readily available product documentation.

During a pre-clinical or prototyping stage, it is not overly difficult or resource-intensive to put in place a few formal processes around the management and control of documents and records. With a Design Control procedure and a Documents and Records Management and Control procedure (and perhaps one

or two other procedures), those engaging in the early stage engineering of a product can begin building a credible Design History File (DHF) by formally authoring and approving Design Reviews Product Requirements, Design and Development Plans, Product Specification Matrices and other DHF content.

Note that this approach does not assume the implementation of an entire QMS, only a few procedures. Nor does it assume the need to finalize the DHF into an FDA submission-ready state. Instead, the approach advocates using documents the early engineering intensive stage of product development naturally creates, such as specifications, design decisions, drawings, and BOMs, with the addition of some formalized procedures and controls.

The benefits of this approach are numerous. In addition to establishing competence around FDA Design Controls, it positions a company to more easily transition to a compliant Medical Device Manufacturer. It further demonstrates the company's competence as a potential partner who can support regulatory obligations.

[ANECDOTE: IMPLEMENT FORMAL PROCESSES EARLY ON]

A medical device company comprised of three Biomedical Engineers asked for regulatory advice for when they should begin preparing their FDA documentation. Rather than starting the process as soon as possible (as recommended), they took their own advice, deciding it was too early to begin addressing such "inconvenient" concerns as compiling documentation in a way that satisfied Design Controls. Within a year, they successfully developed product prototypes, which garnered the interest of a large established medical device manufacturer. The founding engineers claimed to understand the value of product documentation, BOMs, writing down design decisions, project plans, and narrating how they developed and assembled the prototype; nevertheless, they managed their documents haphazardly, without formalized processes.

The potential licensor requested to review the DHF as part of their due diligence. The engineers scrambled to collect documents scattered across multiple computers. During this chaotic process, they realized they had not conducted Design Reviews to further authenticate the correctness of the documents they bundled together. In other words, they did not really have a DHF. With their funds exhausted by prototype development, they neither had the time to create – nor could they afford professional assistance in developing – what the potential partner was looking for. The potential licensor's due diligence resulted in the observation that the absence of formalized processes for managing product documentation spoke to a lack of maturity as a medical device manufacturer, which they hoped would be resolved in time, and, once resolved, they would consider returning for further discussions.

The lesson from this is very simple: get over the 'inconvenience' of implementing formal processes from the beginning. Medical device innovators must decide early on why they should be involved in a medical device project. If the purpose is only to innovate and engineer concepts that may never go to market, then there is no need to be concerned with detailed documentation and processes. However, if the purpose is to commercialize a medical device, then creating formalized processes during early design phases are critical. Without early implementation, you will likely face lost opportunities and costly delays.

Understanding the FDA Approval Process

As you are engineering your device, it is helpful to keep FDA requirements in mind. The FDA utilizes a risk-based approach when licensing medical devices for the US market. The FDA segments devices into three risk classifications (see Table). The higher the risk, the higher the evidentiary threshold for demonstrating product safety and efficacy.

[TABLE: US MEDICAL DEVICE CLASSIFICATION]

Class I examples: stethoscopes, bandages, wheelchairs	Class II examples: ultrasonic diagnostic equipment, x-rays, needles	Class III examples: balloon catheters, pacemakers, heart valves
• Low risk devices that are simple in design	• Medium risk devices that are more complex in design	• High risk devices
• Self-register product with the FDA	• 510(k) pre-market approval process is required for most	• FDA shall inspect facility
• Most are exempt from pre-market requirements	• QMS must comply with 21 CFR Part 820: Special Controls (Design Controls)	• QMS must comply with 21 CFR Part 820
• QMS normally comply with 21 CFR Part 820 General Controls, though some devices are exempt		• Clinical trials likely
		• Malfunction is absolutely unacceptable

Much in a device commercialization strategy's cost and time to market is determined by the product's risk classification. That is, a Class II product has a significantly easier path to market than a Class III product, and a Class I product has the easiest path to market. Determining the risk profile of any product is much more than simply developing a risk management policy. The correct risk approach must be applied with an intimate and detailed understanding of the product, which, in turn, means the product's engineering team should be involved in the risk assessment process. Through collaboration, the device designers and the quality team will build a more detailed assessment with deeper knowledge of the product.

From time to time we see companies try to 'manage' the risk profile of a product and 'thread a needle' to an easier path to market. In our experience, FDA regulations, guidances and internal review processes are designed to prevent such 'motivational judgements' that stray away from appropriate medical device classification. If the FDA disagrees with your product classification, they will kick back the application without a care about the time and expense doing so costs your company. Utilizing the engineer's knowledge and capabilities to fully understand and correctly classify the product will save time and money and reduce risk.

There is a lot more to say about all three of these regulatory pathways for medical devices than space here allows. The most common pathway, and the one we field the most questions about, is Pre-market Notification or the 510(k). Our purposes here can be satisfied with a focus on the 510(k).

The 510(k) process is designed to demonstrate the *substantial equivalence* of an unapproved device to an already approved, or predicate, device. This means that rather than proving safety and efficacy via clinical trials, medical device companies can take the more efficient path of proving their device is as safe and effective as a device that has *already been approved*. This is done by showing it is *substantially equivalent* to a predicate device that has already been shown to be safe and effective.

Establishing Substantial Equivalence

One of the FDA's missions is to approve beneficial medical devices as efficiently as possible, while assuring the public interest that a device is effective and safe when it is used as intended. By establishing substantial equivalence to a predicate device, you are making it easier for the FDA to review your device and give it the proverbial stamp of approval.

So, what exactly is substantial equivalence? A device is substantially equivalent if, in comparison to a predicate, it has:

- *The same intended use as the predicate; and*
- *The same technological characteristics as the predicate;*

OR

- *The same intended use as the predicate; and*
- *Has different technological characteristics and the information submitted to FDA:*
  - *Does not raise new questions of safety and effectiveness; and*
  - *Demonstrates that the device is at least as safe and as effective as the legally marketed device*

At this stage of the game, the engineering staff or device designers can help establish substantial equivalence with technical comparisons to candidate predicate devices or by helping to clearly demonstrate that despite technical differences the device is demonstrably at least as safe and effective as the predicate.

[ANECDOTE: INNOVATION ISN'T SIMPLY FOR THE SAKE OF INNOVATING]

Creating truly innovative medical devices (or anything else for that matter) is genuinely difficult work. Commercializing innovation is a different kind of work altogether and often results in recommended changes and compromises to the original design and intended use of the innovation for the sake of moving the product into the market place. We see this quite often with IVDs.

Truly unique IVDs will likely travel a non-traditional 510(k), or de novo, pathway or a PMA pathway, both of which incur more expense and effort than the traditional 510(k) route. For some emerging companies…

such alternatives are not financially possible. A commonly considered alternative is to try removing the diagnostic capabilities for the license application in order to achieve a more modest commercial goal that might financially enable the next diagnostic device application.

…continued from previous…

On occasion, we have witnessed device designers resist these kinds of alternatives, seeing them as a kind of 'betrayal' to the innovation or even to themselves. If a compromise for moving forward in a commercially sensible way cannot be found, all parties involved may find themselves with a fancy prototype that will amount to bragging rights, rather than a marketable device.

What if there isn't a Predicate?

Sometimes, you'll find yourself in a situation where your device has no substantially equivalent predicate. If this is the case, you may still have a 510(k) pathway available if you can clearly demonstrate that the risks posed by the device when it is used as intended do not rise above a moderate level of risk. In plain language, this means you are able to show the device's risk profile qualifies the device as either a Class I or Class II device. If you can do this, then the FDA may grant permission for you to file a *de novo* application.

The *de novo* process requires pre-submission meeting(s) with and permission from the FDA. Though *de novo* may represent a less expensive route to market than a Pre-Market Approval because it will not require clinical trials, it may require clinical and or performance data and the *de novo* process can add 6 months or more to the normal 510(k) clearance process.

Pre-submission meetings with the FDA represent an incredible opportunity to clearly establish Agency expectations for product approval. The FDA will always ask questions and challenge assumptions in 'pre-sub' meetings, but you never want to be stumped in a FDA meeting because you did not understand something *knowable* about your own product. As part of your preparations to meet with the FDA, the product's design team should contribute to meeting preparations to ensure the presenter's knowledge of the product is both thorough and as complete as possible.

Get an Early Practical Handle on 21 CFR Part 820

FDA product licensing carries with it the expectation that you will comply with all relevant regulations. For medical device companies, this typically means at least compliance with 21 CFR Part 820, also known as Good Manufacturing Practices (GMPs). GMPs are designed to ensure that a medical device manufacturer operates in a way that produces devices that are safe and what the FDA approved for the market place. You should know that 21 CFR Part 820:

- *Is an FDA-mandated system of product design*
- *Requires you to document the evolution of the life of your product*
- *Applies a market-first product development focus*
- *Requires a team-oriented approach to product commercialization*
- *As a process, tends to challenge product design to the point of improvement*

Compliance is a necessary expense and typically involves all functional aspects of a company; don't put yourself in a position where it costs more in dollars or opportunity than it should because you avoided compliance. Take extra care early on to develop processes that, when followed, meet your compliance obligations and support your business goals.

Design Controls Ensure a Quality Product that Safely and Effectively Meets a Real Market Need

21 CFR Part 820 prescribes specific design controls, or processes, for bringing Class II medical devices to market. Generally speaking, design control implementation occurs in phases that move a product along a commercialization path and are often characterized in the following way:

- *Design and Development Planning*
- *Design and Development Input / Output*
- *Design and Development Verification*
- *Design Validation*
- *Design Transfer*
- *Design Changes*
- *Design History File*

Design controls should work as a risk prevention approach to the quality of your medical device. Risk prevention is an efficient and cost-effective way to control manufacturing processes and maintain quality. While it may not be possible to eliminate all potential risks, we consistently observe in our clients a very poor appetite for realized risk that was otherwise mitigable. Design controls often include:

- *Establishing intended use and design inputs*
- *A design plan*
- *Periodic design reviews throughout the design process*
- *Confirmation that the design outputs conform to the design inputs through design verification ("Are we making the device according to the design?")*
- *Design validation ("Are we making the right device?")*
- *Translation of the design into manufacturable specifications*
- *Clear documentation of the entire process in a design history file or DHF*

Clearly, design controls frequently overlap with what the engineers know, and more often than not, depend upon then engineers input. If implemented well, design controls create a number of surprising benefits, including a better-documented product that is more attractive to buy or acquire. They result in a more efficient development cycle due to a reduction of mistakes thanks to early analysis of key questions and a clear distribution of a team's responsibilities.

[ANECDOTE: COMMUNICATION & COLLABORATION ARE KEY]

A Class III manufacturer was developing a software-dependent medical device. The software engineers and developers utilized an Agile methodology for their Software Development Life Cycle (SDLC). The manufacturer's Quality Assurance team understood well in advance the need for a validation package (User Requirements, Traceability Matrix, Qualifications, etc.), which the software engineers committed to

Though the software was developed using an Agile methodology, the SDLC and Validation Procedures were written to reflect a Waterfall development model. While documentation creation is relatively straightforward in a Waterfall model, it is far more complex and difficult to plan for and create documentation in an Agile environment. Because of this misalignment, the software engineers

…continued from previous…

experienced difficulty figuring out how to develop and maintain the appropriate documentation using the Procedures – causing the documentation to fall behind. As the planned PMA submission date approached, it became clear it would be missed as the team rewrote the procedures to accurately reflect the work methodology, and then, retrospectively generate the appropriate documentation for product validation.

We often see Software Engineering departments siloed from other parts of the company. Their lack of integration into Quality and Regulatory company functions usually result in poor communications and crisis management. Software engineers can manage and lead more effectively by proactively reaching out to Quality and Regulatory teams to ensure mutual understanding of need and plan for compromises that result in smoother operations.

Don't Forget Safety Testing and the Value of Risk Management

Depending on the technology incorporated into your medical device, applicable safety standards must be identified during the design stages of the product. The most widely accepted benchmark for establishing safety for electrical medical devices is a standard called IEC 60601-1 3rd Edition Amendment 1 and its collateral standards.

While complaints about the complexity and cost of safety testing in general, and 60601-1 in particular, have many sympathetic ears, safety testing has significant benefits. Meeting the demands of safety testing is a necessary step for electrical medical devices in the commercialization process. Through test house examination and risk assessment, it forces a very deep understanding of your product, which can be invaluable for product improvement, market positioning and sales, and exit strategies.

Failing to conform to a safety testing standard is a sure way to halt a device's commercialization progress. As a consequence, we see more and more engineers from medical device and medical device contract manufacturing companies work through what it means to satisfy safety testing requirements early in the design phase. Taking this kind of proactive approach can identify not only documentation needs, but also design requirements that must be met in order to satisfy Test Laboratory product evaluations. By building conformance to a safety standard into a medical device as early as possible, the medical device engineer saves their company the pain and expense of redesign work due to testing failures after the company thought the design was locked down. As always, an ounce of prevention out performs in money and efficiency a pound of cure!

Key Players in the Commercialization Process

Engineers play a vital role in the medical device approval process – a role that is often minimized or overlooked completely. Engineers can be more effective in this role by:

- *Familiarizing yourself with relevant compliance requirements and develop an understanding of what the FDA expects of a medical device company.*
- *Communicating with the Quality Assurance and Regulatory Affairs staff and understanding their needs as they seek to ensure products can get to market and your company's legal compliance obligations are met.*
- *Sharing your needs with the Quality and Regulatory team so they have the opportunity to enable you in kind. You might be surprised by their efforts to support your work.*

- *Proactively working as a team, regularly exploring how collectively you might anticipate needs and seek to address those needs in a timely manner. Such needs may evolve around processes, documentation, design controls, intellectual property management, risk management, and much more.*
- *BEING PREPARED TO COMPROMISE! Bringing a device to market is a lot of work, which only becomes harder and more expensive if individuals or departments become entrenched in a particular way of doing things that fails to dovetail effectively with other functions of a medical device company.*

As engineers, it is important to remember that you are not only an innovator, but you play a tremendous role in facilitating the commercialization process as well. Thinking of the commercialization strategy from concept through completion will enable you to develop processes that will bring your product to market faster, easier and quite possibly more affordably… allowing you to move on to your next brilliant idea!

About MethodSense, Inc.

MethodSense, creators of the regulatory document management software InfoStrength Smart Enterprise Suite, is a Life Science consulting firm that helps clients deliver medical and technological breakthroughs by effectively meeting the requirements needed to bring their products to market. We guide medical device, biotech and pharmaceutical companies with quality, regulatory and technology solutions. Our guidance enables clients to operate more effectively during the commercialization process and beyond. MethodSense is located in the heart of Research Triangle Park, North Carolina – home to one of the world's largest biotechnology clusters and a hub for technology-based innovation. We invite your communication: Russ King, 919.313.3962, rking@methodsense.com, www.methodsense.com.