



Product Development and Quality Improvement Consulting

Integrating Medical Device Product Development, Design For Six Sigma and Quality System Regulation – Part II

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Part 1 of this article described how the rigor of Design for Six Sigma fits within a new product development process. To recap, Design for Six Sigma (DFSS) “is both a business management and a product development process that uses metrics, data, statistics, team dynamics, risk management and project management tools. It takes products from concept to commercialization using data-driven decision making processes, delivering a “six-sigma” capable, defect-free product or service by focusing on design and process parameters based on the customer and market needs. New products are designed, developed and distributed to six sigma quality and capability for those critical to quality requirements specified by the customer, market, or intended use. In addition, DFSS allows a company to comply with all the elements of the Quality System Regulation (QSR) (1) in the product development process”. Figure I describes a six phase product development process detailing some of the major activities including a risk assessment at the end of each phase.

FIGURE I – Design for Six Sigma and New Product Development

The Business Case	The Technical Requirements	Product Development	Pilot, beta-test and validate	Full scale production and commercialization	Monitor, track and control
Define	Assess	Develop	Validate	Launch	Sustain
Intended use requirements Voice of the customer Market assessment and analysis	Finished device specifications Measurement capability analysis Design options	Product prototype Product capability by design Prototype verification/ clinical trials	Product scale-up, pilot run Product capability at scale-up Product validation/ clinical trials	Product capability in production Distribution and logistics Sales and services	Monitor and track product capability Document controls Full scale transition to operations
Financials Risk assessment	Financials Risk assessment	Financials Risk Assessment	Financials Risk assessment	Financials Risk assessment	Risk assessment Project close out

The process covers the entire product development cycle from idea to eventual sales. Numerous studies over the years have clearly shown that companies that have a cross-functional team integrally involved throughout the product development life cycle have had greater success rates in launching sustainable new products. Figure II illustrates how a cross-functional team can be involved in the new product development life cycle.

FIGURE II – The DFSS Cross Functional Team Matrix

Cross-Functional Team Matrix	Define	Assess	Develop	Validate	Launch	Sustain
Business/Management	P	P	I	I	P	I
Marketing	L	L	I	I	L	P
Design	P	L	P	P	P	I
Technology/Engineering	P	L	L	L	P	I
Manufacturing	I	P	P	L	L	L
Quality	I	P	P	P	P	P
Analytical/Testing	I	P	P	P	P	I
Environmental, Health and Safety	P	P	P	P	I	I
Finance	P	I	P	I	I	P
Legal	I	P	P	I	I	I
Sourcing/Purchasing	I	P	P	P	P	I
Sales	P	P	I	I	L	L
Customer Service/Support	I	I	I	I	P	L

Lead	L
Participant	P

These functions might take on different levels of responsibility in the process. For example, marketing takes the lead in defining the product development strategy and identifying the applications and customers in the beginning stages of the product development cycle. They take on a participant’s role during the actual design and development of the product, but re-emerge in the commercialization stages to drive the marketing initiatives of the new product. Even though various functions assume the lead in different phases of the product development cycle, the project manager is the glue that holds it all together, and maintains continuity.

The Quality System Regulation (QSR)

The QSR for medical devices “governs methods used in, and the facilities and controls used for, the design, manufacture, packaging, labeling, storage, installation and servicing

of all finished devices intended for human use” [1]. The QSR ensures that medical device companies design, develop, manufacture and distribute products that are safe and effective for the end-user. Elements of the QSR include controls related to design, purchasing, production and process, acceptance activities, labeling and packaging, quality and documentation.

DFSS is a natural fit with the QSR as this product development process can incorporate all the elements of the QSR with quantifiable metrics, controls, statistical techniques for quality control and documentation. Figure III details a six-stage product development process incorporating the requirements and documentation of QSR 21 CFR Parts 820. The rest of the article will describe how the various QSR elements (*highlighted in italics*) fit into each phase of a rigorous product development process.

FIGURE III – Integration of Design for Six Sigma and Quality Systems Regulation

Define	Assess	Develop		Validate		Launch	Sustain
Define the Business Case and Customer Requirements	Assess the technical requirements and product options	Design and develop and verify the product		Pilot the product and validate internally and with the customer		Launch the product - full scale manufacturing and commercialization	Monitor and track product capability internally and at the end-user
Design Controls							
Design Input							
	Design plan						
		Design output					
		Acceptance criteria					
		Design review					
		Design Verification		Design Validation			
			DMR				
DHF							
					Design Transfer		
Test methods							
Process Controls							
Purchasing controls							
						Receiving, in-process, finished goods	
						Traceability	
						Labeling	
						Packaging	
						Handling, storage, distribution	
						Monitoring and feedback	
Change Controls, CAPA							
Document Controls							
							DHR

DFSS and Product Development Phases integrated with the QSR:

Phase 1: Define – Define the business case, customer requirements and the intended use

The Define Phase is a critical step in crystallizing the “fuzzy front end” to detailed product, packaging and labeling requirements for the intended use. One of the biggest challenges is to identify that unmet need and obtain the critical requirements of the device for its intended use. This information is typically analyzed by marketing, with input from design and engineering.

Some of the basic questions that need to be answered for this phase are:

1. What unmet need will the new product fulfill for the market, customer or end-user?
What are its benefits?
2. What is its intended use? How will the end-user use the device? What are the requirements for the intended use (e.g. safety, efficacy, performance and user interfaces)?
3. How does the new product fit into the business strategy? Does this make business sense for the company?

The business case must also include a thorough market and competitive analysis. In six sigma terminology, the “Voice of the Customer” is used to identify the device performance, labeling and packaging requirements for the intended use. Lawrence Friedman gives an excellent treatise on targeting the right markets and aligning with customers in his book “Go to Market Strategy” (2). A detailed analysis of the human factors (3) in both form and function to ensure ergonomic handling, aesthetics, error-free performance and ease of use must not be ignored. Various methods can be used to obtain the “Voice of the Customer” and “Voice of the Market” including interviews, focus groups, surveys, observation and behavior modeling. Information from the Voice of the Customer is distilled down to quantifiable finished device performance specifications. Quality Function Deployment (QFD) is a very powerful tool that takes high level customer needs and correlates those needs with the critical performance specifications of the device. The performance specifications can in turn be correlated to the device design component specifications which in turn can provide the processing controls. Figure IV illustrates how the QFD can be used to identify critical production and processing

parameters that will produce a consistent product with the right performance requirements.

The information from this phase is documented as the *design inputs* which are part of the *Design History File* for the QSR (Figure III)

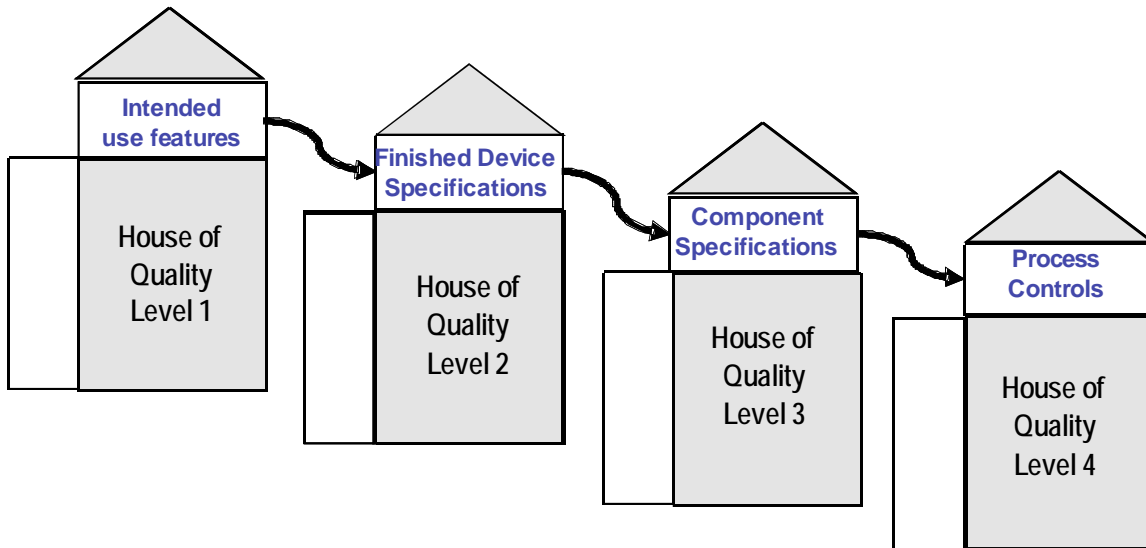
Phase 2: Assess – Identify the technical requirements, specifications and the technical options

The activities of the second phase are focused on identifying:

1. The detailed product/device properties, specifications and acceptance criteria (including performance needs after sterilization, biological or chemical fluid contact etc.)
2. The right test measurements for the acceptance criteria, and evaluating test measurement capability.
3. Prototyping and design evaluation, and
4. The appropriate development path and plan.

This phase is led by marketing, design and engineering (Figure II). From the end-user requirements, the detailed (critical-to-quality) product properties, specifications and tolerances are quantified using the QFD (Figure IV). Examples are exact dimensions and tolerances, clarity, toughness, electrical outputs, aesthetics and color, compliance needs, etc. Designing and developing the product becomes much easier once the device outputs are well defined. Design options are whittled down to the one design that meets all the product requirements.

FIGURE IV – Quantifiable flow down from customer’s requirements to process controls



Before embarking on developing the product, it is of primary importance that the test measurements used for the acceptance of the components, sub-assemblies and the finished device are capable. Large variations in a measurement system will make it impossible to differentiate whether or not a product is within specification or out of specification. Standard methods of evaluation are the %Gage Repeatability and Reproducibility (%GR&R) or the % Precision to Tolerance Ratio (%P/T). Preference should be given to ANSI, ASTM, ISO or other industry standard test methods.

The outcomes of this phase include criteria for *inspection, measurement and test equipment*, which is part of the *Production and Process Control* in the QSR. Product specifications, design options and design selection (i.e. *design inputs*) are recorded in the *Design History File*. The cross-functional product development team formulates a detailed *design and development plan* also part of *the Design History File* (Figure III)

Phase 3: Develop – Develop and verify the new product

Technology and engineering take the lead in developing the new product based on the selected design (Figure II). After a design review, a prototype is developed. The prototype’s properties and performance, including clinical trials, are evaluated with respect to the customer specifications and the intended use. Various techniques can be

used to evaluate the sigma capability of the product using predictive models and information obtained from statistical techniques like design of experiments, regression analysis, analysis of variance and capability scorecards. An example of a design capability scorecard is shown in Figure V. Model equations are generated based on first principles, modeling or design of experiments. These equations highlight the sensitivities of those components that influence the critical properties of the finished device. The benefit of this scorecard is that it identifies those components and parameters that need to be controlled during production. It also assesses the capability of the device based on the existing design. Redesign may be necessary if the prototype is not six sigma capable by design.

This information is documented for QSR compliance in the *Design History File* and is the source of information for the *design inputs, design outputs, design verification* and the *Device Master Record*.

FIGURE V – Design Scorecard example

Design Components	LSL	USL	Target value	Std. Dev.	Capability
Raw material Component a	12	26	19.3	1.39	6.3
Raw material Component b	65	85	72.3	2.2	4.8
Processing Condition c	100	140	115	4.3	5.0
Processing Condition d	255	355	290	7.1	6.4
Device Output 1	6700	7700	7216.75	133	5.0
Transfer Function : Y = f (X₁, X₂, ..., X_n)	Device Output 1 = 253-3.5*Component a +4.75*Component b + 12.5*Component a*Componentb - 10.3*Process x - 33*Process y				
LSL = Lower Specification Limit USL= Upper Specification Limit	Enter transfer function formula in green cell				
	<ul style="list-style-type: none"> • Improve low performing components to six sigma capability. 				

Phase 4: Validate – Pilot and test the product internally; validate with the customer/end-user

A minimum of five consecutive lots of the product is made on a pilot scale. Five lots are required to obtain a statistically significant standard deviation. The finished device capability is then evaluated on the critical-to-quality characteristics for the intended use using a capability scorecard (Figure V). This scorecard details the performance of the influencing components, processing conditions and the device properties. It also provides an overall capability of the product. Low capability components must be identified and their performance improved via a root cause analysis. The product must also be validated by the end-user or customer. This part of the product development process could take a significant amount of time depending upon the complexity of the validation at the end-user and any additional clinical testing that is required.

There are three critical documents that result from the development phase (Figure III):

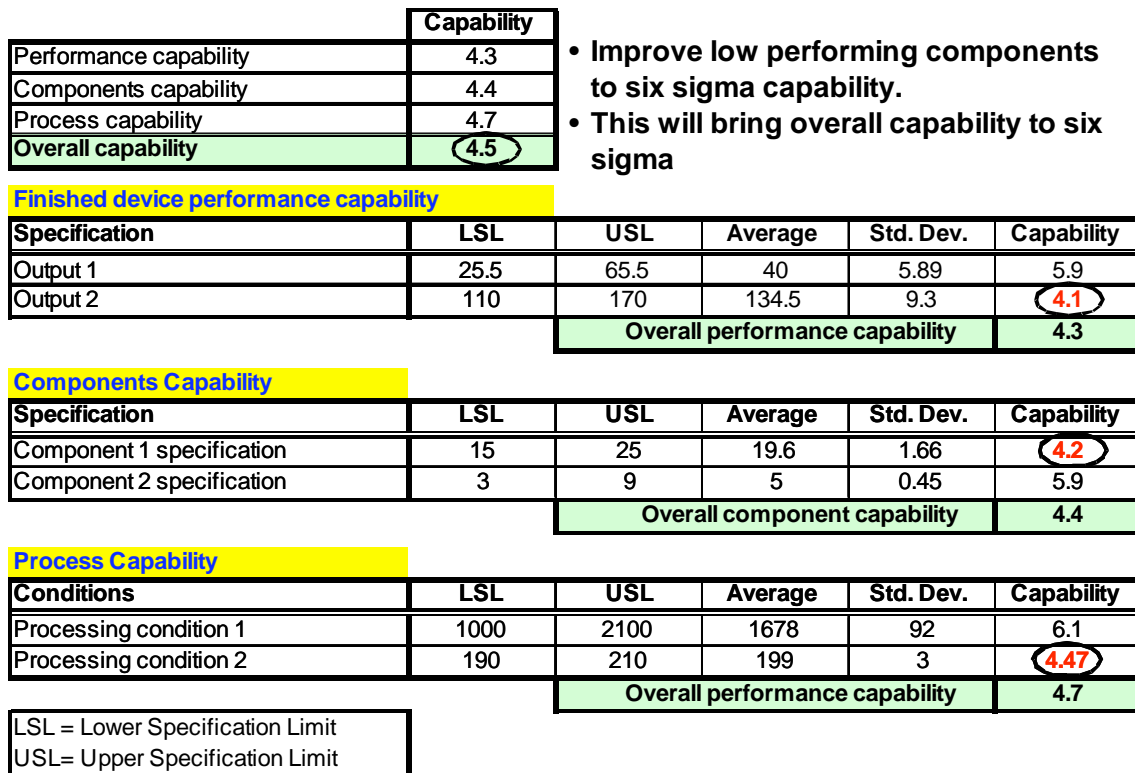
1. The *Device Master Record (DMR)* that details the description of the intended use, specifications for the device outputs and the raw materials, production protocol, *packaging and labeling, acceptance activities* (raw materials, in-process and finished device), *storage, handling, distribution and servicing* of the finished device.
2. The *Design Transfer* that contains all the standard operating procedures, tests and acceptance activities for the production, assembly and distribution of the finished device. It includes the identification and disposition of *non-conforming products* from incoming raw materials (*purchasing controls*) to finished goods.
3. The *Design History File (DHF)* that contains all the information during the design and development of the device including the *design inputs, design outputs, design verification and validation, design reviews*, and the design changes.

Phase 5: Launch – Product launch; full-scale production and commercialization

Full-scale production is led by manufacturing and the commercialization process is led by sales and marketing (Figure II). Product, process and performance capabilities are continually evaluated for six sigma performance both in production and at the end-user. The intent of Design for Six Sigma is designing the new product to be robust and

consistent during production, taking into account the raw material and manufacturing variability (4). Ideally, production and process controls (with minimal testing and inspection) should be adopted. Statistical techniques like statistical process control (SPC), statistical quality control (SQC), and product capability scorecards (Figure VI) are used to control and monitor the product and the process.

FIGURE VI – Product Capability Scorecard example



One of the major reasons for unsuccessful product launches is the quality of the product launch itself (5). Insufficient resources or attention is paid to the marketing and sales of the product to the industry, resulting in sluggish sales and poor market acceptance.

Commercial activities should include advertising, sales and marketing highlighting the value proposition of the product. End-user feedback is monitored to ensure the product meets the intended use and is safe and effective.

For QSR compliance, all production, testing, distribution, installation and servicing data are documented in the *Device History Record (DHR)* through the life cycle of the product.

Changes to processes and product should be captured in the change management and CAPA process.

Phase 6: Sustain - Operationalize, monitor, track and sustain the new product through the entire supply chain

The finished device should be monitored and tracked through the entire supply chain for a determined amount of time or a pre-determined number of lots to evaluate the capability of the entire process. This can be accomplished by setting up a regular audit schedule with a list of attributes to monitor. Such practices will also aid in preparing for FDA inspections. Product capability should be monitored over a pre-determined period of time to identify any major shifts and drifts which are related to changes in the process or raw materials over time. The root causes of these shifts and drifts must be identified and corrected. Any changes must be recorded in the CAPA system.

Before closing out the product development project and making it self-sustainable and operational, one should review the results (sales, revenue, quality, margins, product capability, development cycle time etc.) versus the original plan. Thus information is used in the continuous improvement loop of the quality systems process. The *Device History Record* is the repository for all the product data (Figure III).

Conclusion:

Companies should review their product development processes and assess how to bring rigor and quality regulations compliance into a single business process. Using the rigor of Design for Six Sigma tools and methodologies and integrating the Quality System Regulations within a company's new product development process can bring structure, clarity, reduced risks, speed-to-market and regulatory compliance. Finished devices can be designed, developed, manufactured, and sold with six sigma capability, meeting the end-user needs for its intended use as a safe and effective product. This leads to product consistency and reliability and sustainable sales, revenues and profits. Simplification of many processes into one integrated, manageable process allows for better control and compliance in producing the right product for the desired intended use and providing total customer value.

This may mean changing the way product development is conducted within a company. The challenge is to devise and implement a meaningful, sustainable process that becomes second nature in conducting business and is not perceived as additional or extra work.

REFERENCES

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