On

Process Validation

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Straight Talk

on

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Introduction

The Medical Device Industry should be very proud of their many wonderful accomplishments….but there is so much more to be done! Medical Device manufacturers have developed some amazing products that are truly making the quality of life fundamentally better for a huge number of people, but there are some tremendous challenges to be better and to do more. In the developed world, we have access to some phenomenal device and treatments but are finding it increasingly more difficult to pay for these solutions. Regarding the third world and emerging economies, the cost is far beyond the reach of all but a small percentage of wealthy members of these countries. If costs were to be dramatically lower, more people in this world would have access to the advanced procedures and human suffering could be reduced.

Let's briefly discuss some innovative devices that have had a dramatic impact on our quality of life. One example is a nebulizer. A nebulizer is a medical and health product that has been used as a way of transforming respiratory medication from liquid form into vapor form so that it can be breathed in through the lungs. This allows it to be absorbed far more quickly into the body than by simply ingesting it as commonly practiced in the past. Those that are suffering from health conditions like asthma and COPD find great comfort in such a device to help them relieve their symptoms and live a more normal life. My neighbor, Doug, recently had hip replacement surgery as an out-patient! He was doing great in a matter of weeks. A leading class II medical manufacturing company has a device that can annihilate cancerous cells without surgery. It is particularly helpful in cases of brain, prostrate and lung cancer. Another company is marketing a device in Europe (attempting to get FDA approval in USA) for people with a heart condition called atrial fibulation. Those fortunate to benefit from these devices and procedures can now go back to living more normal lives.

Developing these innovative medical devices also includes risks. (NOTE: For a recall listing see www.fda.gov/safety/recalls). When there are problems in the field, it can lead to catastrophic problems including loss of life or decreased quality of life. One recent example involves infusion pumps used in the medical device industry. These devices can deliver up to three different medications to a patient intravenously. Unfortunately, a number of companies have experienced problems with these devices in the last decade. One of the most infamous cases involves an infusion pump marketed by a world renowned medical device company. In 2010, the FDA asked this company to pull all of their units of a particular model from the market place. The FDA required the company to destroy many thousands of units due to field failures. According to a FDA News Release on May 3, 2010, over 500 deaths have been attributed to malfunctions in this device. Several problems were identified. One involved an interaction between the batteries and the controlling software. It seems that if the batteries died the software allowed for a "free flow" of medications to the patient. In August of 2010, another U.S. medical device company issued a global recall of two hip aid systems after more people than expected suffered pain which required additional surgery. According to the company, 1 in 8 patients who received the ASR total hip replacement needed a second surgery to fix issues. These recalls demonstrate that risks must be properly identified during product development and risk management must be continued after process validation.

Why do we have the above stated crises with medical devices? How can a medical device company enhance their probability of success in the market place and minimize these risks? What can management do to assure products being produced are timely, low-cost, reliable, FDA compliant, customer delighting, and hit their market window? As delineated in Chapter 1 of this book, medical device providers need to complete three phases exceptionally well in order to mitigate risk.

- Step 1: Complete Pre-validation activities in a seamless manner.
- Step 2: Validate processes
- Step 3: Conduct on-going monitoring and control the process.

All three are essential to mitigate risk. For the previously described catastrophic examples, it is not entirely obvious from the public accounts as to where the root cause(s) lie. There may have been issues with any of the above three steps or some combination thereof.

Process validation is one integral element of a company's risk reduction strategy. Process validation is a requirement of the Good Manufacturing Practices Regulation for Medical Devices, 21 CFR Part 820. It is applicable to companies that design and manufacture medical devices, pharmaceutical, and bio-medical devices. Regardless of whether you are producing a class III, class II, or class I device, compliance is the law. Completed in an efficient and effective manner, process validation does not have to add excessive cost or bureaucracy to your company, yet many companies have taken paths that do just these things. As an integral part of an overall product and process design and manufacturing strategy process validation can be an invaluable tool in minimizing risk and cost in a lean manner.

Some organizations new to the medical device community are convinced that it is not necessary to validate any processes. Their mode of operation is to test/assemble/test/assemble/and test again at the system level. This strategy is high cost and not effective. Even simple tests are not 100% reliable. Testing of complex systems is even worse. With any test, there are two fundamental risks. One is declaring good product bad. The other is calling bad product good. This strategy will guarantee you have field failures and excessive manufacturing costs. It leads to lots of rework and scrap. It is the antithesis of a low-cost and lean strategy.

There are a lot of medical device manufacturers doing an excellent job with their process validation initiatives. They got there by thinking through their products and processes and developing process validation strategies that are appropriate for their unique needs. Unfortunately, there are *some* in the medical device industry that don't want to think…..just tell me the proper course and I will blindly follow (consultants and company gurus are frequently the guilty party in this regard). Design verification/validation teams need to have profound design and process knowledge and a working knowledge of company SOP's and be willing to logically think through the risk and make a logical decision. The team then needs to document their logic and decision. *You* should be the expert on your design and process, not an outside consultant or the FDA.

Process validation need not be a painful process. In the end, a common understanding of process validation across the organization will actually make everyone's job easier. Our belief is that the

FDA really wants you to look at process validation from a common sense approach. You just need to understand the FDA's requirements, ensure your company policies and procedures are in sync with these requirements, and then rigorously follow these procedures. A fundamental tenant being driven at FDA presentations we have attended is:

- Understand risk.
- Document the level of risk.
- Take action as appropriate.
- Document what you have done,
- As new information is obtained update your risk assessment and take actions as deemed appropriate.

It is also important to remember that just because your process validation effort is completed does not mean you are done. You must have a system of timely, rigorous controls in place. You must do Process Control! Dr. Edward Deming, a noted guru on Quality and Management, stated that getting a process to attain a state of statistical control requires a great deal of team work and effort. This has been our experience as well. After the process has been validated, it is key to have on-going statistical process control techniques in place.

In this book we will attempt to provide a proactive, logical, thought provoking approach to the process validation, and continued control of a process. Process validation cannot be completed in a vacuum after design work has been completed. It must be part of a proactive, integrated, cross-functional team effort. Individuals need to have a working knowledge of FDA requirements, company Standard Operating Procedures, and profound knowledge of customer needs, product design, and processes.

Chapter 1 – Process Validation Basics

Conceptually Process Validation is not all that difficult.

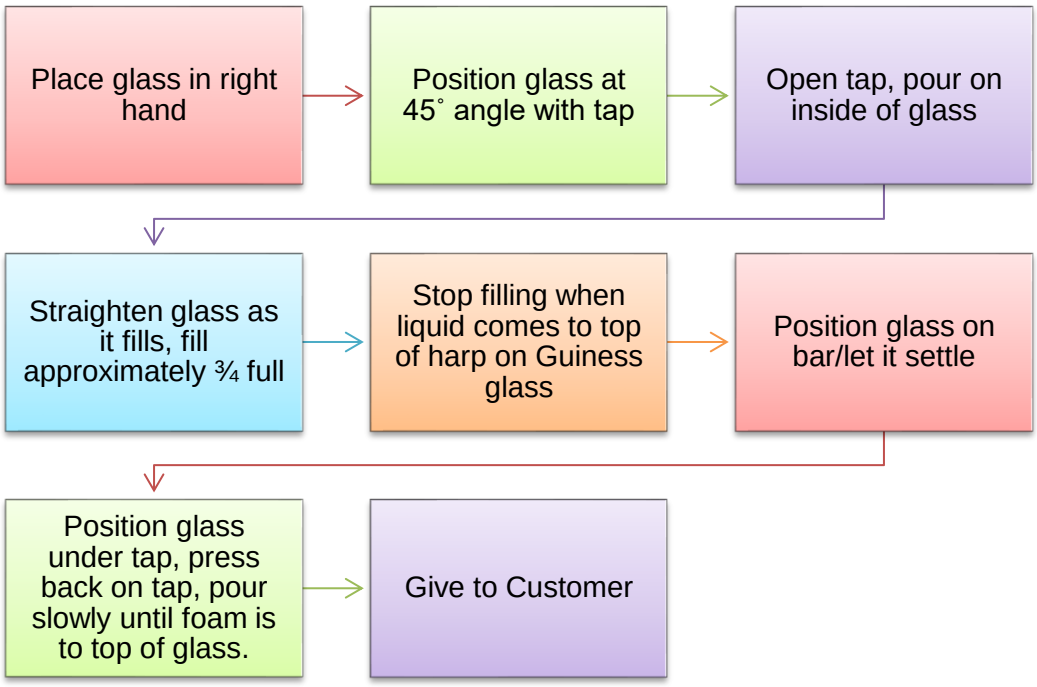
Back in the early 1990's, I made my first trip to Ireland. After flying all night from Boston to Cork International airport, I finally checked into the Killkarney Hotel mid-afternoon. By late in the afternoon, I was in the pub and decided to order a pint of Guinness. Patrick, the bar keeper, was behind a beautiful, big, dark, wooden bar. In Ireland, pouring a glass of beer is an ancient art form. After I asked for an Imperial pint of Guinness, Patrick began the exacting process of preparing the pint. First he selected a Guinness glass (20 ounces), positioned the glass at a 45 degree angle with the down flow of the spout on the tap, pulled the tap arm all the way forward and began filling the glass. The flow from the tap was directed at the inside wall of the side of the glass. As the glass filled he gradually straightened the glass until the bottom of the glass was perpendicular to the flow. Once the glass was ¾ full he turned off the tap and placed the partially filled pint on the bar. Waiting for what seemed to be hours (until bubbling below the foam had stopped), Patrick slowly filled the remainder of the glass by pushing back on the tap arm. The glass filled slowly until full. After commenting to Patrick about this amazing process, he went into great detail regarding the training he had received at the local brewery in Cork and the rigorous controls that the brewer, distributor, and Inn had in place to ensure the integrity of the product.

So how does this relate to process validation of medical devices? In order for anything to be of consistent high quality, there must be an outstanding optimized process that is followed meticulously. This applies not only to pouring a glass of Guinness but to a host of products and services including medical devices. The major topic in this text is process validation, not pouring beer, but perhaps there is an interesting parallel to be drawn between process validation and the above activity.

Actual validation of a process involves team work, discipline, great planning, profound process knowledge, understanding risk, and documentation; however, at the conceptual level it is not all that complex. In fact, process validation makes a great deal of sense for anyone attempting to provide a consistently great customer experience. The process validation team should generate a plan, map the process, identify key characteristics, and then decide on where to begin.

The Guinness Example

Let's look at the steps involving the pouring of a pint of Guinness and how process validation could apply. First we will create a high-level Process Map of the process. Process Maps are useful tools to use during your process validation efforts. It is as follows:



First Major Stage of Process Validation
The first major stage of process validation addresses the following question: *Is all of the equipment functioning properly and installed correctly?*

In the "beer" scenario, suppose the key output characteristic is taste**.** Items of interest regarding equipment would be flow rates from the tap, storage temperatures of the kegs, and pressure in the kegs.

Second Major Stage of Process Validation
In the second major stage of process validation, we need to demonstrate we can create good product at nominal process conditions and then worst case process conditions. Worst case or extreme conditions might include newly tapped keg vs. one that is nearly empty, keg storage temperature at extremes or other variables that the team knows can have impact on taste of delivered pint**.**

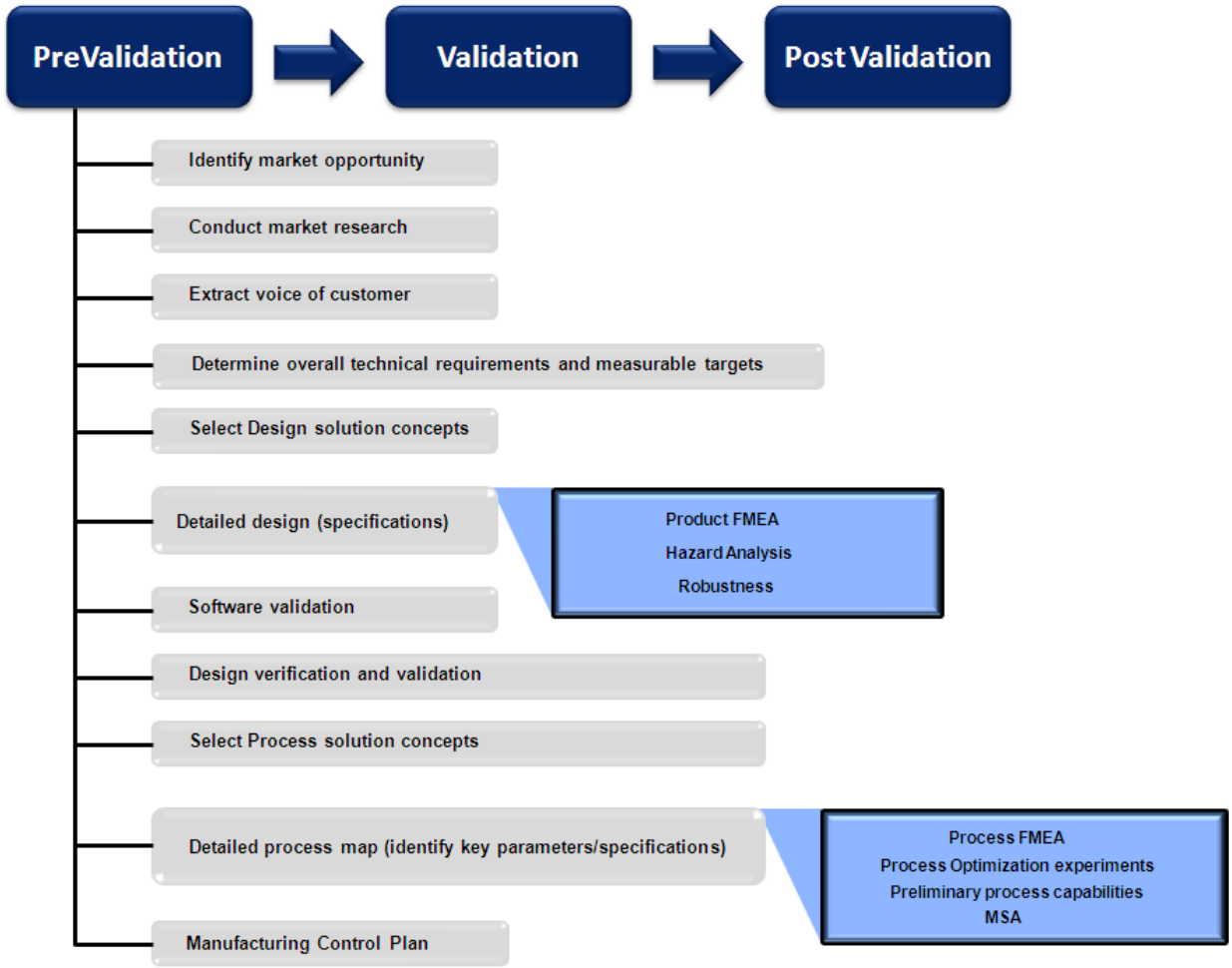
Third Major Stage of Process Validation
In this stage, we need to demonstrate that the process will consistently produce great tasting pints in a production setting**.** Once all the above have been demonstrated, we need to plan for things like on-going production controls, plotting of data, and revalidation of the process.

Successful completion of the above stages constitutes a validated process.

But Many are Confused!

Why does process validation leave so many people "scratching their heads"? The flow chart below shows the correct sequence for process validation. Often times, pre-validation activities are done in conjunction with other steps in the flow chart when, in fact, the pre-validation activities should have been done first. This is a large source of the confusion.

Although the primary focus of this book will be on the Validation portion of this flow chart, it is important to discuss pre-validation activities and post-validation activities as well. Post validation activities will be discussed later in the book. Since pre-validation activities appear to be a major source of confusion, let's discuss them now. Below is an expanded version of the flow chart from above.



There are a lot of activities that need to occur prior to even considering validation of the process. These pre-validation activities include, but are not limited to, the following:

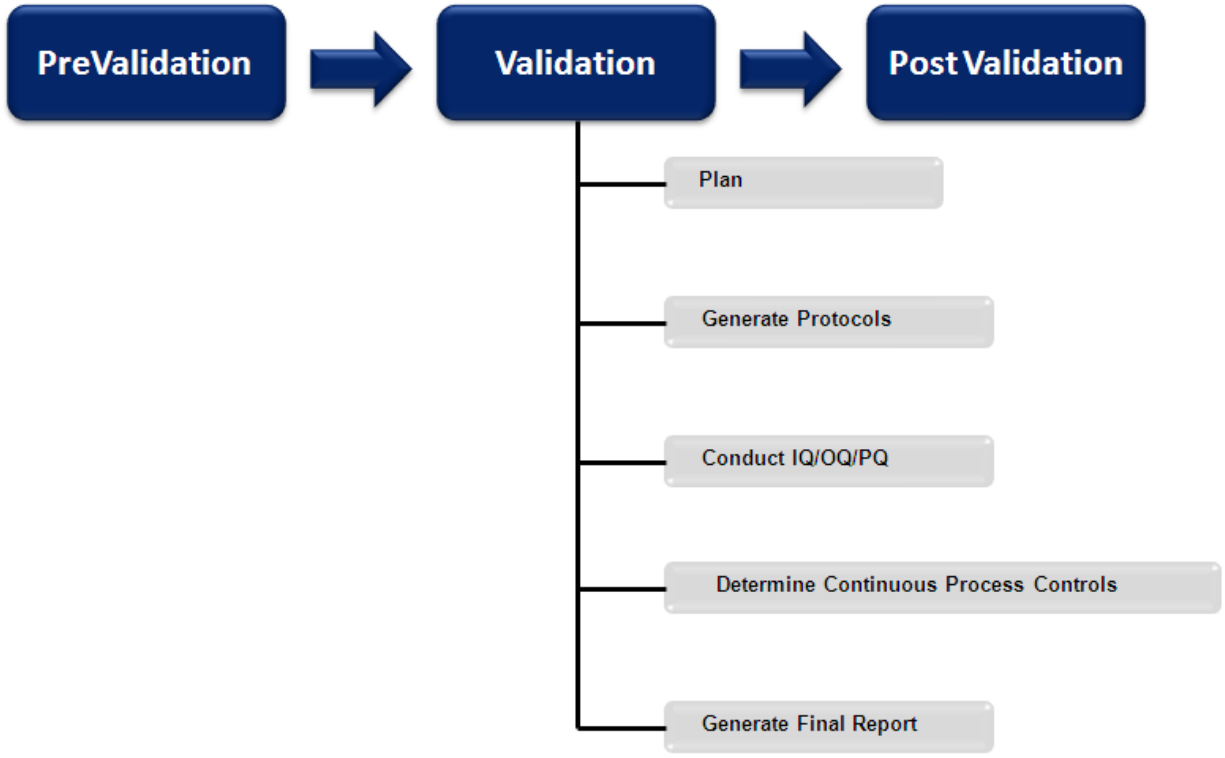
- Identify market opportunity
- Conduct market research
- Extract voice of customer
- Determine overall technical requirements and measurable targets
- Select Design solution concepts
- Detailed design (specifications)
    - Product FMEA (Failure Mode and Effects Analysis)
    - Use/Misuse FMEA
    - Hazard Analysis
    - Robustness
- Software validation
- Design verification and validation
- Select process solution concepts
- Detailed process map (identify key parameters/specifications
    - Process FMEA
    - Process Optimization experiments
    - Preliminary process capabilities
    - MSA (Measurement Systems Analysis)
- Manufacturing Control Plan

The authors of this book have consulted with numerous companies over the years. The biggest problem at most of these companies is that they try to incorporate pre-validation activities into their process validation protocols. This leads to a great deal of confusion. These activities should be done ***first***. This will lead to a more streamlined and efficient process validation effort…oh, and it will be less confusing too! NOTE: Pre-Validation activities will be discussed in more detail in Chapter 2.

Process Validation Steps

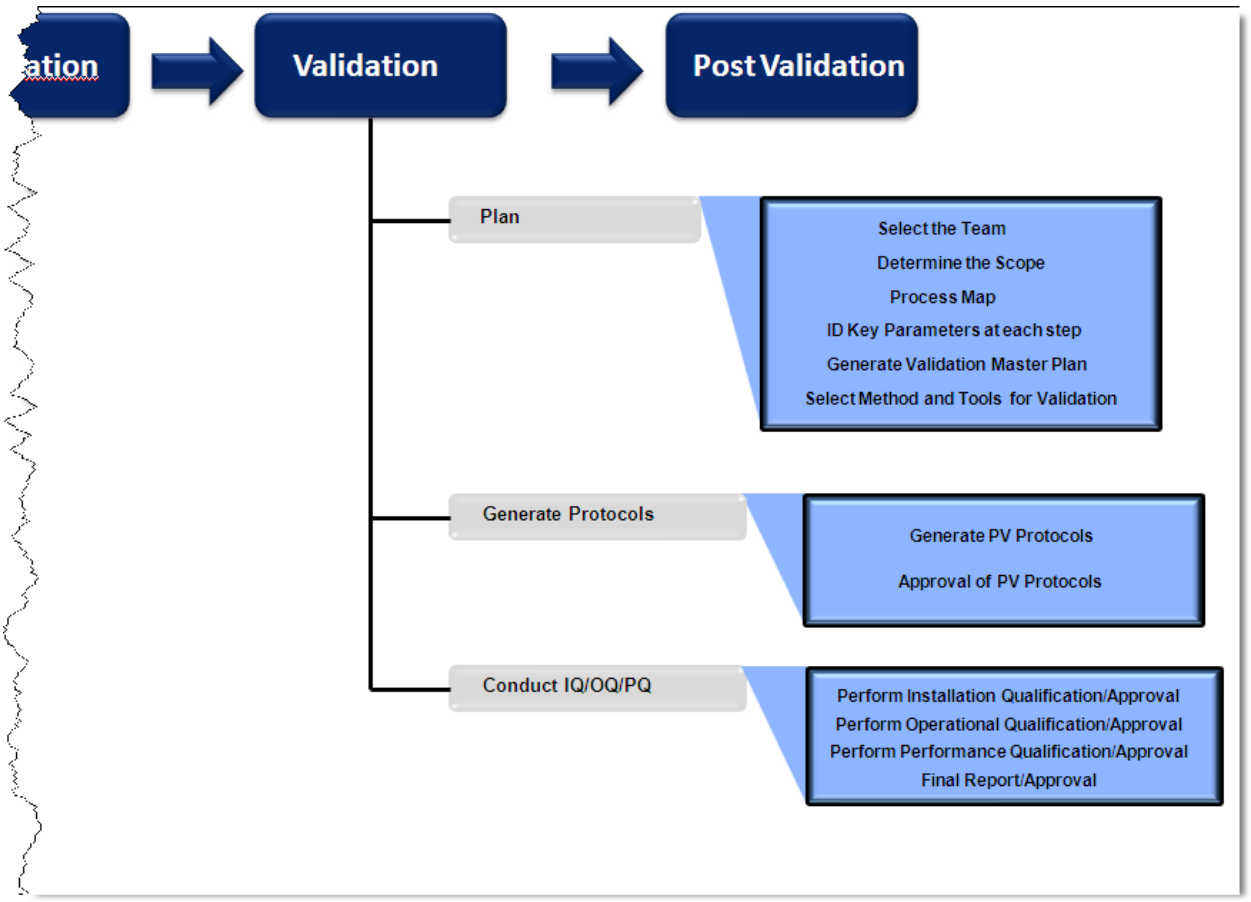
Now that you understand what pre-validation activities must occur, let's move to the Validation portion of the flow chart in Figure 1.0. Process validation is all about taking a fundamentally sound, optimized, documented process and demonstrating with data that it consistently produces a good product. Guinness has worked for hundreds of years to perfect their process. It is foolish to attempt process validation until you are certain you have a fundamentally sound optimized process. Just document the completed studies in the appropriate company approved systems.

The steps in process validation are simple and logical. They are shown in the flow chart below.



Really. Those are the basic steps to process validation. Don't make it more difficult than it needs to be. And while performing each step, never lose sight of why you are performing process validation in the first place. No, it's not to simply satisfy FDA requirements…it's to PROTECT the potential users of your product and to DO NO HARM. Instead of viewing process validation as a negative requirement imposed upon you by the FDA, view it as an opportunity for you to help protect your customers. It just makes good business sense.

The following chart expands on each of the process validation steps:



Step 1: Plan

- Pull together a cross-functional process validation team.
- Determine the scope of the process validation effort.
- Create a process map.
- Determine the critical inputs and outputs for the entire process and at each process step (you need support from product design to do this)
- Create a Master Validation Plan (MVP). Using this simple spreadsheet the team will determine actions required (validation, verification, qualification, timing, responsibilities, etc.) at each process step
- Select the methods and tools you will use for process validation

Step 2: Generate Protocols

- Generate Process Validation Protocols
- Get Signed Approval of Process Validation Protocols.

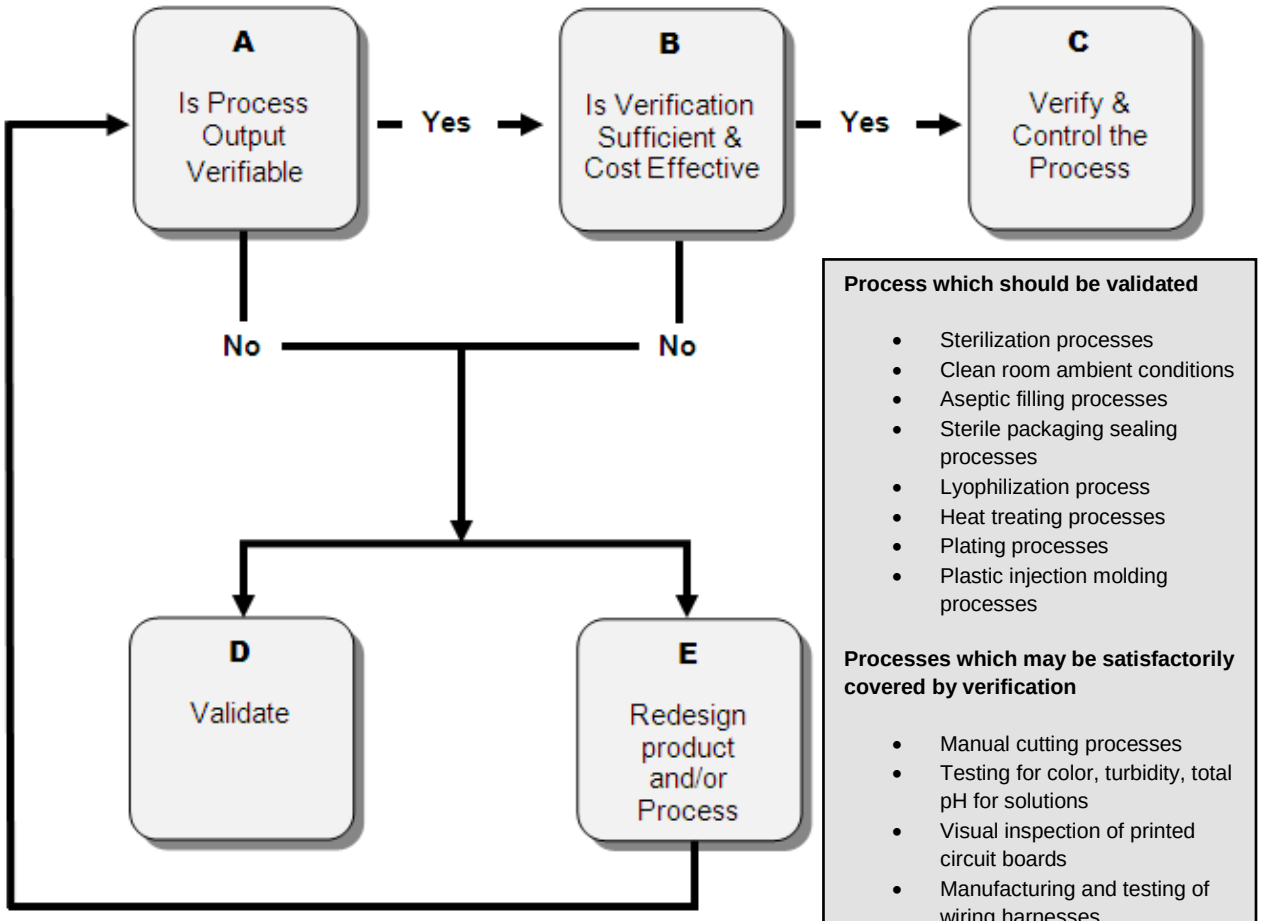
Step 3: Conduct IQ, OQ, PQ

- Conduct the IQ (Installation Qualification that demonstrates we installed all equipment correctly). Once this is completed, have the appropriate parties review and sign-off.
- Next conduct the OQ (Operational Qualification which demonstrates the process can make good stuff at nominal conditions and at worse-case settings). Once this is completed, have the appropriate parties review and sign-off.
- Next conduct the PQ (Performance Qualification which demonstrates the process will create consistently good product in a production setting. Once this is completed, have the appropriate parties review and sign-off.
- Generate a final report that summarizes the above IQ, OQ and PQ. Once this is completed, have the appropriate parties sign-off.

We will discuss each step in more detail in the following chapters of this book. At this point, we are trying to show that there really are some basic steps and process validation does not have to be a confusing topic.

Guidelines on when you should validate

Below is a simple flow chart that indicates when your company should validate a process.



Process which should be validated

- Sterilization processes
- Clean room ambient conditions
- Aseptic filling processes
- Sterile packaging sealing processes
- Lyophilization process
- Heat treating processes
- Plating processes
- Plastic injection molding processes

Processes which may be satisfactorily covered by verification

- Manual cutting processes
- Testing for color, turbidity, total pH for solutions
- Visual inspection of printed circuit boards
- Manufacturing and testing of wiring harnesses.

Note from the above diagram: It is sometimes ok to 100% verify as opposed to validating a process. The GHTF (Global Harmonization Task Force) provides recommendation of common processes that should be validated and those where it is ok to verify the process. Ultimately, the decision regarding verification or validation rests upon you and your team's shoulders.

Warning: If you decide to do 100% verification of a process that the FDA guidance document suggests should be validated, you better have a documented, logical, technology-based thought process in place justifying your position…and be ready to sell your case to the applicable regulatory body.

What is required to be good at Process Validation?

The following is a list of some key items to continually strive to achieve within your organization.

- Planning
- Cross functional team THAT CAN WORK TOGETHER!!!
- Profound process knowledge
- Long term commitment
- Roadmap reflecting regulatory guidelines
- Good procedures and forms in place that are easily understood.
- Metrics to map progress
- Passion for excellence

Barriers to Process Validation

Unfortunately, organizations and people by their nature can pose barriers to achievement of these attributes. Some barriers we have witnessed first-hand in industry are:

Organizational segmentation:

In highly segmented organizations, communication is good up and down an organizational silo but poor across organizations. Unfortunately, this type of structure is rampant in many medical device companies. The Marketing group communicates poorly with the Product Design group. Product Design communicates poorly with Advanced Manufacturing Engineering. Advanced Manufacturing Engineering, in turn, communicates poorly with Manufacturing. The Quality group tends to live outside this circle, functioning in a classical "quality cops" role. The FDA contributes to this organizational malaise by generating separate documents for design control, process validation, test methods, and software validation. The FDA's attempts at communicating that an overall "systems approach" is necessary is not being received by all in the medical device community.

Many organizations have had excellent success by using truly cross-functional teams. One approach is to have teams that actually wear different hats as the primary product activity shifts

from pre-design to detailed design to prototype to volume manufacturing. Additionally, having the cross-functional teams use tools such as quantitative market research, KJ diagrams, simplified QFD (Quality Function Deployment), and Designed Experiments can greatly enhance the combined organizational intelligence about the product and process required to create the product.

Utilizing a truly cross-functional team that can communicate and work together toward a common goal is especially important for process validation efforts. Recently I was working with a medium sized medical device company on some experimental design and process validation activities. The process validation team consisted mainly of manufacturing operations and mechanical engineering personnel. The function of quality was to generate procedures, then audit and critique protocols and completed qualifications. Audit is certainly an important role within a medical device company but wouldn't the team be in a better position to conduct process validation activities in an effective and efficient manner if the quality engineers were part of the process validation activity from its initiation? Quality engineering concerns could then be raised and resolved early in the development of the process validation protocols, not after they had been prepared. Quality engineering needs to partner in the process…not just be the "quality cops".

Organizational dysfunction:

My daughter, Cass, is a grade school teacher. She was telling me about some conflicts her teaching team was working through. One of the other teachers and Cass seemed to be having trouble communicating with each other. About this same time, the school district decided to give each teacher a profile-exam to determine their primary approach to problem solving. It seems Cass was a classical "green". Green's tend to start with getting a handle on the big picture first then working down to the details. The other teacher with whom she was occasionally having communication problems was "gold"…the opposite of a "green". "Gold's" tend to start with the details first then gradually work their way up to understand the whole picture. The risk with being a "green" is never being able to get down to the details. The risk with being "gold" is getting so immersed in the details that you never get the big picture. Most effective teams should have both personality types in order to solve various challenges. Team members need to appreciate the special talents (and limitations) of the other problem solving types and ensure there is a working balance on the cross-functional team.

We frequently see seriously conflicted teams within medical device organizations. Both green and gold types are needed. If the greens tend to dominate the team, there is a tendency to complete only cursory level validations….they may gloss over important details. If the gold's dominate the team, they can get wrapped up in minute details while making only incremental progress. Allow each member to become aware of their primary approach to learning and problem solving. Make sure all have an appreciation for other team member's strengths and weaknesses. It is usually the Project Manager's job to think "Green", while most technical contributors are thinking "Gold". That is why solid Project Management is critical.

Preplanning tools can be of great assistance to both problem solving types on the process validation team. Design Failure Mode Effect and Criticality Analysis (DFMECA) and Process

Failure Mode Effect and Criticality analysis (PFMECA) can guide the team regarding focusing on the key risks both at the design and process level. These tools help them go after the big risk items first! Detailed process maps supplemented by Design of Experiments (DOE) characterization studies can delineate the key input factors for the key output characteristics. Control plans can provide useful insight into key parameter management. This information can be of great assistance in focusing the process validation team on the essential parameters so they can get on with their important work.

Below are some examples of strange things people can do if they have not prioritized risk.

1) The following story was relayed to me by a battery manufacturer for a Class III device. A customer auditor (not FDA) told supplier personnel that when gathering test data manually, the recording of the data needed to be witnessed by another individual within the company as an assurance measure. This is certainly not an FDA requirement.

2) A customer auditor from a major medical device manufacturer was reviewing the use of an oscilloscope in the gathering of data from an electronic module being tested. The auditor asked about the cleaning solution being used occasionally to clean smudges off the oscilloscope screen. The cleaning solution was a commercially available window cleaner and used for occasional screen cleaning. The auditor wanted to see a certificate of compliance for the commercial screen cleaning solution.

3) In a facility geared toward the manufacture and test of printed circuit boards and modules, a paper build log system was being used. As a process operation was completed on the hardware, the person doing the actual build would use a stamp to provide ownership and traceability. Once the process step was completed, it was submitted to a quality inspector. After the quality inspector had completed their inspection and approved the process step, they would in turn stamp the completed build folder with their unique stamp. A third group, internal audit, would review all completed build documentation. Incredible concerns would be raised if assembler or inspection stamps were even slightly smeared yet still obviously identifiable.

Plan for success

A few years ago, my 27 year old son, Randy, was at my place on a Sunday evening. We were watching an edition of Sunday night football and having some refreshments. Randy brought up the fact that there was a marathon in Colorado Springs planned for two weeks from that weekend. During the summer, we had both completed a couple of 5k's but never anything longer. We naively decided that doing a marathon should be no big problem for us. After all, the course map showed the marathon to be nearly all down- hill. We enthusiastically signed up! Needless to say, we had no concept of what we were in for. The first couple of miles were just fine but at about the 12 mile marker, bad things began to happen. At mile 16, I totally cramped up in my right hamstring muscle

and started to walk. I was unable to run anymore and I finished the course by walking the last 10 miles. My finish time was an embarrassingly slow 5:37. After the race I decide to sit for about 15 minutes before embarking on the journey to my vehicle. This turned out to be problematic as I was barely able to stand up and walk by now. With much effort, I eventually was able to get into my vehicle and drive the 30 minutes home. By this time, I was even in worse shape and literally had to crawl out of the truck, across the yard and up to my house.

Some medical device companies approach process validation with a similar amount of pre-planning as above. Suddenly they are about to manufacture a device when someone realizes they need to consider FDA requirements for process validation. Confusion in this context is rampant. Should we validate, verify, or qualify the process? Can we just 100% test? What about suppliers? Can we afford to do all of this? What about a hazard analysis? Where do we start?

Much like being successful in a marathon, effective, low-cost, risk reducing process validation requires great cross-functional team work, appropriate tool applications to support product and process design, profound technical knowledge, and a passion for low-cost, risk mitigating excellence.

Process validation planning needs to begin long before the product design is completed. Process flow charts, detailed process maps, DFMEA, PFMEA, hazard analysis, control planning, requirements maps, VSM (Value Stream Mapping), and DOE characterization studies all need to be completed before process validation is initiated. By doing this, an organization can provide low-risk, low-cost, compliant products that delight the customer.

Summary

Process validation need not be complex or confusing. Organizations need to do the necessary pre-work up front and early in the product and process development cycle. Compelling product and process design activities coupled with excellent process characterization studies should be completed *before* process validation activities are commenced. By doing the upfront work, process validations will be timely, efficient, and effective.

Chapter 2 – Some Pre-Process Validation Considerations

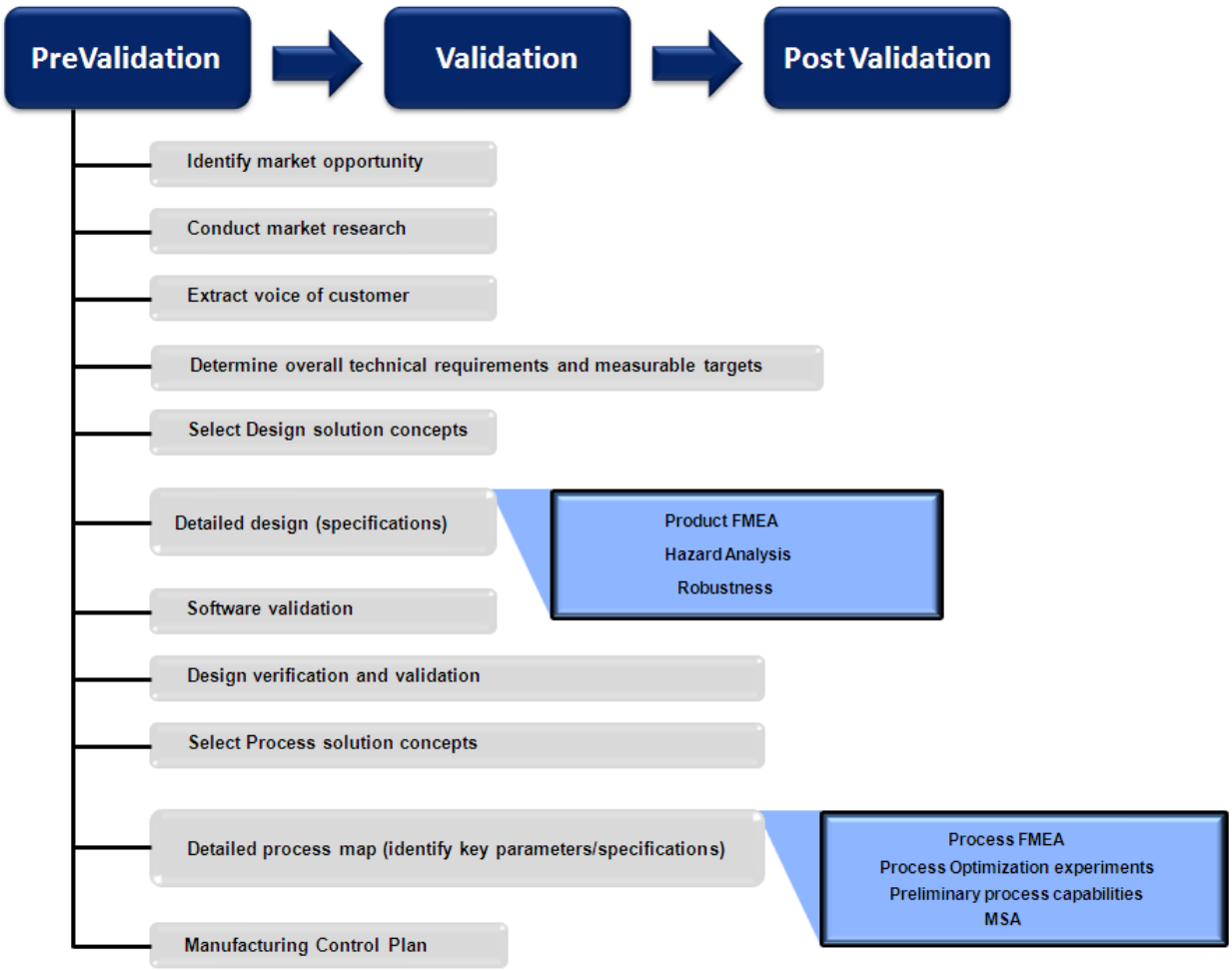
It Doesn't Have To Be Overwhelming

Process validation can appear to be an overwhelming task to organizations first embarking upon this initiative. Should we do verification or validation? What is the difference between these two terms? What is a protocol? What should be in a protocol? Who should sign-off on the final report? How does process validation play with ISO 13485? Do we need to conduct software validation? When is re-validation necessary? What are the engineering requirements we are attempting to validate against? What process steps are we considering for validation? These are just a few of the multitude of questions that can come up when discussing process validation of medical device processes. In this book, we will discuss some important questions to answer before embarking on process validation as well as some simple graphical and planning tools that can be used to help your team focus, clarify, and move forward with a proactive validation effort.

Regarding product and process validation, it all starts with Designing the Product and Process for the medical device. The FDA document "Design Control Guidance for Medical Device" provides a roadmap for this process. Of particular interest to folks embarking upon the validation of manufacturing processes, is the section regarding "Design Transfer". In this section it is stated that "Production specifications must ensure that manufactured devices are repeatedly and reliably produced within product and process capabilities. If a manufactured device deviates outside those capabilities, performance may be compromised. Thus, the process of encapsulating knowledge about the device into production specifications is critical to device quality." Design transfer is the process of creating manufacturing specifications (processes, tooling, fixturing, work instructions, Quality Assurance specifications, etc.) from the design output (design specifications). Design transfer identifies controls in the manufacturing process while ensuring manufacturing specifications do not introduce residual risk to the medical product.

The focus of this chapter will be on the Pre-Validation phase.

Before the first step of process validation can occur, a number of key actions need to have been completed. Don't confuse your Pre-Validation activities with Validation activities. The key pre-validation activities are shown in the graph below.



The above activities are listed so as to suggest the activities are sequential in nature but in fact concurrency in activity can and should be utilized as appropriate. Standard Operating Procedures will differ from company-to-company but many of the last items in the above graph would be addressed in the design transfer documentation.

In what follows, we provide a very brief description of key activities and identify some popular tools used to support data and information gathering. It is important to remember that there is no substitute for outstanding market research, product engineering, and process engineering knowledge and talent. Upon this foundation, the tools can have an incremental impact on decision effectiveness and risk management. Effective and efficient utilization of the tools discussed in the following sections allows a good team to become a great team. Learning to use the tools discussed in the following session requires training and numerous applications.

Do not lose sight of the big picture. You (and the FDA) care tremendously about product design, process design and other pre-validation activities. Please see the FDA documents listed below.:

1. http://www.fda.gov/RegulatoryInformation/Guidances/ucm126954.htm?utm_source=fdaSearch&utm_medium=website&utm_term=software validation&utm_content=4 "General Principles of Software Validation"
2. http://www.fda.gov "Design Control for Medical Device Manufacturers"

Identify Market opportunity

Briefly, in this step we need to carefully assess the niche in the market that our product or service would meet. Questions such as:

- What is the value proposition?
- Is this opportunity financially viable to us?
- Is this opportunity a good business fit with our other offerings?
- Do we know how to be successful in this niche?
- Do we have the right technological, sales, and marketing know-how to be successful?

These are just a sampling of key assessment questions to be answered at this stage.

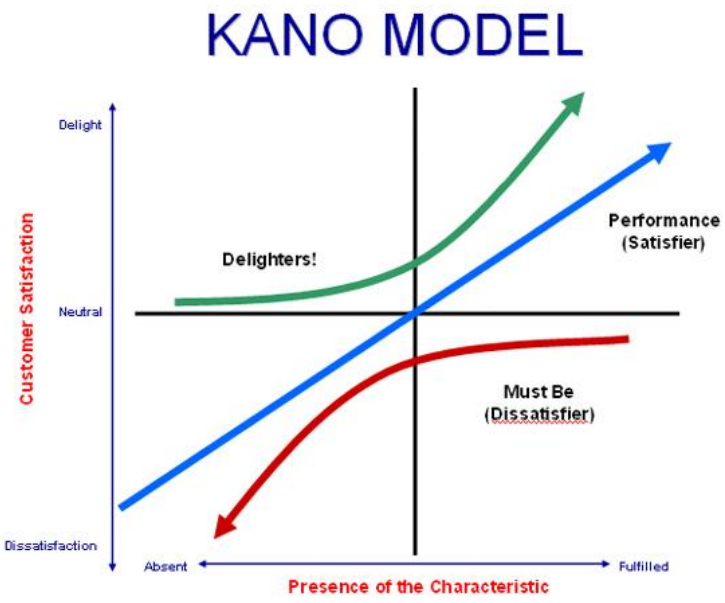
Conduct Market Research

In this step, we need to take the time to understand the basic, spoken, and latent needs of the market. Tools such as contextual inquiry, focus groups, one-on-one interviews, interactive prototyping, etc. are used by leading organizations to ensure a complete understanding of the needs and the value proposition to the customer. Additionally, it is important to consider the competition from products offered by other companies, especially their strengths and weaknesses.

Extract Voice of the Customer

Once we have conducted exhaustive market research and collected statements from the customer, we need to make sense of this information. Tools such as Voice of the Customer tables, affinity diagrams, and KJ analysis are hugely valuable in this activity. In particular, these tools support the Design Control requirement of "determination of design inputs".

Below is an example of the Kano Model. It is important to determine which product characteristics are considered "Performance", "Must Be", and "Delighters".



After interviewing customers, it is typical to use a table to summarize their "voices".

1ml. Syringe			
Characteristic	elderly	under age 40	nurse
Appealing pkg.	performance	delighter	must be
Pilfer evident pkg.	must be	must be	must be
Clear graduation on barrel	performance	must be	must be
Quick fill	performance	performance	performance
Needle cover safe	must be	must be	must be
low pain injection	delighter	performance	performance
Easy to dispose	performance	must be	must be

Medical Device and Diagnostics has an excellent article regarding this topic. For more information, go to:
http://www.mddionline.com/article/psst-your-customer-knows-something-you-don%E2%80%99t

Determine overall technical requirements and measurable targets

Tools such as QFD (Quality Function Deployment) or Simplified QFD are powerful tools the team can use to translate leading customer needs into overall, measureable engineering (technical) requirements for the product. These tools are most effective when used to focus on the most important needs as measured by customer ratings. Importantly, each technical requirement

needs to be measureable with a target value and specification. Target values and specifications are primarily driven by customer expectations and/or technical benchmarking of competitor products.

Here is a QFD example from the University of the West of England:
http://www.cems.uwe.ac.uk/amrc/KTP/CODA/Paper2.htm

Select Design Solution concepts

The engineering team needs to consider multiple concepts before focusing upon the final concepts. This can and should be completed at the sub-system/part level as appropriate. Competitive benchmarking, trade-shows, and tools such as TRIZ can be useful in the concept generation stage. Tools such as Pugh's Concept Selection techniques (or modifications thereof) can be helpful in allowing the team to trade-off concept level alternatives against technical, business, and customer requirements. Below is an example of a Pugh concept selection matrix for a revised needle shield. The datum is the current design, Shields A, B, and C are alternatives being considered by the design team.

Criteria	Datum	Shield A	Shield B	Shield C
Manufacturing Cost		1	-1	0
Appearance		-1	-1	-1
Ease of use		1	1	-1
Storage		0	1	-1
Color options		0	1	0
Recyclable?		1	1	-1
Size		-1	0	-1
Max. Temperature		1	0	1
Max. Humidty		1	-1	0
Total of "-1"		2	3	5
Total of "+1"		5	4	1
Total of "0"		2	2	3

Detailed design (Specifications)

Product FMEA

FMEA (Failure Mode and Effect Analysis) is a popular, systematic bottoms-up approach to risk assessment, risk mitigation, and risk documentation of products. The FDA is typically very interested in this document. A cross-functional team starts at a part or component level and assumes a failure at this low-level. The team then identifies potential effects at a higher (usually) system level. The team assigns a Risk Priority Number (RPN).

For higher RPN's, follow-up actions are identified and correction action is taken as appropriate.

Function	Potential Failure Mode	Potential Effects of Failure	SEV	Causes of Failure	OCC	Current Design Controls	DET	RPN	Recommended Actions	Responsibility and Target Completion Dates	Action Results				
											Actions Taken	SEV	OCC	DET	RPN
Close orifice on down stroke	Leaks air from the chamber into the atmosphere.	User unable to pressurize bottle	7	Won't slide to top/bottom position.	2	Lifetest (RD - 107)	2	28	None at this time.	J. Lahey 7/29/05	None	7	2	2	28
			7	Fails to seal against chamber wall.	3	Lifetest (RD - 109)	3	63	Monte Carlo Analysis	M. Ryan 8/1/05	Design Change New Tolerances DOC 5548	7	1	3	12
			7	Particle prevents sealing.	5	Environmental Particle Test (ENV - 22)	7	245	Develop new test to evaluate particle generation.	R. Lopez 8/1/05	New test procedure DOC 4977	7	2	2	28
			7	Material loses resiliency.	2	Resiliency Test (MECH - 101)	2	28	None at this time.	B. Goode 7/21/05	None	7	2	2	28
			7	Material cracks/breaks.	4	Fatigue Test (MECH - 104)	2	56	Conduct Designed Experiment on new resin formulation.	B. Goode 7/21/05	Material change DOC 3784	7	3	2	24

Hazard Analysis

Hazard Analysis is another popular risk assessment/risk mitigation tool. This is a top-down approach to risk management. Typically a failure is assumed at the system (or highest level) and then traced down to the sub-system or component level. As appropriate, actions to reduce risk are taken and documented. A brief example of a hazard analysis for a hypothetical infusion pump:

ID	Hazard Type
1	No flow of medication to patient
2	Free flow of all medications
3	incorrect amount of medication
4	Incorrect ratio of medications
5	Wrong medication

Likelihood of Occurrence	Catastrophic	Significant	Marginal	Trivial
highly				
moderate	hazard 2			
remote	hazard 3	hazard 5		
improbable	hazard 4	hazard 1		

The above table can provide guidance to the design team in terms of prioritization of which hazards to address first.

Robustness

Low-cost, rugged products are a goal for all designers. Not only do we want our products to provide their intended function under best-case conditions, but over a range of usage conditions as well. Robust design techniques are a special application of experimental design techniques. Using Robust design, the experimenter attempts to find settings for controllable variables where the outputs of interest are sufficiently insensitive to the influence of noise variables. Some typical examples of noise factors are:

- environmental temperature
- humidity
- air quality
- operator techniques
- part variation

The overall theme of Robustness popularized by an engineer named Taguchi is to strive to design robust or rugged products in a low-cost, timely mode. Properly applied these approaches can lead to significant market place advantage.

Suppose a medical device injection molder wanted to have a process that was robust to cavity number changes. Here is an example of the designed experiment they might run. Notice there is an inner orthogonal array and an outer array for cavity number.

DOE Wisdom Work Sheet

			Run	1	2
			Cavity	1	2
Run	Mold Temp	Melt Temp	Fill Time	Diameter	Diameter
1	160	375	3.7		
2	160	405	2.2		
3	160	425	0.7		
4	180	375	2.2		
5	180	405	0.7		
6	180	425	3.7		
7	200	375	0.7		
8	200	405	3.7		
9	200	425	2.2		

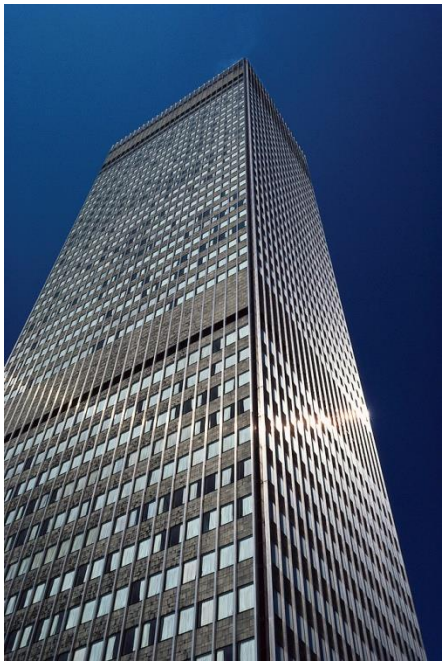
Software Validation

More and more systems, test equipment, and products have a software element. It is essential for designers to demonstrate that the software is doing its job (without error). The FDA has guidance documents on software validation.
http://www.fda.gov/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm085281.htm

Design verification and validation

Design Validation means establishing by objective evidence that device specifications conform to user needs and intended use(s**).** Verification means confirmation by examination and provision of objective evidence that specified requirements have been fulfilled.

The FDA provides an excellent example what Design verification and validation imply in the following:



To illustrate the concepts, consider a building design analogy. In a typical scenario, the senior architect establishes the design input requirements and sketches the general appearance and construction of the building, but associates or contractors typically elaborate the details of the various mechanical systems. Verification is the process of checking at each stage whether the output conforms to requirements for that stage. For example: does the air conditioning system deliver the specified cooling capacity to each room? Is the roof rated to withstand so many newtons per square meter of wind loading? Is a fire alarm located within 50 meters of each location in the building?

At the same time, the architect has to keep in mind the broader question of whether the results are consistent with the ultimate user requirements. Does the air conditioning system keep the occupants comfortable throughout the building? Will the roof withstand weather extremes expected at the building site? Can the fire alarm be heard throughout the building? The broader concerns are the essence of validation.

Select Process solution concepts

Depending upon the uniqueness of the proposed manufacturing process, process concept selection can be considered. Similar tools used in Design Concept selection are used in this phase.

Detailed process map (Identify key parameters/specification)

Process mapping can be conducted at several levels dependent upon the teams needs. Process mapping is a useful tool for teams to use to help visualize the process and identify key inputs, outputs, and parameter set points. Many teams use these approaches as an early step in process validation.

Process FMEA

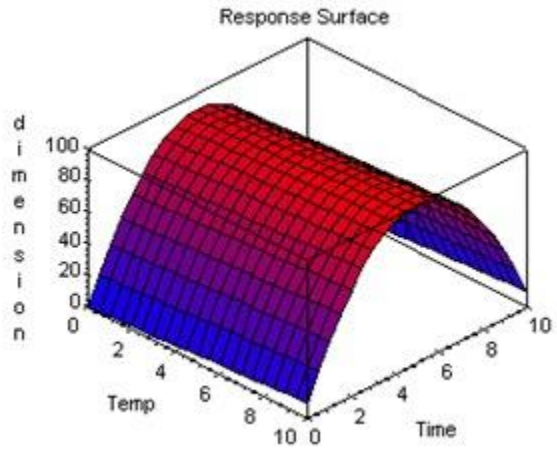
Earlier in this chapter, we discussed a Product FMEA. The Product FMEA focuses on the "product". Process FMEA focuses on the process…..not the product. The focus is on risk identification, risk assessment and risk reductions

Potential Failure Mode	Potential Effects of Failure	SEV	Causes of Failure	OCC	Current Process Controls	DET	RPN	Recommended Actions	Responsibility and Target Completion Dates	Action Results				
										Actions Taken	SEV	OCC	DET	RPN
tensile strength of bond below spec.	detachment of ZZZ in-vivo, distal portion left in patient	9	Laser parameters set incorectly	1	Operator training	2	18	none						
					SPC on process on tensile strength	4	36	none						
					100% NDT test	1	9	none						

Process Optimization experiments

Popular tools to support this objective include mathematical, multi-variable design of experiments. Controlled studies typically consist of two or more independent variables (factors) at more than two levels. One or more responses can be studied for each family of experiments. Thanks to popular software using desirability functions, acceptable trade-offs of multiple outputs can be achieved.

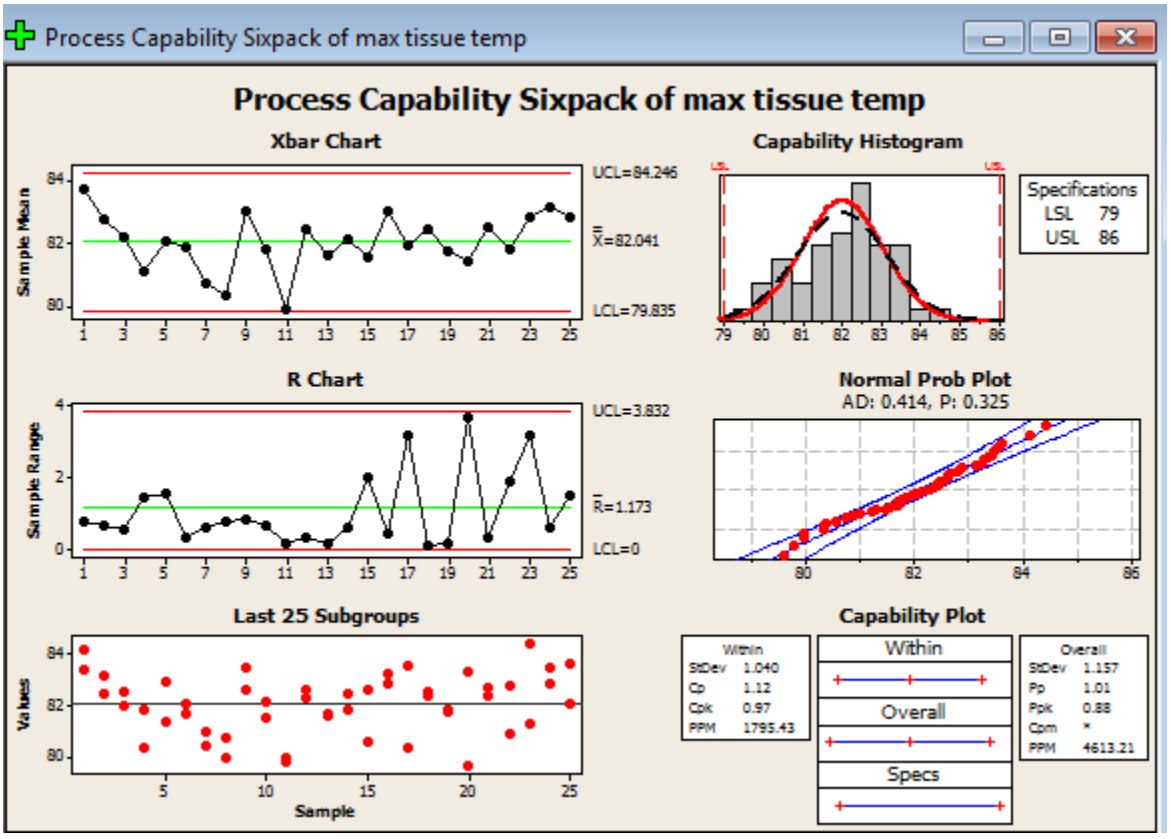
Design of experiments allows you to generate a model of your process. Here is an example of a response surface graph from a medical device experiment.



Preliminary process capabilities

We want to demonstrate with valid data that our manufacturing processes are capable of consistently meeting pre-determined specifications. Since these studies are typically not completed under high volume conditions, we use the term preliminary to reflect the fact that the data may only represent what will happen under short-term conditions. Control charts and data analysis techniques are used to support this determination.

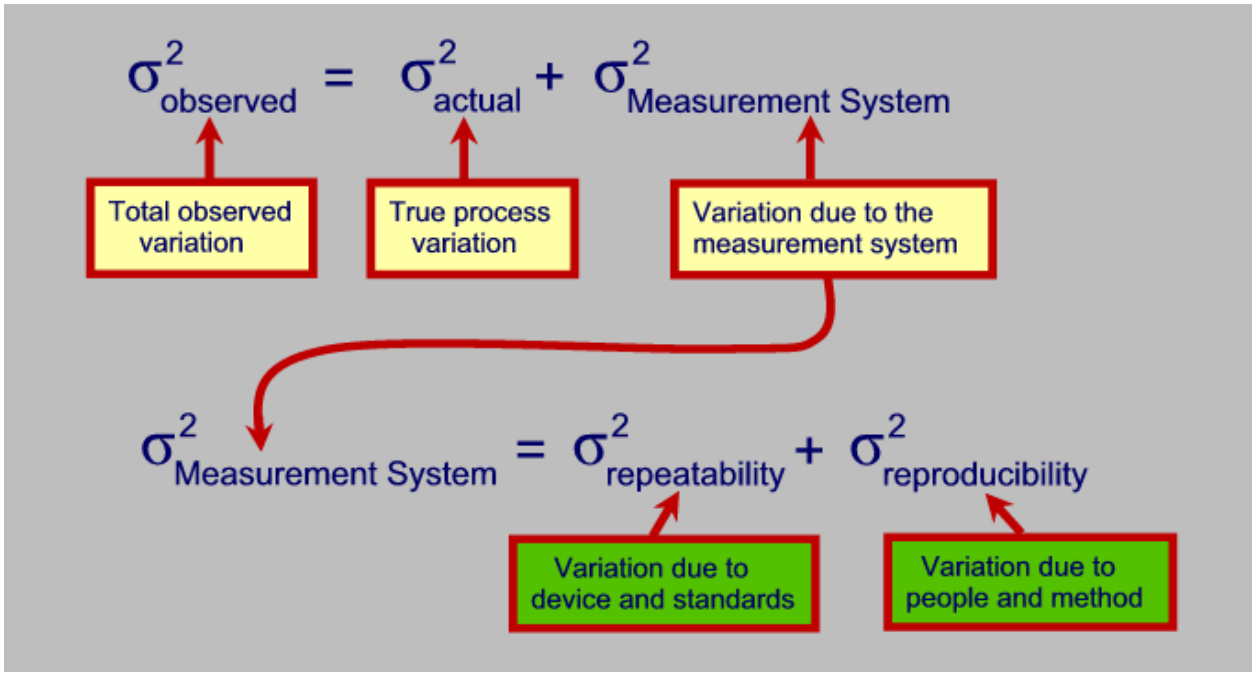
Here is an example of a typical control chart and resultant data that might be generated during this phase:



Output from Version 16 of Minitab Software

Measurement System Analysis

Measurement System Analysis (MSA) is a tool used to demonstrate that our measurement devices are generating reliable data. Many decisions will be based on data generated by various measurement devices. It is extremely important to understand the uncertainty of the measurement system. Years of industrial experience suggest this is an essential first step before taking variable or attributes data. Major software packages support the set-up and analysis of these types of studies.



Manufacturing Control Plan

A control plan typically manifests itself as an Excel spread sheet. The first column identifies the process steps in a sequential manner. Additional columns are relegated to identification of key process step input and output variables, sampling considerations for key variables, and process controls (inspections, sampling plans) as well as data analysis approaches. The Control Plan takes into consideration all activities to ensure compliance to acceptance criteria and specifications.

Process step	Process step	Machine/ device	Characteristic	Specification
1	Receiving of Ti bars		Material cert	alloy grade
		XXXX	Length	5.0 +/- .005
		FFFFF	Diameter	2.0 +/- .004

Need for Lean!

We cannot over stress the need for a lean, optimized, low-cost, low-risk manufacturing processes before you embark upon process validation or verification. The theme in the organization needs to be:

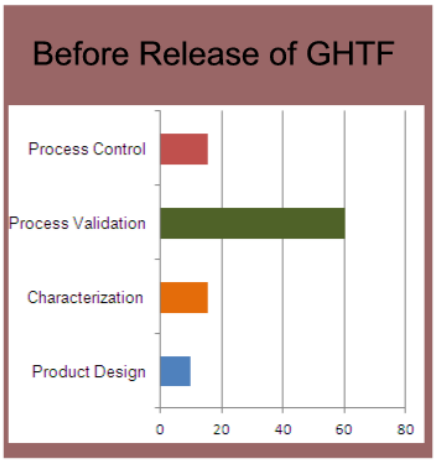
- develop a detailed knowledge of the equipment and process (characterize the equipment and process)
- conduct the validation activities….should be a snap if the upfront activity has been completed
- control the production process
- revalidate as required in your plan.

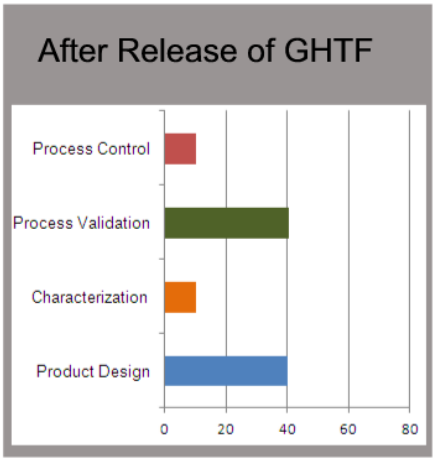
Our experience with some medical device companies and suppliers is that process validation is almost an afterthought for companies. At the last minute or based upon an audit or new focus from a customer, there is a realization that there is an immediate need for validation activity. In the rush some forget to perform the necessary planning, equipment characterization, and process characterization work that is essential to fast, low-cost, low-stress validation activity. Poor planning and inadequate pre-validation activities could lead to overlooked parameters that influence the processes. As a result defective products are shipped and everybody wonders how this happened since the process is validated.

If the upfront work has been completed, process validations can be done with few false starts. Without the preceding, it can be a very time consuming and frustrating experience for the organization. There is another issue with packing everything into process validation. A validation protocol is typically reviewable by the FDA. It is therefore highly advisable to have a good understanding of the process and to have a high level of confidence that the process validation will pass. This high level of confidence is only attainable by diligent upfront characterization and testing.

Where We Need to Be

The first two graphs on the left illustrate the amount of resources companies have historically dedicated to the various phases before and after the release of the GHTF guideline document on design controls. The last graph shows where companies need to be in the future.





If the company has done their work upfront regarding Product Design and Characterization, then process validation will be “a piece of cake”.

The above graphic does not mean that process validation is unimportant. It suggests that if we have done great things from a product design and characterization standpoint, process validation should be very straight forward and simple for us to demonstrate. Importantly, we are not done after process validation. Process control and process monitoring are huge and require continuous focus to ensure process integrity.

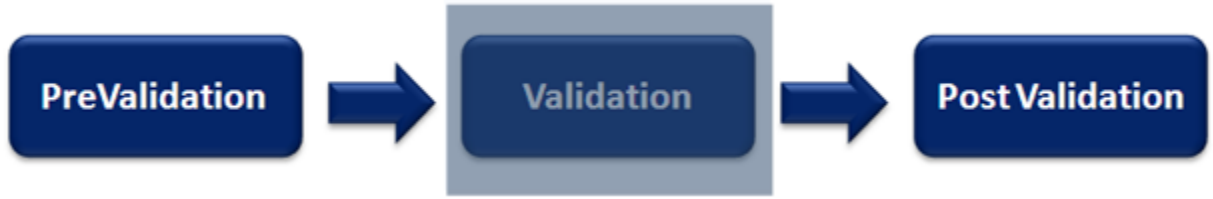
Summary

In this chapter you were introduced to a three phase approach to effective process validations: Pre-validation, validation, and post validation. As pointed out in this chapter, a host of good work needs to be wisely completed in the pre-validation phase. We briefly introduced you to a number of powerful tools that, when combined with great market research and design activity, can be of huge benefit to smooth sailing through the validation and post-validation phases.

Chapter 3 – IQ, OQ, PQ – Breaking Through the Confusion

Straight Talk on IQ, OQ and PQ

The previous chapter discusses all the issues that need to be addressed before beginning the actual process validation. Now that those items are completed, it is time to start the process validation. This chapter will address the Validation section of the flow chart shown below:



Installation Qualification, Operational Qualification and Performance Qualification are the foundation of process validation. Just like building a new home, this foundation is the key to a successful process validation effort. There is good news, though. It really doesn't have to be a mystery. Let's first take a "30,000 foot" view of process validation.

Consider the waffle maker shown below.

You are assigned the task of performing a validation on this waffle iron. The first question you must ask yourself is, "Is the waffle iron (equipment) installed correctly? This is essentially what Installation Qualification addresses.

Is it plugged in correctly?

Is the temperature correct?

Is the time correct?

The next thing to consider is “Can we make a good product at best settings? Can we make a good product at extreme conditions?” This is Operational Qualification.

Finally, we need to perform Performance Qualification: “Can we make numerous products under production settings?”





It really is as simple as that. As you get into the documentation surrounding Installation Qualification, Operational Qualification and Performance Qualification, be sure and go back periodically and as yourself the basic question(s) associated with each. If you get confused during Installation Qualification regarding what exactly needs to be done, STOP and ask yourself what exactly you are trying to accomplish? You are trying to answer the question, “Is the equipment installed correctly?” Don’t make it more difficult than it needs to be.

Simple example – Getting Started with Process Validation

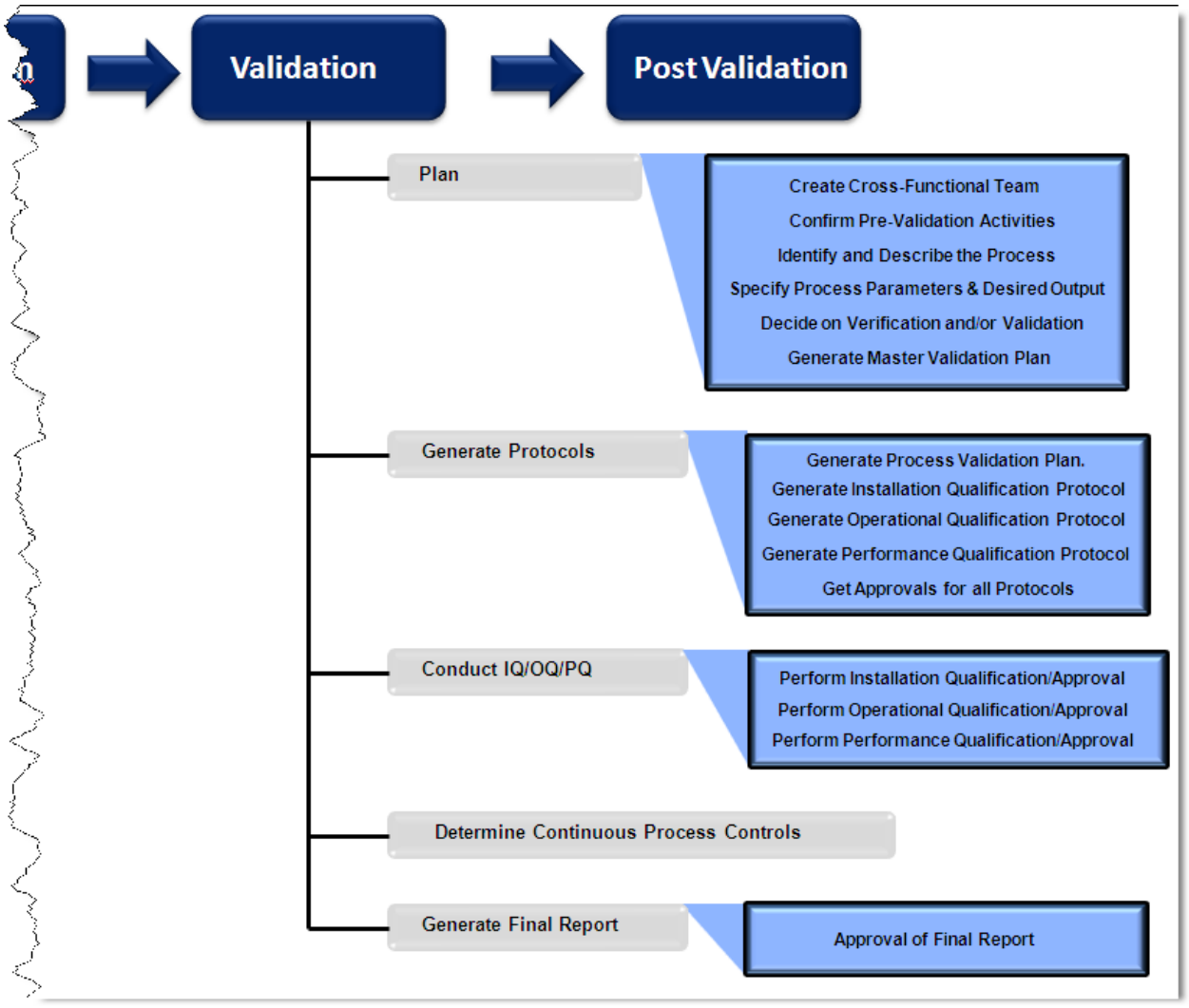
Of course the FDA wants more than a “30,000 foot” view. They want an upfront and personal view of your process validation efforts. But what exactly are they expecting to see? Appendix B of the Global Harmonization Task Force, Quality Management Systems – Process Validation

Guidance (http://www.ghtf.org/documents/sg3/sg3_fd_n99-10_edition2.pdf) document lists a general format that you may follow.

Our experience suggests some companies have a hard time getting started with process validation. In what follows we will work through a conceptual example with a simple device to demonstrate at a couple of levels what needs to be done.

As an example, suppose our task is to validate a waffle making process. We will demonstrate the key process validation stages with a waffle Iron commonly used in hotels in North America. The process in question makes use of the *Professional Belgian Waffle Iron* by Waring.

The following flow chart shows the steps for process validation:

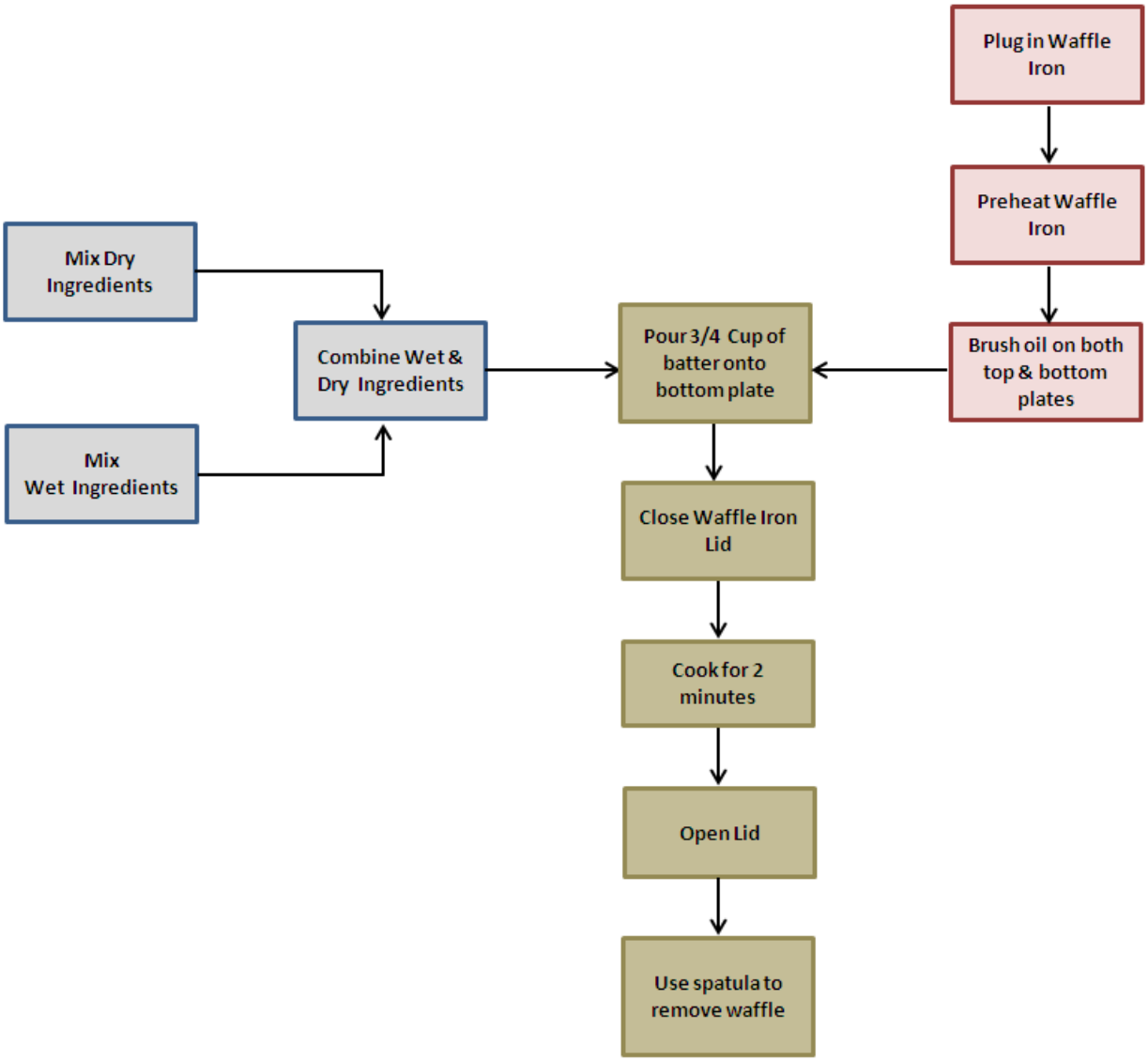


Planning Phase

Create Cross-Functional Team - First we would define a cross-functional validation team consisting of internal company experts responsible for the process.

Confirm Pre-Validation Activities - For the Waffle Iron, the company has already conducted a number of pre-validation activities. All of these activities have been documented.

Identify and Describe the Process – A Process Flowchart will be created to help visualize the process. The flowchart shows the separate steps of the process and the key process inputs and key process outputs for each step. Below is a flow chart for our waffle example.



Specify process parameters and desired output – The purpose of this step is to ensure that customer requirements and technical requirements are fully understood, documented, and translated into key process characteristics. The following form shows some of the steps for the Waffle example.

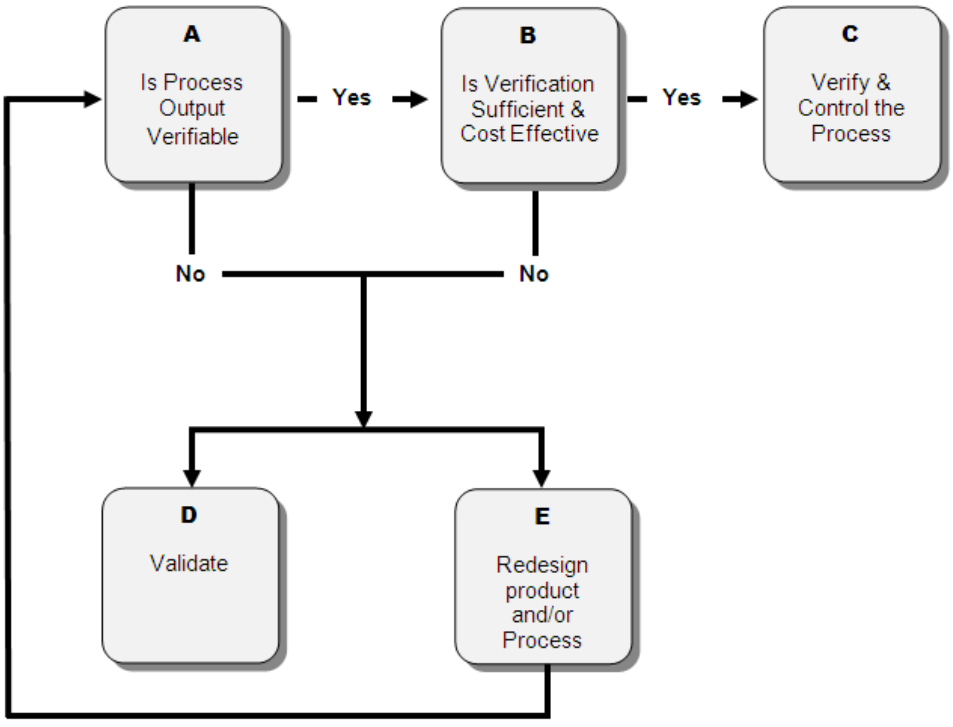
Process Parameters and Desired Outputs

Process Validation Protocol Number: PV8752X | Date: January 31, 2012

Prepared By: Robert G. Launsby | Approved By: J. Torell, B. Walker, S. Taylor, G. Greene, K. Long, V. Barker

Process Step	Process Name	Process Element	SOP	Characteristic	Specification
1	Dry Ingredient Prep	Flour	SOP563D	Mixability Ratio	98 +/- 0.5%
		Salt			
		Sugar			
		Baking Powder			
2	Wet Ingredient Prep	Eggs	SOP563W	Viscosity	101 +/- 3 poise
		Milk			
		Vanilla			
		Oil			
3	Batter Preparation	Dry & Wet Ingredients	SOP563B	Color	20-34 mm (per Pfund Grader)
				Viscosity	300 +/- 5 poise
4	Waffle Iron Prep	Heating	SOP588H	Temperature	250 +/- 3 degrees F

Decide on verification and/or validation – The following model is taken directly from "GHTF Quality Management Systems – Process Validation Guidance" document, Edition 2 – January 2004. The model describes a decision tree that a company can follow when deciding on whether a process needs to be validated. The process under consideration in this model is the simplest possible – many processes may be large and/or a complex set of sub-processes.



Generate Master Validation Plan - Next the team would put in place a Master Validation Plan which delineates whether we would qualify [operator, raw material (batter)], verify, or validate (the actual waffle making process) an element of the process. The Master Validation Plan (MVP) serves as a planning tool for Installation Qualification, Operational Qualification and Performance Qualification work as well as a record of completed process validation activities. Below is an example of the Master Validation Plan for the Waffle example.

Master Validation Plan

				Process Validation Protocol Number: PV8752X		Date: January 31, 2012		
				Prepared By: Robert G. Launsby		Approved By: B. Walker, S. Taylor, G. Greene, K Long, V. Barker		
Process Step	Process Name	Process Element	Characteristic	Validation - Yes/No (If yes, enter qualification type - IQ,OQ,PQ. If no, enter rationale)	Who is Responsible?	Target Start Date	Target Completion Date	Software Validation Completed
1	Dry Prep	Flour	Mixability Ratio	Yes/OQ,PQ	J. Torell	2/7/2012	2/21/2012	N/A
		Salt						
		Sugar						
		Baking Powder						
2	Wet Prep	Eggs	Viscosity	Yes/OQ,PQ	K. Long	2/7/2012	2/21/2012	N/A
		Milk						
		Vanilla						
		Oil						
3	Batter Prep	Dry & Wet Mix	Color	Yes/OQ,PQ	G. Greene	2/21/2012	3/9/2012	N/A
			Viscosity	Yes/OQ,PQ	G. Greene	2/21/2012	3/9/2012	N/A
4	Waffle Iron Prep	Heating	Temperature	Yes/IQ,OQ, PQ	V. Barker	2/7/2012	3/9/2012	N/A

Protocol Phase

An overall Process Validation Plan will be generated and approved before initiating any validation activities. This plan will describe the protocols for all three phases (Installation Qualification, Operational Qualification and Process Qualification. The Process Validation Plan differs from the Master Validation Plan in that it gives specifics regarding aspects of the process validation effort.

Following is a flow chart describing the activities associated with this phase of the process validation effort.

Process Validation Plan Activities

The next few pages are the Process Validation Plan for the Waffle Iron example. This is one of many formats that could be used for this document. Your process may lend itself to a different format.

Process Validation Plan
Title: Larson Hotel Waffle Making Process

Document Number: PV8752X
Document File Name: Waffle 7645

Revision Level	Revision Date	DCO/ECO Number	Description of Revision	Revision Author
0	1/31/2012	10477	New procedure to implement Process Validation Plan	Robert Launsby

Role	Approval Name	Signature	Date
Author			
Quality Manager			
Engineering Program Manager			
Manufacturing Engineering Manager			

1. **Products to be covered**
   1.1 Belgian Waffle formulation 21-0501
2. **Equipment/Process to be Validated**
   2.1 The scope of this protocol is to evaluate the Waffle Iron model WMK300a
3. **Objective**
   3.1 Customer requirement is to produce a visually appealing and tasty waffle in a short amount of time using the Waring Professional waffle iron. The process to be validated consists of an operator loading the iron with a predetermined amount of batter (formulation 21-0501), creating the waffle using the standard operating procedure (SOP #578) then removing the finished waffle from the device. Key outputs from the process are waffle appearance (quality standard #2011 AQW). Process capability is planned to be Cpk of 1.33 or better.
4. **Reference Documents**
   4.1 Standard Operating Procedure for Dry Ingredient Preparation, SOP563D
   4.2 Standard Operating Procedure for Wet Ingredient Preparation, SOP563W
   4.3 Standard Operating Procedure for Batter Preparation, SOP563B
   4.4 Standard Operating Procedure for Waffle Iron Preparation, SOP588H
   4.5 Standard Operating Procedure for Waffle Baking, SOP578
   4.6 Process Validation Master Plan, PVP2011
   4.7 Statistical Methodologies, SOP435
   4.8 Maintenance Guide for Waring Waffle Iron, #FW M232

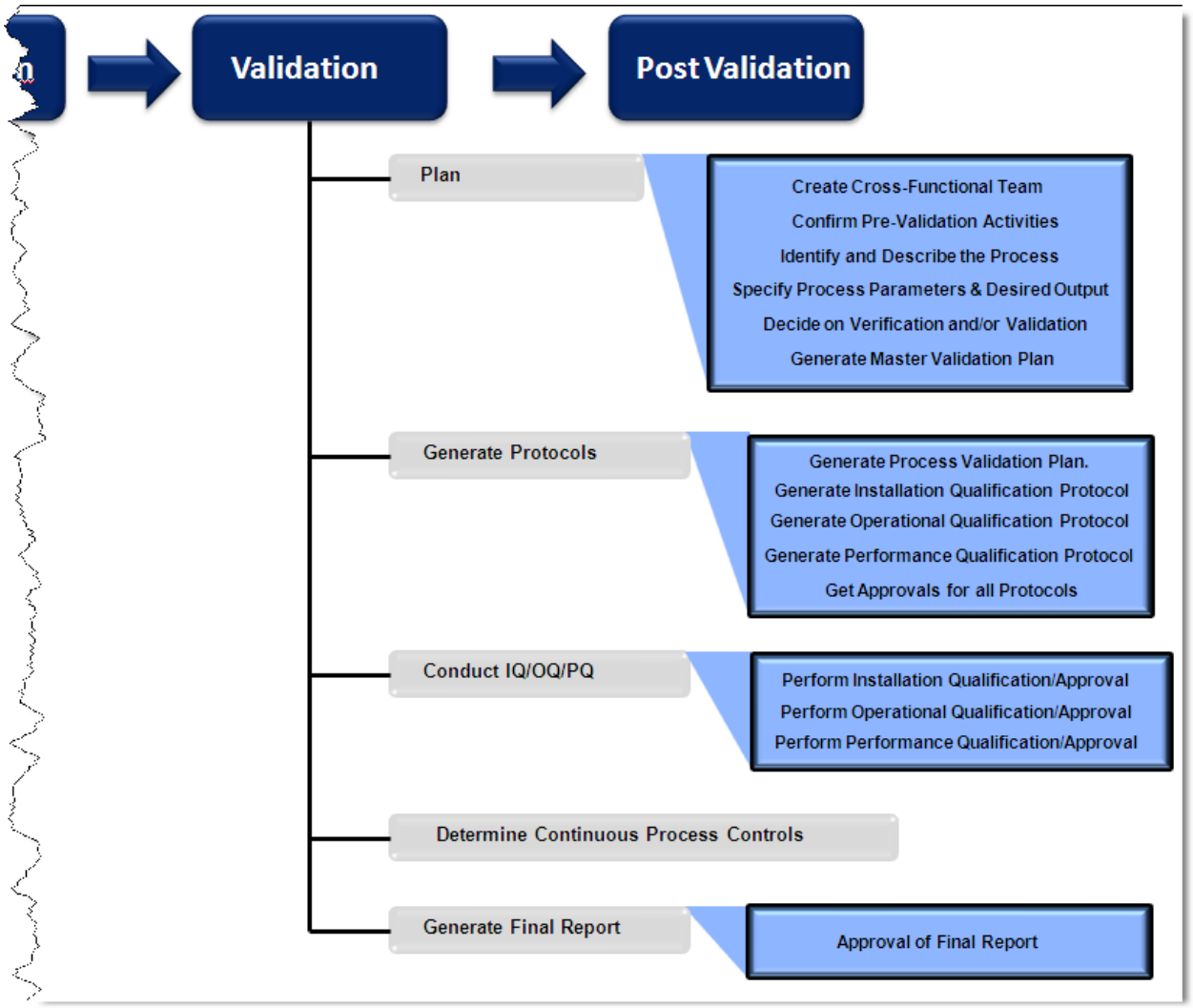
4.9 Incoming inspection plan for waffle formulation, #FM IM32
4.10 Quality lab book #QE09

5. Validation Plan
   5.1 Waring Waffle Iron model WMK300A will be subjected to the Installation Qualification, Operational Qualification, and Performance Qualification procedures outlined in the Master Validation Plan, PVP2011.
   5.2 The Installation Qualification will make use of the Waring Waffle Iron operation manual to define requirements for setup of the device. The waffle iron will be installed, checked, and calibrated before commencement of the Operational Qualification Plan. A checklist of requirements will be completed and results approved.
   5.3 The Dry Preparation, Wet Preparation, and Batter Preparation will be subjected to the Operational Qualification and Performance Qualification procedures outlined in the Master Validation Plan, PVP2011.
   5.4 Operational Qualification will be completed in two phases. In the first phase, optimal settings previously determined using Designed Experiments (Lab Book #QE09, pp21-56) will be used to demonstrate waffles of the right color can be made using this process. Fifty(50) waffles will be produced in order to demonstrate short term process capability. In the second phase of Operational Qualification, worse case process conditions will be tested to demonstrate sufficient process capability for waffle color under worse case conditions. Control charting techniques will be utilized to determine short-term process stability and Cpk will be calculated and reported. A Cpk of 1.33 (or better) will need to be achieved before commencement of the Performance Qualification phase.
   5.5 Performance Qualification will commence after satisfactory completion of Operational Qualification. Optimal settings for the waffle process will be used for this activity. Production personnel will be used to gather the data. Additionally, color will be measured and recorded. Values will be control charted to demonstrate adequate process stability. Data will be gathered over a one-week period. When the process is sufficiently stable and Cpk values of 1.33 (or better) have been achieved, the process will consider to be validated.
6. Measurement/Testing Equipment and Calibration
   6.1 Colorimeter Number 233
   6.2 Gage R&R Study for Colorimeter Number 233, GRR547
   6.3 Viscometer Number 475
   6.4 Gage R&R Study for Viscometer Number 475, GRR548
   6.5 Thermometer Number 215
   6.6 Gage R&R Study for Thermometer Number 215, GRR549
   6.7 Calibration/Maintenance Procedure for Colorimeter Number 233, CP209
   6.8 Calibration/Maintenance Procedure for Viscometer Number 475, CP210
   6.9 Calibration/Maintenance Procedure for Thermometer Number 215, CP212

7. Resource Requirements (Labor and Materials)
   7.1 It is estimated that 120 hours of manpower will be required to complete the Installation Qualification, the Operational Qualification, and the Performance Qualification.
   7.2 The following materials will be needed to complete the IQ, OQ, and PQ. NOTE: All materials will be sourced, qualified, and documented per company procedures.
       Flour
       Salt
       Sugar
       Baking Powder
       Eggs
       Milk
       Vanilla
       Oil
       Waffle Iron
       Measuring Cups
       Spatula
       Mixer
       Bowls
       Measuring Spoons
8. Responsibilities
   8.1 Dry Preparation OQ and PQ – J. Torell
   8.2 Wet Preparation OQ and PQ – K. Long
   8.3 Batter Preparation OQ and PQ – G. Greene
   8.4 Waffle Iron IQ, OQ and PQ – V. Barker
9. Safety Requirements
   9.1 All Qualifications will be completed following Safety Procedure SP544
10. Revalidation
    10.1 Revalidation must be considered anytime there are significant changes in formulation, equipment, processes or product characteristics.

Let's review the process validation steps we have covered so far. We have:

- Created a Cross-Functional Team
- Confirmed pre-Validation Activities
- Identified and Described the Process
- Specified process Parameters and Desired Output
- Decided on Verification and/or Validation
- Generated a Master Validation Plan
- Generated a Process Validation Plan



It is now time to generate the IQ, OQ and PQ Protocols.

Installation Qualification Protocol

The purpose of Installation Qualification is to demonstrate and document that the equipment is installed correctly and will perform as intended. Following is the IQ for the Waffle Iron example.

The following requirements were established from the Waring maintenance guide (FW M232) and Waring Operations Manual (SOP588H).

Requirement	Acceptance Criteria	Actual	Pass/Fail
Leveling of device	<0.8 degrees		
Line voltage	120 ± 3 VAC		
Functional Pre-heat Light	Must see red light during pre-heat		
Preheat time	4 ± 0.2 minutes		
Beeps at end of Preheat	6 beeps		
Preheat end Light	Must turn green at end of pre-heat		
Control Setting	location 4 (Temperature = 250 ± 3ºF)		
Cook completion sound	3 beeps		

4.0 Equipment Maintenance Plan

Document Title	Document Number	Document Location	Verification Date/Initials
Maintenance Guide for Waring Waffle Iron	FW M232		

5.0 Spare Parts List

Part Number	Description	Location	Verification Date/Initials
WB789214	Leveling bubble		
WSP85429	Pre-heat light		
WSK76591	Control Setting knob		

6.0 Calibrated Instrument List

Instrument Number	Instrument Description	Next Calibration Due Date	Instrument within calibration at time of qualification? Y/N	Check Performed by: Initials/Date
C42301	Digital Leveling Device	3/1/12		
C76540	Thermometer	3/1/12		
C86522	Viscometer	2/23/12		
C98303	Colorimeter	2/29/12		

7.0 Report Conclusion

Report Conclusion

Operational Qualification Protocol

The purpose of Operational Qualification is to establish confidence that the process is effective and reproducible over the process parameter range. Process parameters will be challenged to ensure that they will result in a product that meets all defined requirements under all anticipated worst case conditions of manufacturing. Following is Phase 1 OQ for the Waffle Iron example.

Operational Qualification Protocol (Phase 1 – Nominal Settings)
Title: Larson Hotel Waffle Making Process

Document Number: OQ8752X
Document File Name: Waffle 7645OQ

Role	Name	Pre-Approval Signature	Date	Final Approval Signature	Date
Research and Development					
Manufacturing Engineering					
Quality Engineering					
Manufacturing					
Regulatory					
Marketing					

1.0 Validation Purpose

The purpose of this protocol is to document the studies done to establish confidence that the process is effective and reproducible under nominal conditions.

2.0 Procedure

A designed experiment was previously conducted to determine the optimal settings for the waffle iron (see controlled lab book #QE09 for details). The customer requirement is to hit a color score of 6.0 ± 1.0 with a Cpk of 1.33 or greater. 50 consecutive waffles will be generated at the previously defined optimal conditions for the waffle iron.

3.0 Set-up Conditions

Parameter	Setting	Performed by: Initials/Date	Comments
Batter Amount	**¾ Cup**		
Waffle Iron Control Knob Setting	**4**		
Time	**190 seconds**		

4.0 Process Output Requirements

Characteristic	Acceptance Criteria	Actual	Pass/Fail	Measurement Method	Sample size	Performed by: Initials/Date
Color Rating	6.0 ± 1.0					

5.0 Associated Graphs

Graphs associated with the analysis of data generated during this procedure are shown in the table below.

Associated Graphs

6.0 Report Conclusion

Report Conclusion

Following is Phase 2 OQ for the Waffle Iron example.

Operational Qualification Protocol (Phase 2 – Worst Case Settings)
Title: Larson Hotel Waffle Making Process

Document Number: OQW8752X
Document File Name: Waffle 7645OQWC

Role	Name	Pre-Approval Signature	Date	Final Approval Signature	Date
Research and Development					
Manufacturing Engineering					
Quality Engineering					
Manufacturing					
Regulatory					
Marketing					

1.0 Validation Purpose

The purpose of this protocol is to document the studies done to establish confidence that the process is effective and reproducible under anticipated worst case conditions of manufacturing.

2.0 Procedure

Characterization studies were previously completed and indicated that the worst case conditions consist when the batter amount is less than ½ cup or greater than 1 cup. (see controlled lab book #QE09 for details). The customer requirement is to hit a color score of 6.0 ± 1.0 with a Cpk of 1.33 or greater. 25 consecutive waffles will be generated using ½ cup of batter and 25 waffles will be generated using 1 cup of batter.

3.0 Set-up Conditions

Parameter	Setting	Performed by: Initials/Date	Comments
Batter Amount	½ Cup		
Batter Amount	1 Cup		
Control Knob Setting	4		
Time	190 seconds		

4.0 Process Output Requirements

Characteristic	Acceptance Criteria	Actual	Pass/Fail	Measurement Method	Sample size	Performed by: Initials/Date
Color Rating	6.0 ± 1.0					

5.0 Associated Graphs

Graphs associated with the analysis of data generated during this procedure are shown in the table below.

Associated Graphs

6.0 Report Conclusion

Report Conclusion

Performance Qualification Protocol

The purpose of Performance Qualification is to demonstrate that the process will consistently produce acceptable product under normal operating conditions. Challenges to the process will simulate conditions that will be encountered during actual manufacturing. Following is the PQ for our waffle making process.

Performance Qualification Protocol
Title: Larson Hotel Waffle Making Process

Document Number: PQ8752X

Document File Name: Waffle 7645PQ

Role	Name	Pre-Approval Signature	Date	Final Approval Signature	Date
Research and Development					
Manufacturing Engineering					
Quality Engineering					
Manufacturing					
Regulatory					
Marketing					

1.0 Validation Purpose

The purpose of this protocol is to demonstrate that the waffle making process will consistently produce acceptable product under normal operating conditions.

2.0 Procedure

Production lots will be run under standard production conditions for a one week period.

3.0 Set-up Conditions

Parameter	Setting	Performed by: Initials/Date	Comments
Batter Amount	¾ Cup		
Control Knob Setting	4		
Time	190 seconds		

4.0 Process Output Requirements

Run or Batch #	Characteristic	Acceptance Criteria	Actual	Pass/ Fail	Measurement Method	Sample size	Performed by: Initials/Date
	Color Rating	6.0 ± 1.0					

5.0 Associated Graphs

Graphs associated with the analysis of data generated during this procedure are shown in the table below.

Associated Graphs

6.0 Report Conclusion

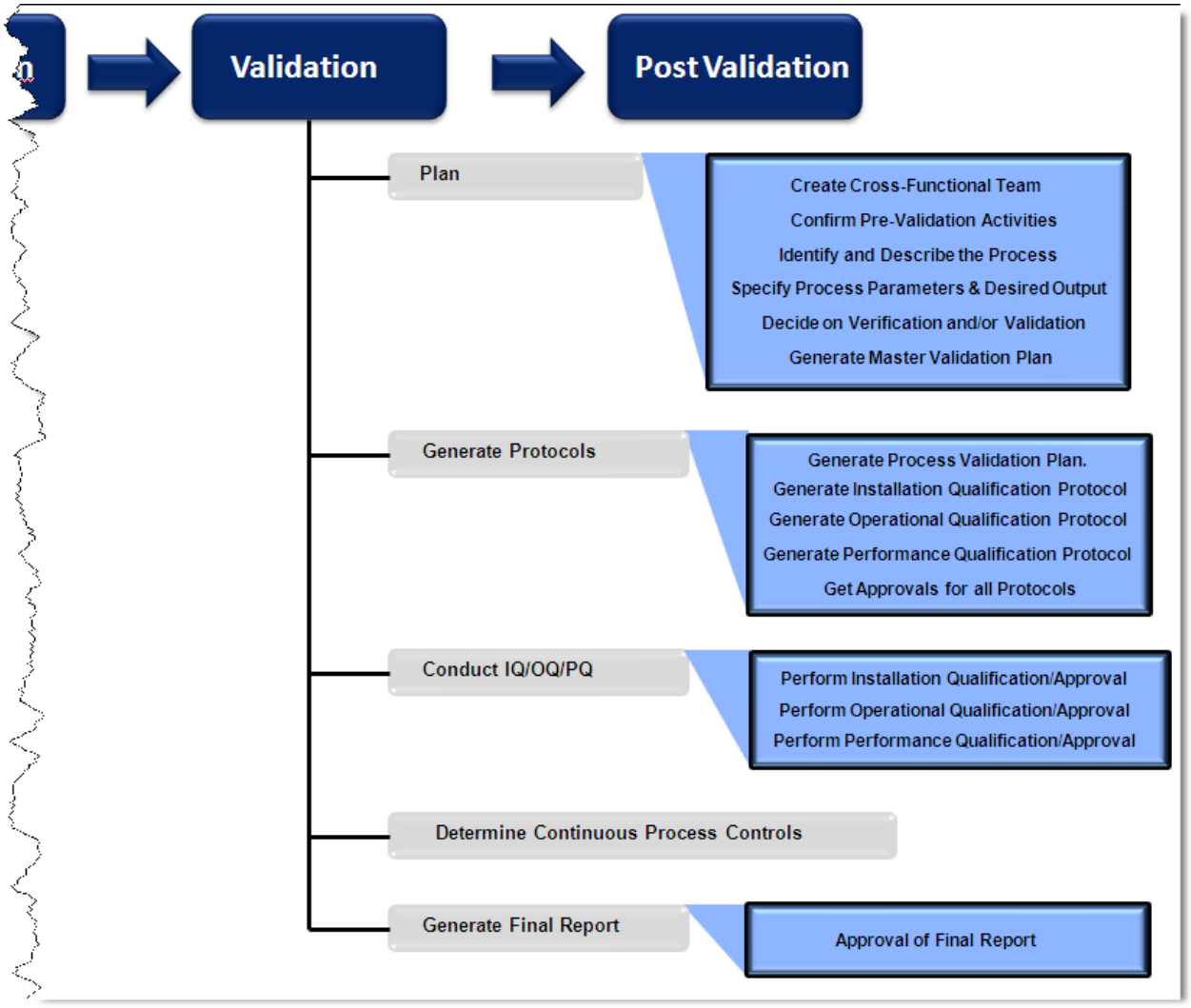
Report Conclusion

Conduct IQ, OQ, and PQ

Let's review the process validation steps we have covered so far. We have:

- Created a Cross-Functional Team
- Confirmed pre-Validation Activities
- Identified and Described the Process
- Specified process Parameters and Desired Output
- Decided on Verification and/or Validation
- Generated a Master Validation Plan
- Generated a Process Validation Plan

It is now time to conduct the Installation Qualification, Operational Qualification and Performance Qualification.



Installation Qualification will be performed first. The IQ protocol generated in the above section will be completed and signed off before performing the Operational Qualification.

Both phases of Operational Qualification will be completed, reviewed and signed off before Performance Qualification begins. Below is the completed Phase 1 Operational Qualification for the waffle example. Phase 2 would be completed in a similar manner.

Operational Qualification Protocol (Phase 1 – Nominal Settings)
Title: Larson Hotel Waffle Making Process

Document Number: OQ8752X
Document File Name: Waffle 7645OQ

Role	Name	Pre-Approval Signature	Date	Final Approval Signature	Date
Research and Development	Brian Taylor	Brian Taylor	2/3/12	Brian Taylor	3/1/12
Manufacturing Engineering	Sue Jones	Sue Jones	2/3/12	Sue Jones	3/1/12
Quality Engineering	Mary Curtis	Mary Curtis	2/3/12	Mary Curtis	3/1/12
Manufacturing	Bill Murphy	Bill Murphy	2/3/12	Bill Murphy	3/1/12
Regulatory	Greg Lawson	Greg Lawson	2/3/12	Greg Lawson	3/1/12
Marketing	Mike Gray	Mike Gray	2/3/12	Mike Gray	3/1/12

1.0 Validation Purpose

The purpose of this protocol is to document the studies done to establish confidence that the process is effective and reproducible under nominal conditions.

2.0 Procedure

A designed experiment was previously conducted to determine the optimal settings for the waffle iron (see controlled lab book #QE09 for details). The customer requirement is to hit a color score of 6.0 ± 1.0 with a Cpk of 1.33 or greater. 50 consecutive waffles will be generated at the previously defined optimal conditions for the waffle iron.

3.0 Set-up Conditions

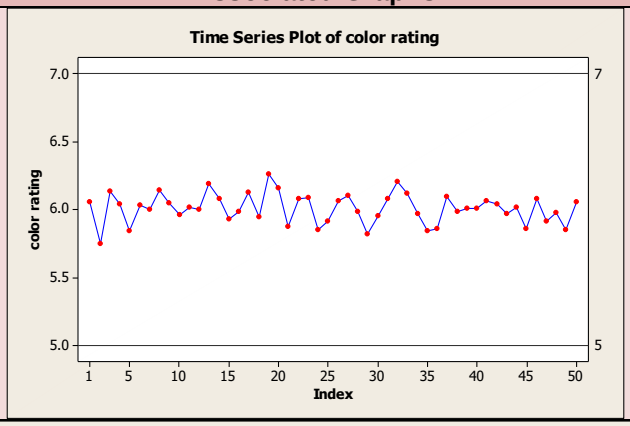
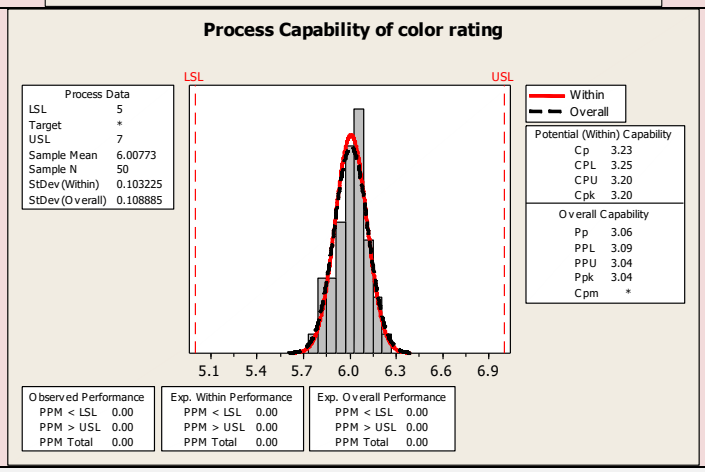
Parameter	Setting	Performed by: Initials/Date	Comments
Batter Amount	¾ Cup	S.Jones/SJ 2/8/12	
Waffle Iron Control Knob Setting	4	S. Jones/SJ 2/8/12	
Time	190 seconds	S. Jones/SJ 2/8/12	

4.0 Process Output Requirements

Characteristic	Acceptance Criteria	Actual	Pass/Fail	Measurement Method	Sample size	Performed by: Initials/Date
Color Rating	6.0 ± 1.0	6.0 ± 0.103	**Pass**	**MM4532**	**50**	**MDL/2/9/12**

5.0 Associated Graphs

Graphs associated with the analysis of data generated during this procedure are shown in the table below.

Associated Graphs



6.0 Report Conclusion

Report Conclusion
Under nominal conditions, the color rating for waffles was 6.0 +/- 0.103. The Cpk value for our 50 samples was 3.2. This value is greater than 1.33 and satisfies our Qualification requirements.

Once both phases of the OQ have been completed and signed off, the Performance Qualification can be completed and signed off.

Determine Continuous Process Controls

Continuous process controls are an integral part of the process validation effort. In order to ensure that the validated condition is maintained in the future, adequate process control and monitoring must be performed. Here is the Control Plan for the waffle example.

Control Plan

Control Plan Number: VR4572 | Date: 2/3/12
Revision: 0 | Approved By: B. Walker, S. Taylor, G. Greene, K. Long
Process Validation Protocol Number: PV8752X
Prepared By: Robert G. Launsby

Process Step	Characteristic	Specification LSL, USL & Target	Control Limits LCL & UCL	Measurement System	Sample Size	Sample Frequency	Control Method	Reaction Plan	Responsibility
1	Dry Ingredient Prep.	98 +/- 0.5%	97.8 - 98.2	Mixability Ratio	5	every 2 hours	CM354	RP3	S. Taylor
2	Wet Ingredient Prep.	101 +/- 3 poise	99 - 101	Viscometer	5	every 2 hours	CM355	RP5	S. Taylor
3	Batter Prep (color)	27 +/- 7 mm	25 - 29	Pfund Grader	5	every shift	CM 422	RP9	K. Long
	Batter Prep (viscosity)	300 +/- 5 poise	298 - 302	Viscometer	5	every shift	CM313	RP4	K. Long

Generate Final Report/Approve Final Report

At the end of the process validation, a completion report shall be written to summarize all validation activities and a conclusion of all validation efforts. Here is the report for the waffle example.

Final Process Validation Report
Title: Larson Hotel Waffle Making Process

Document Number: FR8752X
Document File Name: Waffle 7645FR

Role	Name	Final Approval Signature	Date
Research and Development	Brian Taylor	Brian Taylor	3/9/12
Manufacturing Engineering	Sue Jones	Sue Jones	3/9/12
Quality Engineering	Mary Curtis	Mary Curtis	3/9/12
Manufacturing	Bill Murphy	Bill Murphy	3/9/12
Regulatory	Greg Lawson	Greg Lawson	3/9/12
Marketing	Mike Gray	Mike Gray	3/9/12

1.0 Scope

This report covers the Larson Hotel Waffle Making Process.

2.0 Summary

Installation Qualification, Operational Qualification and Performance Qualification protocols were all completed and signed off. No issues with the waffle process were identified. The process appears to be able to produce waffles at an acceptable level at optimal (normal operating conditions) as well as worst case conditions. Appropriate controls have been implemented to ensure that all quality performance parameters will remain within specification.

3.0 Revalidation

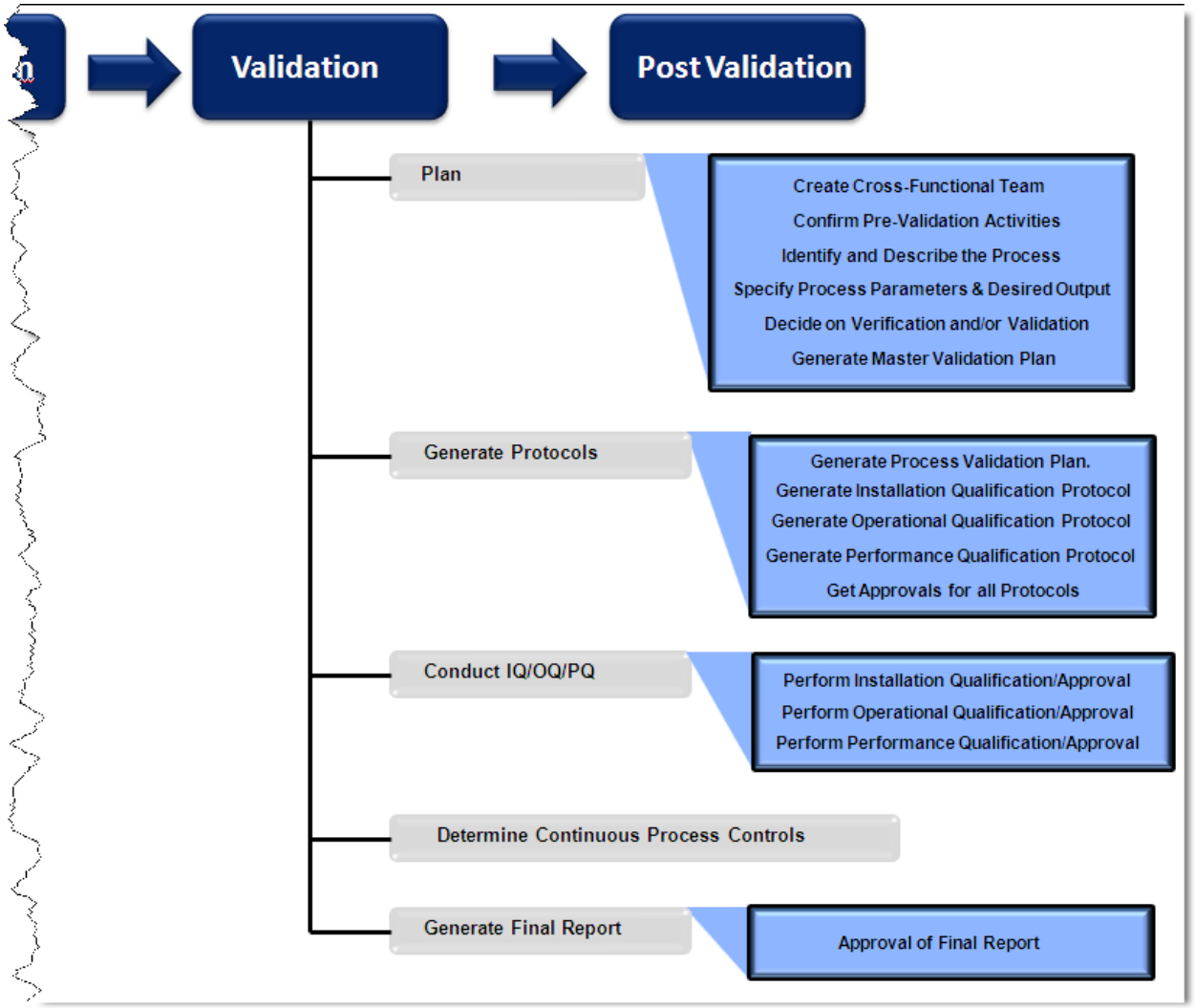
Revalidation must be considered anytime there are significant changes in the formulation, equipment or processes associated with the Waffle Making process. Negative trends in quality indicators, transfer of the process from one facility to another or any change in suppliers would initiate a revalidation of the process.

4.0 Conclusion

The Larson Hotel Waffle Making Process has been successfully validated.

Summary

This chapter discussed the Validation portion of the flow chart shown below.



In this chapter we made use of a simple waffle making process to demonstrate the different process validation steps. Initially, we looked at process validation at a high level, then at a more detailed level. We used an increasingly popular approach based upon an example from GHTF, appendix B. It is important to understand this is only one approach to structuring a process validation effort. Other approaches can be acceptable as well.

Chapter 4 – Post-Validation Considerations

You have accomplished a lot! Your organization designed a product and an applicable manufacturing process. The design has been validated. You likely conducted Robust Design and Modeling experiments to better understand product and process variables while enhancing cost effective customer driven performance. You conducted product and process risk assessments and took proactive step to document and mitigate risk. Using your Master Validation Plan (MVP) your team has likely conducted numerous verification, certification, process validation, and software validation activities. It was a great deal of work but you learned a great deal about process drivers and essential variables that need monitoring and control over the production life of the process. You feel great about the fact that you have real confidence in documenting and mitigation of risk to the customer. But there is more to do!

This chapter will discuss Post Validation considerations.

Your process validation team will likely be bombarded with changes over the manufacturing life of the product. Regardless of whether you validated or 100% verified a particular process step you still need to perform process monitoring and control. In addition, if you have validated a process, the team needs to consider when revalidation is needed. For some processes it is likely you will consider revalidation on a scheduled basis. For others you will need to reconsider re-validation on a case by case basis as changes to the process emerge. In this chapter, we will first discuss on-going process monitoring and control and then re-validation of processes.

What the FDA Has to Say.
Regarding validated processes, the following FDA quotation is appropriate:

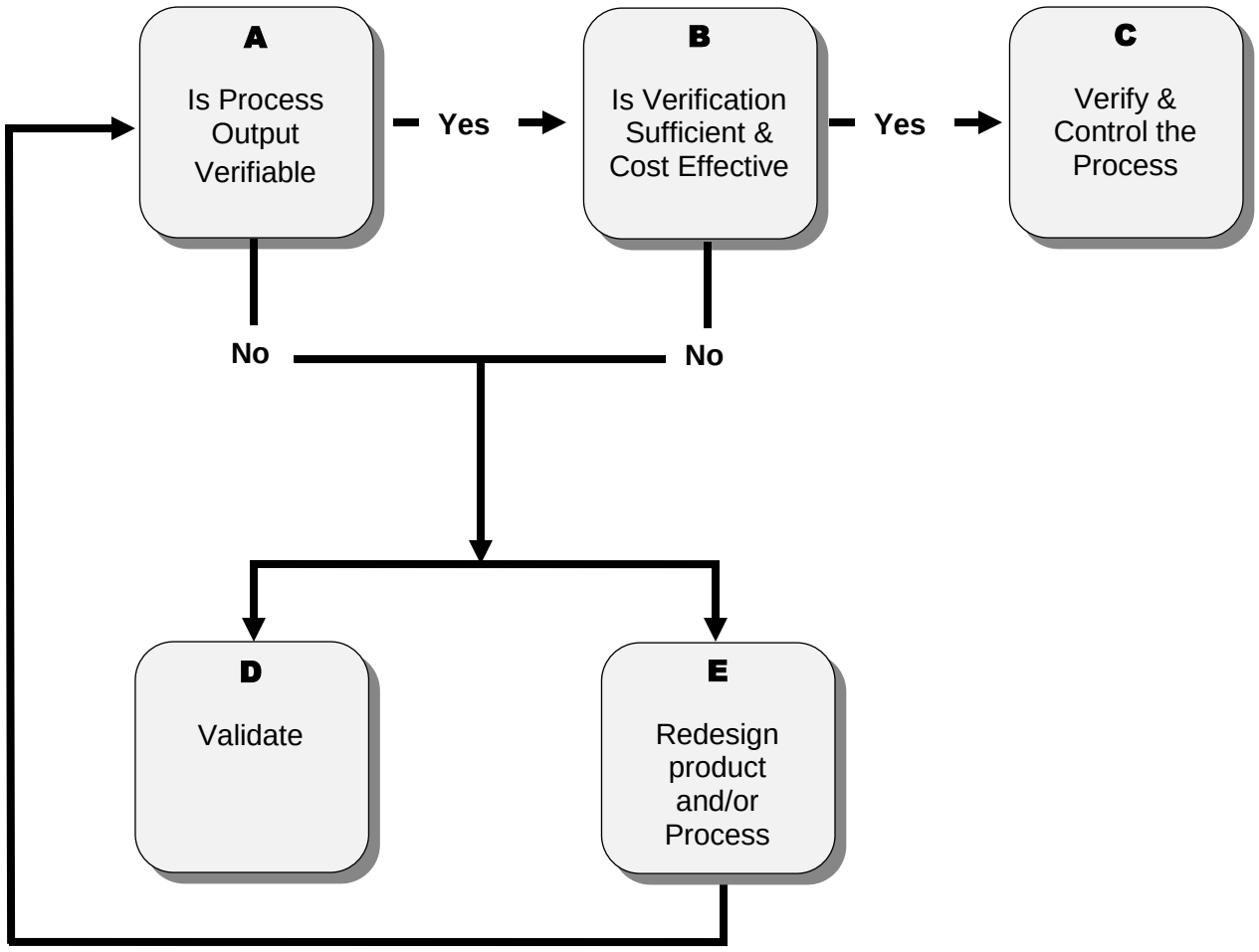
"Each Manufacturer shall establish and maintain procedures for monitoring and control of process parameters for validated processes to ensure that the specified requirements continue to be met. " 820.75

This indicates we need to be collecting useful, reliable data on a real-time basis and conducting analysis of the data as appropriate. Our experience suggests that many who perform process validation have an understanding of the above FDA quotation and strive to meet these criteria.

On the other hand, those who are conducting 100% verification of processes through test seem to be unaware of this criterion. Not only this, but there is in some companies little understanding of the value of this activity. "Why would we ever want to trend chart data from burn-in and final system test? As long as we meet specifications what possible benefit could this activity have for us?" This was a recent statement from a VP at a Class 3 medical device complex system provider. There was an element of truth to this statement, of course. If an organization has never

characterized (some folks refer to this as a requirements flow-down) their processes and product design they really have no systematic way of knowing if what they are measuring (and testing for) has a direct relationship with providing value. If they have adequately characterized processes and designs, then trending of test data can be of huge value in understanding a marginality situation is nearing or if down-stream processes are shifting off target.

The following flow chart (from GHTF/SG3/N99-10:2004, Edition 2) states in the decision box titled as "C" that even if you decide that verification is sufficient and cost effective, you still **are required to control the process**. In order to determine if a process is controlled, you must gather reliable data on key parameters and conduct analysis of the data on a real-time basis.



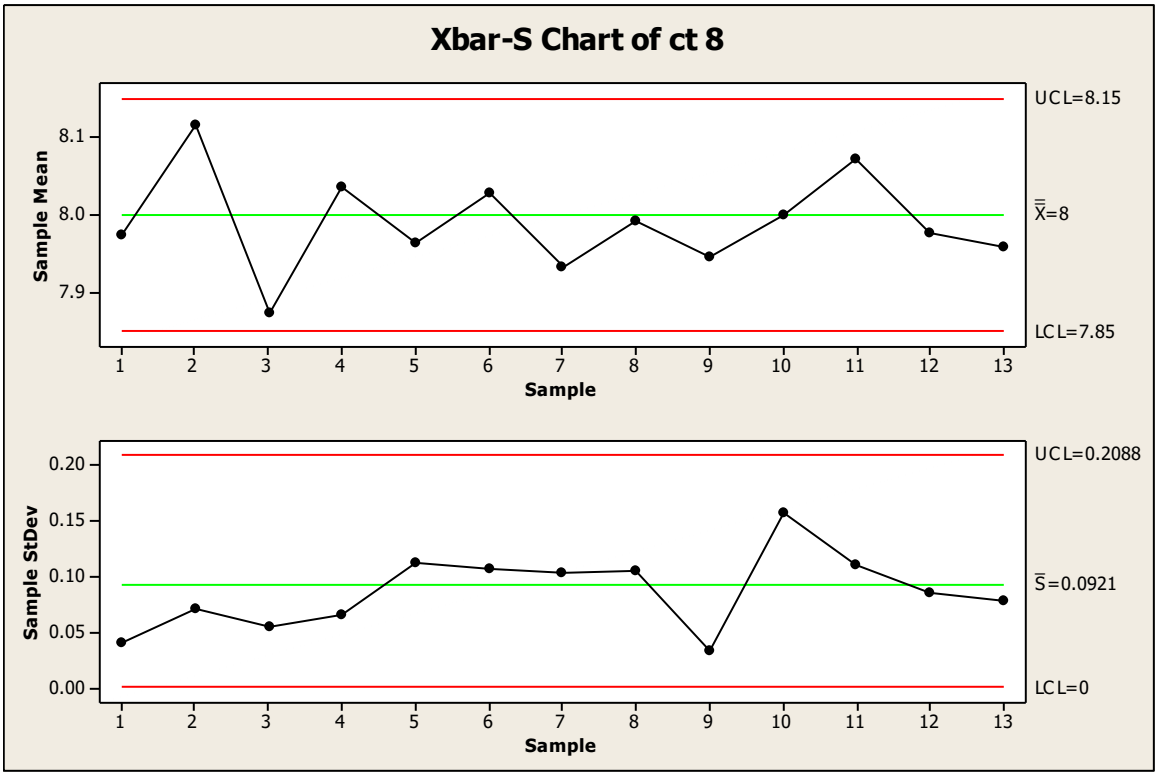
Continuous on-going monitoring and control of a process (validated or verified) is important and essential to avoid a potential field recall or catastrophe. This is not a book on the details of process control. A host of references abound including the following:

- "Statistical Quality Control", Grant and Leavenworth
- "Introduction to Statistical Quality Control", Montgomery
- "Statistical Process Control", AIAG

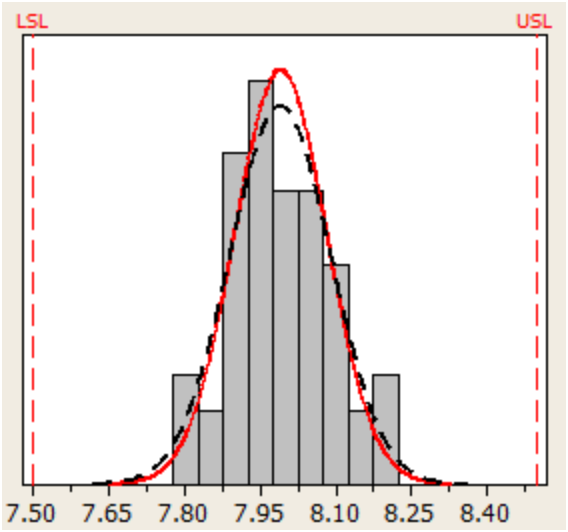
Example

As an example, suppose our company mixes 225 kilogram batches of elastomers, fillers, colorants, accelerators, curing agents, and other ingredients in a Banbury mixer. Approved batches are molded into closures for containers that hold various drug reagents that are used for humans. The critical output parameter of the batch is cure time. Suppose the mixing process has just been validated and our on-going process controls are to check a small random sample from each Banbury batch and determine the cure time. The specification for the formulation of interest is 8.0 +/- .50 minutes. Every 5 minutes another batch is completed. Our factory operates on three shifts, 24 hours per day. Our process control strategy is to sample 4 consecutive batches; calculate the average and standard deviation of cure time in each subgroup and plot the values on an average and range chart. The charts are monitored on a continuous basis. Standard AT&T rules for control charts are employed to interpret the control chart. The target Cpk for the process is "equal or greater than" 1.2.

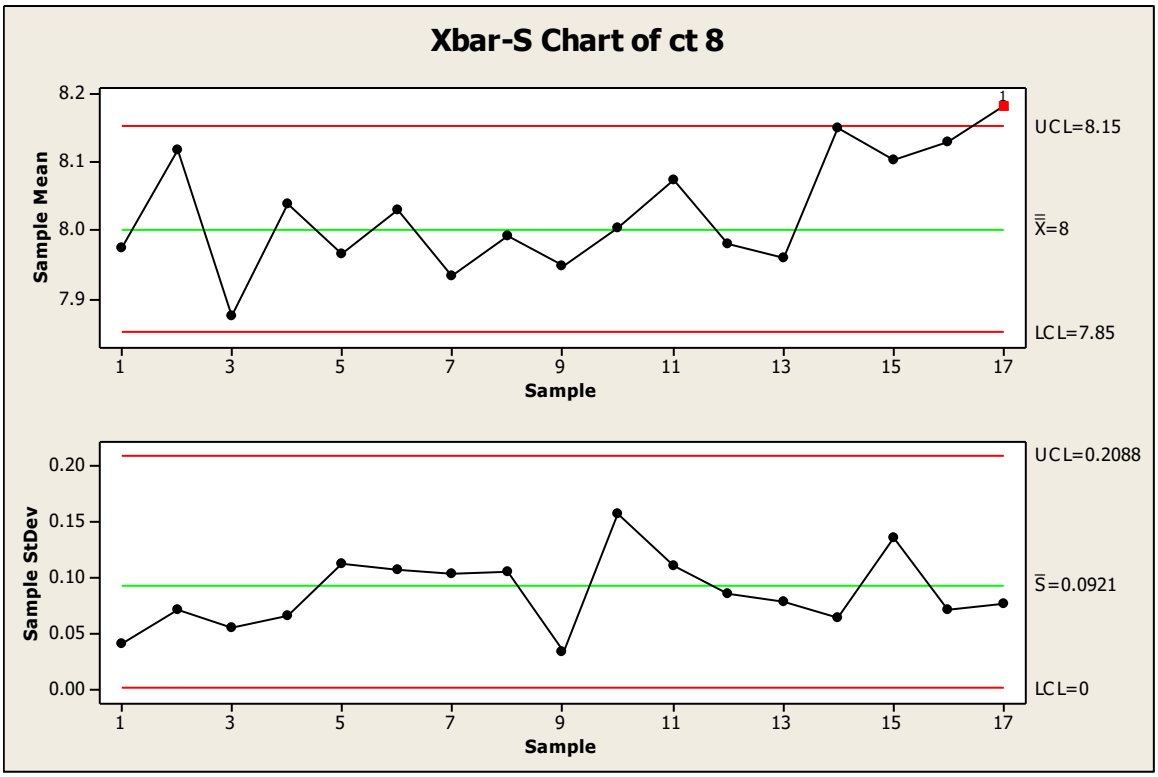
Scenario 1: Suppose the control charts for the last 13 subgroups and process capability information is as follows:



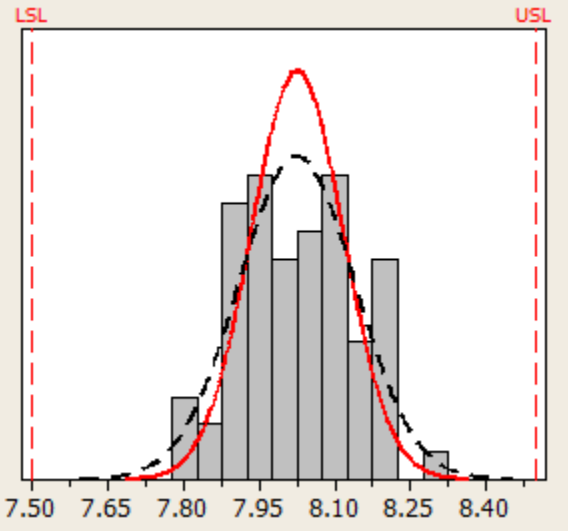
The above control charts suggest that for the last 13 subgroups there appears to be no evidence of assignable cause and the histogram shown below suggests the process is centered near nominal with a CPK of approximately 1.77.



Suppose we gather additional real-time data and plot values as they become available. This on-going process monitoring is shown on the Control Chart below:

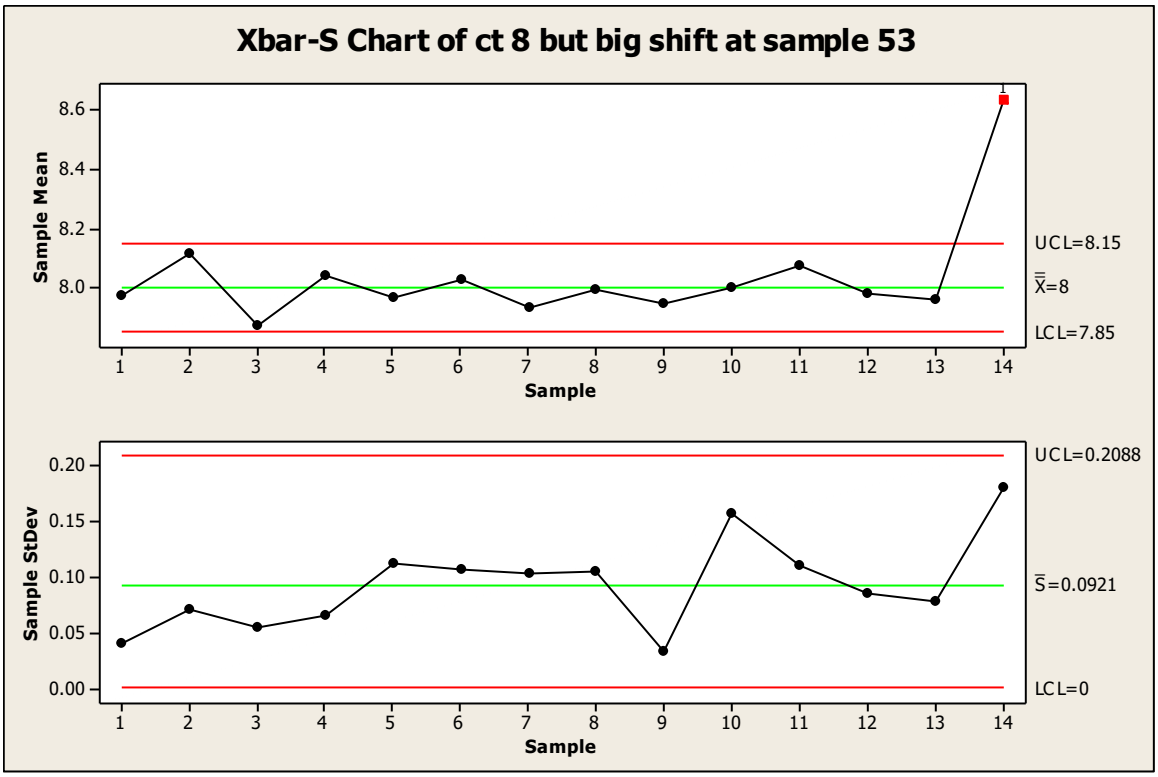


The above x-bar chart suggests an out-of-control point with sample 17 and what appears to be a shift in the process mean after sample 13. The histogram shown below shows this shift.



The team investigates this shift and determines the increase in the process mean is attributable to a particular lot of accelerator. Further investigation suggests the new lot of accelerator met the specification for all critical characteristics. In this case the process validation team evaluated the risk, documented the issue and assignable cause and continued to monitor the process. Since outputs were still meeting specification, revalidation was not necessary.

Scenario 2: Instead of a small increase in the subgroup mean as indicated in scenario 1, suppose the mean shift had been very large as follows:



As shown in the above chart the process is dramatically above the UCL on the X-bar chart. Additionally, suppose the last 4 observations are 8.55, 8.90, 8.50, and 8.60. Recall the specification for cure time is 7.5 to 8.5. The above suggests the process has seen a statistically significant increase in the mean and a number of observations are out of specification….obviously suggesting that the specified Cpk for the process is no longer being obtained. In this case the team would document the event, determine root cause, quarantine the out-of-specification batches and determine the extent of the revalidation activities that would be necessary.

Revalidation

As long as the process operates in a state of control and no changes have been made to the process or output product, the process does not have to be revalidated.

After a process has been validated, there will be a number of things that impact the process that the team will need to assess on an on-going basis. The team needs to consider risk based upon a profound knowledge of the product and/or process. An excellent understanding of the product and process technology is necessary in order to accurately assess risk. Determine the risk associated with the impact, document the risk, document your assessment, and determine your course of action. Leading medical device organizations do much of the risk assessment work up front using the tools of FMEA (Failure Mode and Effects Analysis), FMECA (Failure Mode, Effects and Criticality Analysis), FTA (Fault Tree Analysis) and Hazard Analysis.

Example: A potential decision matrix regarding an injection molding process is as follows:

Concern	Root Cause	Probably Action by Team
Burn marks on last 15 shots from cavity #4	Investigation determines molding vents are clogged	Quarantine parts, Send to MRB, shut down process, clean vents,

		re-start per standard procedures. If all ok, document event. Re-validation not required.
New Lot of Resin	(no problem, lot meets all receiving inspection requirements)	None other than what is called out in the standard operating procedures for new lot of resin.
Technician on 2nd shift blocks cavity #2 (damage to part). 2nd and 3rd shift run with blocked cavity	Cavity damaged on second shift by operator attempting to remove material with unapproved tool. Blocked cavity will have big impact of plastic flow likely resulting in big changes in dimensions and visual requirements	Quarantine all parts from all cavities. Send to MRB, shut down process, repair cavity re-start per standard procedures. IQ on machine/tool. If all ok, document event. OQ and PQ probably not required. Check/update approved tool list for operator/technician.
Catastrophic molding machine failure	Maximum available pressure no longer adequate. Machine repair required by machine manufacturer. Need to run tool on another machine for 2 months.	New machine will be different. IQ, OQ, and PQ will be required (unless original validation conducted using Scientific Molding Principles…then perhaps only IQ)
New Operator	(no problem, new person has been certified)	None other than following standard operating procedures
Cavity 16 is showing sink marks for last 20 shots	Surface temperature probe detects relative high mold temperature near questionable cavity. Further assessment determines clogged cooling line in area	Quarantine all parts, Send to MRB, shut down process, clean lines, re-start per standard procedure. If all ok, document event. Re-validation not required. Review/modify mold maintenance procedures as appropriate
Process monitor on end-of-fill mold cavity sensor displays out of control negative trend on control chart (last 20 shots)	Material being used is glass-filled nylon. Check ring is experiencing excessive leakage	Quarantine all parts, Send to Material Review Board, shut down process, replace check ring, IQ required on machine, re-start per standard procedure. If all ok, document event.
Sudden shift in part diameter (all cavities). Last 10 shots are all out of specification	Customer fixture used to mount parts for measurement of diameter not adjusted to nominal for this part #. Operator error.	Adjust fixture as required by Standard Operating Procedure (SOP), Re-measure parts, if all ok, document event and continue to run process. Check/modify SOP for fixture as appropriate
Customer complains of wall burst on our molded housing when assembly is pressurized. Customer conducts 100% pressure test…so no user risk according to customer, but yield problem to our customer	Review of drawing suggests a minimum wall thickness is not originally called out by customer. Customer has now revised engineering drawing to reflect minimum wall thickness.	Need to validate process in lieu of this new requirement. Original IQ can probably be used but new OQ, PQ, will be required.

Engineering recommends a new type of screw be used for production of part in question	Engineering has determined a new screw type for molding machine will provide better overall mixing of polymer during resin melt stage	Need to re-validate (IQ, OQ, and PQ).
Part has historically been molded in green color. Engineering is revising part number to reflect blue as an additional color for part. Resin will be same except for new colorant	Our process knowledge suggests that colorant can have a significant impact on part level critical to quality characteristics	Need to re-validate, IQ is likely ok but OQ and PQ will definitely need to be redone.

On-going process control activity after a process has been validated is essential. In order for a process to maintain a consistent state it must be maintained and monitored rigorously. Without proper attention, processes will have shifts and drifts over time potentially resulting in processes not meeting specification.

Revalidation of a process is addressed during process validation. Based upon the established company guidelines and profound process knowledge, changes in the process need to be assessed to determine the need for process revalidation.

Conclusion for this book

In this book we have attempted to provide a proactive, logical, thought provoking approach to the validation, and continued control of a process. Process validation cannot be completed in a vacuum once design work has been completed. It must be part of a proactive, integrated, cross-functional team effort. Pre-planning for process validation must start with the design of the product and process. Individuals need to have a working knowledge of FDA requirements, company Standard Operating Procedures, and profound knowledge of customer needs, product design, and processes in order to mitigate risk and validate processes. Even after the formal design and process validation has been completed, on-going process control (and revalidation) must be continuously assessed with appropriate actions taken as deemed necessary.

APPENDIX A

INJECTION MOLDING EXAMPLE

Grabow Medical

Injection Molding

Process Validation Protocol

PVP 2011-123

Title: Injection Molding Process Validation

Product to be covered: Left and right housing for Grabow infusion pump, part numbers 8181-21 and 8181-22

Equipment/process to be validated: Horizontal molding machine #1-001, 100 ton; mold # MT-001, facility FAC-01; mold # 005

Process Change Control Number: PPCN 70-329

Objective: Grabow Medical has recently obtained a new family mold for the left and right housing of their highly successful infusion pump. All parts are to be molding using above machine and mold. This process is to be validated so as to insure parts consistently meet engineering specifications using SOP 2212. The SOP has identified 4 critical characteristics for the housing. They are:

- Overall length of right housing = 0.000 +/- .500 (note data has been coded at request of client)
- Overall length of left housing = 0.000 +/- .500 (note data has been coded)
- Gap on right housing = 5 or less (note data has been coded)
- Gap on left housing = 5 or less (note data has been coded)

The target process capability for each of the above is Cpk of 1.1 or greater

Reference Documents:

- Molding process procedure, SOP 2212
- Statistical Methodologies, SOP XY 35
- Device Master Records, Code SSSS
- Nestal Model www-100T operating manual
- Master Validation Plan, MVP QWW12
- Engineering drawing for right housing, D-T001
- Engineering drawing for left housing, D-B001
- Process FMEA for left and right housings, P-XX1

- Design FMEA for left and right housing, D-YY2
- Mold and process set-up guide, pc 8181
- Lab processes and calibration, SOP 9-2-5
- Production Processes and Calibration SOP 1-12-11
- Mold specification sheet, MS-XX1
- Software validation Minitab, SW-785
- Software validation molding machine, SVW-879

Process Validation Plan:

The above reference tool and machine for molding of the left and right housing for Grabow infusion pump, part numbers 8181-21 and 8181-22 will be subjected to an Installation Qualification (IQ), Operational Qualification (OQ), and Performance Qualification (PQ) as planned in Master Validation Plan MVP QWW12. The associated material dryer, #MD-001 has already been validated and is not part of this protocol. The associated temperature controller, #IMC-001 has previously been qualified and is also not part of this protocol. The raw material resin being used, Blue PC/ABS blend, RX123456 is qualified by receiving inspection and is also not part of this protocol.

The Installation Qualification will use the Nestal Model www-100T operating manual to define machine setup requirements. For the installation and setup of the mold and water lines, Mold specification sheet MSS-001 will be utilized. The measurement of steel dimension as part of the IQ will not be required as this has already been completed in Form F-0x1. A checklist of requirements will be completed and results approved.

Operational Qualification will be completed in three phases. In the first phase previously completed characterization studies (Quality Engineering Lab Book RGL 2011-02, pp. 39 -123) and a modeling designed experiment will be used to determine best input variable settings and worst case input variable settings.

In the second phase of Operational Qualification consecutive shots will be completed at optimal process conditions in order to determine short term process capability. Using Statistical Methods SOP XY 35, a sample of 100 shots will be conducted, measured and the critical characteristics control charted on an X-bar, R chart. An assessment of process stability as well as targets Cpk will be made at that time.

In the third phase of Operational Qualification 100 consecutive shots will be conducted, measured and plotted on an X-bar, R chart at worst case settings as identified in phase one (above). Action limits will be determined at this time.

In all three parts of Operational Qualification parts will be measured and quarantined from production. All units will be subject to regrind after being held until the sign-off and successful completion of all phases of this validation.

Performance Qualification will commence after satisfactory completion of Operational Qualification.

Optimal settings for the molding process will be used and the input variable action levels for adjustment will be used. Using Statistical Methods SOP XY 35 samples will be take every 15 minutes for three consecutive days and the results control charted. Unusual variations in response variables will be investigated and root causes determined. When process stability is demonstrated, and the process variation demonstrates a value of Cpk > 1.1 the process will be considered validated and SOP 2212 will be used to control the process.

Measurement / Testing Equipment and Calibration

- Stopwatch, Process Development Lab, Calibrated per SOP 9-2-5
- Remote IR Thermometer RST -12, Process Development Lab, Calibrated per SOP 9-2-5
- CMM, MM-XX1, Calibrated per SOP 9-2-5
- Material Dryer, #MD-001, no calibration required
- Moisture Analyzer, #MA-001, Calibrated per SOP 9-2-5

Equipment Maintenance

During process validation the molding process will be maintained per the Supplier Co. Operating Manual. Upon completion of the validation, Manufacturing Equipment Register, MER 98-1248 will be updated to include maintenance and calibration of the machine and tool.

Revalidation

Upon completion of the process validation, the Process Validation Master Plan: Master Validation Plan, MVP QWW12, will be updated to include the molding process in the master validation schedule.

Process Validation Team Protocol Approval

Role	Name	Pre-Approval Signature	Date	Final Approval Signature	Date
Research and Development	Brian Taylor	Brian Taylor	2/3/12	Brian Taylor	3/1/12
Manufacturing Engineering	Sue Jones	Sue Jones	2/3/12	Sue Jones	3/1/12
Quality Engineering	Mary Curtis	Mary Curtis	2/3/12	Mary Curtis	3/1/12
Manufacturing	Bill Murphy	Bill Murphy	2/3/12	Bill Murphy	3/1/12
Regulatory	Greg Lawson	Greg Lawson	2/3/12	Greg Lawson	3/1/12
Marketing	Mike Gray	Mike Gray	2/3/12	Mike Gray	3/1/12

Installation Qualification Results
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Molding Machine Installation Checklist

Item	Specification (Tolerance)	Source of Requirement	Reading (if appropriate)	Status
Machine Component Calibration	Date to be current	Document MCC459	Due: Jan 26 2012	Conforms
Machine Tonnage	100 Tons	Document MTC457	100.4 Tons	Conforms
Line voltage	480 (+/- 1) Volts	Machine ops. Manual	480.2	Conforms
Machine Level	< 0.01 mm/m	Machine Setup Manual	n/a	Conforms
Maximum Pump Pressure	2200 psi (+/- 22 psi)	Machine Setup Manual	2212	Conforms
Water flow to machine for cooling	7 GPM (+/- 1 GMP)	Machine ops. Manual	6.8 GPM	Conforms
Molding Screw Zero position	0 (+/- 0)	Machine ops. Manual	0	Conforms
Minimum Oil temperature	60 deg F	Machine ops. Manual	65	Conforms
Oil Level	To be visually between the Min and Max lines	Machine ops. Manual	NA	Conforms
Room temperature	70 deg. F (+/- 10)	Document ED765	68.5	Conforms
Room humidity	30 % (+/- 5)	Document ED548	32.0	Conforms

Mold Installation Checklist

Item	Specification (Tolerance)	Source of Requirement	Reading (if appropriate)	Status
Mold maintenance Cycle	Date to be current within required cycles	Document MMC834	Next Required :25000, Current : 18457	Conforms
Mold Temperature Set Point	125 deg F (+/- 5 deg F)	Material Manufacturer's Manual	122 deg F	Conforms
Mold Level	Visual	Document MLD873	n/a	Conforms
Water flow	Per Document XXX	Document MLD574	n/a	Conforms

Auxiliary 1 Installation Checklist: Plastic Dryer

Item	Specification (Tolerance)	Source of Requirement	Reading (if appropriate)	Status
Dryer Component Calibration	Date to be current	Document DC754	Due: Mar 14 2012	Conforms
Set Point	180 deg F (+/- 5 deg F)	Material Manufacturer's Manual	182 deg F	Conforms
Dew Point	-40 deg F (+/- 5 deg F)	Machine ops. Manual	-42 deg F	
Line voltage	220 (+/- 1) Volts	Machine ops. Manual	220.0 V	Conforms
Machine Level	Visual	Machine ops. Manual	n/a	Conforms
Air flow	5 CFM (+/- 0.5)	Machine ops. Manual	5.3 cfm	Conforms
Air pressure	100 psi (+/- 5 psi)	Machine ops. Manual	102 psi	Conforms

Auxiliary 2 Installation Checklist: Mold Temperature Controller

Item	Specification (Tolerance)	Source of Requirement	Reading (if appropriate)	Status
Machine Component Calibration	Date to be current	Document MCC321	Due: Feb 02 2012	Conforms
Line voltage	240 (+/- 1) Volts	Machine ops. Manual	239	Conforms
Water Pressure	50 psi (+/- 5 psi)	Machine Setup Manual	53	Conforms
Water flow to machine for cooling	15 GPM (+/- 3 GMP)	Machine ops. Manual	13 GPM	Conforms
Molding Screw Zero position	0 (+/- 0)	Machine ops. Manual	0	Conforms
Water Set Point	120 deg F	Document MCC432	120 deg F	Conforms

Initial Startup

The machine and tool operated as described in Machine Operation Document 435 and as required by SOP 870.

Calibration

All gauges and measuring devices on the tool, machine, and ancillary equipment were successfully calibrated per SOP 981.

Lab Notebook Reference

Quality Engineering Lab Notebook, JWS, 98-4, pages 46 – 62

Issues / Commentary

No new issues were identified.

The installation for Horizontal molding machine #1-001, 100 ton; mold # MT-001, facility FAC-01; mold # 005 was successful.

Process Validation Team IQ Results Approval

Role	Name	Pre-Approval Signature	Date	Final Approval Signature	Date
Research and Development	Brian Taylor	Brian Taylor	2/3/12	Brian Taylor	3/29/12
Manufacturing Engineering	Sue Jones	Sue Jones	2/3/12	Sue Jones	3/29/12
Quality Engineering	Mary Curtis	Mary Curtis	2/3/12	Mary Curtis	3/29/12
Manufacturing	Bill Murphy	Bill Murphy	2/3/12	Bill Murphy	3/29/12
Regulatory	Greg Lawson	Greg Lawson	2/3/12	Greg Lawson	3/29/12
Marketing	Mike Gray	Mike Gray	2/3/12	Mike Gray	3/29/12

Operational Qualification Results
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Phase I

During process characterization (before process validation activities commenced) a number of essential machine/tool studies were completed. They were:

- On-Machine Relative Viscosity curve
  - Determined optimal injection velocity to be 2 in/sec or greater
  - Determined maximum injection velocity to be 4 in/sec
- Mold-Fill Analysis (25%, 50%, 75%, 95%)
  - Provided valuable information about fill dynamics in tool. Information provided assist us with future potential problem solving analysis
- Gate Freeze Study
  - Determined minimum hold time to be 10 sec
- Cooling Time Analysis
  - Determined hold time needed to be at least 25 seconds
- Mold Balance Study
  - Mold conforms to requirements
- Mold Cooling vs. Time Study
  - Water and cooling lines in tool are sufficient to prevent temperature build up over shifts of continuous use on tool

Details on the above characterization studies can be referenced in Quality Engineering Lab Book RGL 2011-02, pp. 39 -123.

Screening design of experiments studies completed during process characterization indicated that the three key factors influencing the 4 dimension characteristics were mold temperature, injection velocity and hold pressure (Quality Engineering Lab Book RGL 2011-02, pp. 39 -123). Based upon this outstanding characterization work done by the engineering team an eight-run full factorial designed experiment was completed. Levels for the factors studied were:

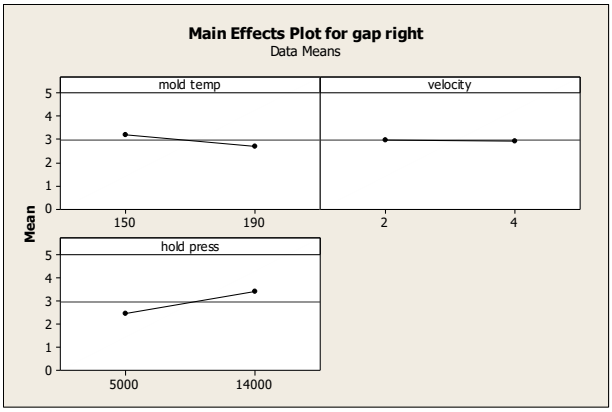
Factor	**Levels**
Mold Temperature	150, 190 degrees F
Injection Velocity	2, 4 inches/sec
Hold Pressure	5000, 14,000 psi plastic

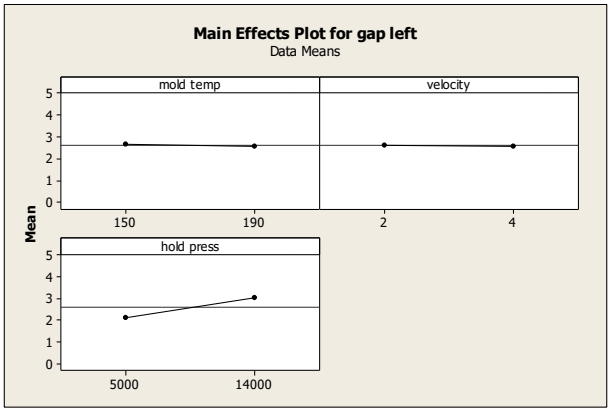
Utilizing Statistical Methodologies SOP XY 35, it was determined that we should conduct 5 shots for each run and measure all parts for the critical responses of interest. Parts were allowed to cool for two hours before measurements of critical dimensions were taken (please refer to Quality Engineering Lab Book RGL 2011-02, pp. 66-69) regarding the two hour time criteria. The data for each response is as follows:

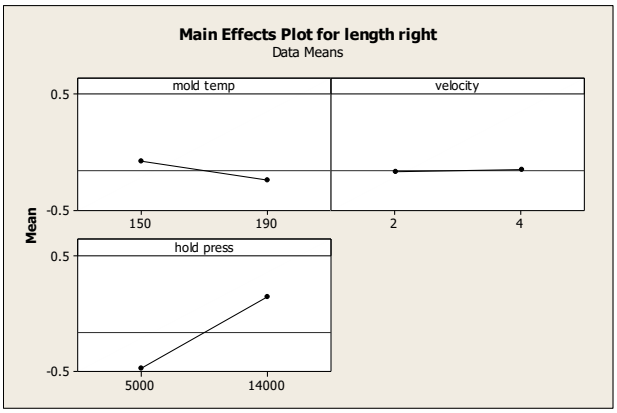
mold temp	velocity	hold press	length right	length left	gap right	gap left
150	2	5000	-0.52	-0.28	2.8	2.2
150	2	14000	0.24	-0.08	3.7	3
150	4	5000	-0.38	-0.24	2.8	2.2
150	4	14000	0.35	0.13	3.8	3.1
190	2	5000	-0.47	-0.15	2.3	2.1
190	2	14000	0.05	0.01	3.2	3.1
190	4	5000	-0.47	-0.31	2.2	2.1
190	4	14000	0.14	-0.02	3.2	3
150	2	5000	-0.42	-0.25	2.8	2.2
150	2	14000	0.16	-0.01	3.7	3.1
150	4	5000	-0.44	-0.23	2.8	2.1
150	4	14000	0.22	0.11	3.7	3.1
190	2	5000	-0.43	-0.37	2.2	2.2
190	2	14000	0	0.02	3.2	3.1
190	4	5000	-0.53	-0.38	2	2.1
190	4	14000	0.21	0.02	3.2	3
150	2	5000	-0.42	-0.29	2.8	2.2
150	2	14000	0.35	0.11	3.7	3.1
150	4	5000	-0.41	-0.25	2.7	2.2
150	4	14000	0.4	0.11	3.8	3.1
190	2	5000	-0.5	-0.36	2.3	2.1
190	2	14000	-0.08	-0.07	3.2	3
190	4	5000	-0.45	-0.35	2.4	2.1
190	4	14000	0.05	-0.06	3.2	2.9
150	2	5000	-0.33	-0.25	2.7	2.2
150	2	14000	0.2	0.02	3.7	3.2
150	4	5000	-0.41	-0.35	2.7	2.1
150	4	14000	0.23	0.03	3.5	3.1
190	2	5000	-0.5	-0.36	2.3	2.1
190	2	14000	0.02	0.08	3.2	2.9
190	4	5000	-0.65	-0.38	2	2
190	4	14000	0	-0.02	3.2	3
150	2	5000	-0.44	-0.27	2.7	2.2
150	2	14000	0.28	0.21	3.6	3.2
150	4	5000	-0.46	-0.34	2.7	2.2
150	4	14000	0.21	0.12	3.6	3.1
190	2	5000	-0.5	-0.36	2.3	2.1
190	2	14000	-0.06	-0.01	3.2	3
190	4	5000	-0.79	-0.38	2	2.1
190	4	14000	0.05	0.02	3.2	3

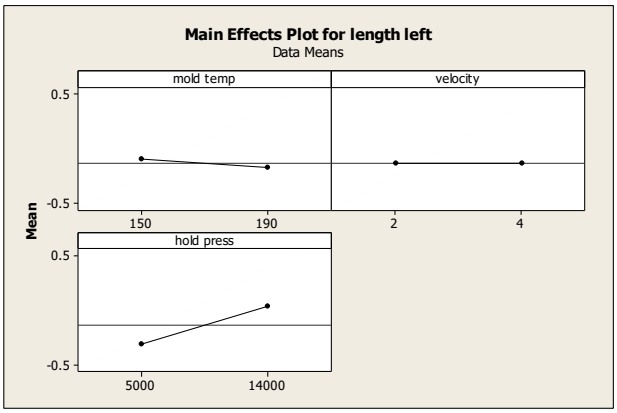
- Note: runs were not randomized. Please see Statistical Methodologies, SOP XY 35.

Main effects plots for each of the 4 responses of interest are as follows:









The plots for left part of tool and right part of tool are similar, as expected. Hold pressure appears to be the most impactful factor for all four responses, followed in importance by mold temperature. Injection velocity appears to have smaller influence on the four responses. Statistical analysis of each response was as follows:

Factorial Fit: gap left versus mold temp, velocity, hold press

Estimated Effects and Coefficients for gap left (coded units)

Term	Effect	Coef	SE Coef	T	P
Constant		2.59750	0.008478	306.38	0.000
mold temp	-0.09500	-0.04750	0.008478	-5.60	0.000
velocity	-0.03500	-0.01750	0.008478	-2.06	0.047
hold press	0.91500	0.45750	0.008478	53.96	0.000
mold temp*velocity	-0.00500	-0.00250	0.008478	-0.29	0.770
mold temp*hold press	-0.01500	-0.00750	0.008478	-0.88	0.383
velocity*hold press	0.00500	0.00250	0.008478	0.29	0.770
mold temp*velocity*hold press	-0.00500	-0.00250	0.008478	-0.29	0.770

S = 0.0536190 PRESS = 0.14375
R-Sq = 98.93% R-Sq(pred) = 98.32% R-Sq(adj) = 98.69%

Factorial Fit: gap right versus mold temp, velocity, hold press

Estimated Effects and Coefficients for gap right (coded units)

Term	Effect	Coef	SE Coef	T	P
Constant		2.9575	0.01358	217.81	0.000
mold temp	-0.5150	-0.2575	0.01358	-18.96	0.000
velocity	-0.0450	-0.0225	0.01358	-1.66	0.107
hold press	0.9650	0.4825	0.01358	35.53	0.000
mold temp*velocity	-0.0350	-0.0175	0.01358	-1.29	0.207
mold temp*hold press	0.0350	0.0175	0.01358	1.29	0.207
velocity*hold press	0.0450	0.0225	0.01358	1.66	0.107
mold temp*velocity*hold press	0.0350	0.0175	0.01358	1.29	0.207

S = 0.0858778 PRESS = 0.36875
R-Sq = 98.08% R-Sq(pred) = 97.00% R-Sq(adj) = 97.66%

Factorial Fit: length left versus mold temp, velocity, hold press

Estimated Effects and Coefficients for length left (coded units)

Term	Effect	Coef	SE Coef	T	P
Constant		-0.1358	0.009998	-13.58	0.000
mold temp	-0.0715	-0.0357	0.009998	-3.58	0.001
velocity	-0.0055	-0.0027	0.009998	-0.28	0.785
hold press	0.3435	0.1717	0.009998	17.18	0.000
mold temp*velocity	-0.0235	-0.0118	0.009998	-1.18	0.249
mold temp*hold press	-0.0065	-0.0032	0.009998	-0.33	0.747
velocity*hold press	0.0215	0.0108	0.009998	1.08	0.290
mold temp*velocity*hold press	-0.0105	-0.0053	0.009998	-0.53	0.603

S = 0.0632357 PRESS = 0.199938
R-Sq = 90.67% R-Sq(pred) = 85.42% R-Sq(adj) = 88.62%

Factorial Fit: length right, length left, gap right, gap left

Factorial Fit: length right versus mold temp, velocity, hold press

Estimated Effects and Coefficients for length right (coded units)

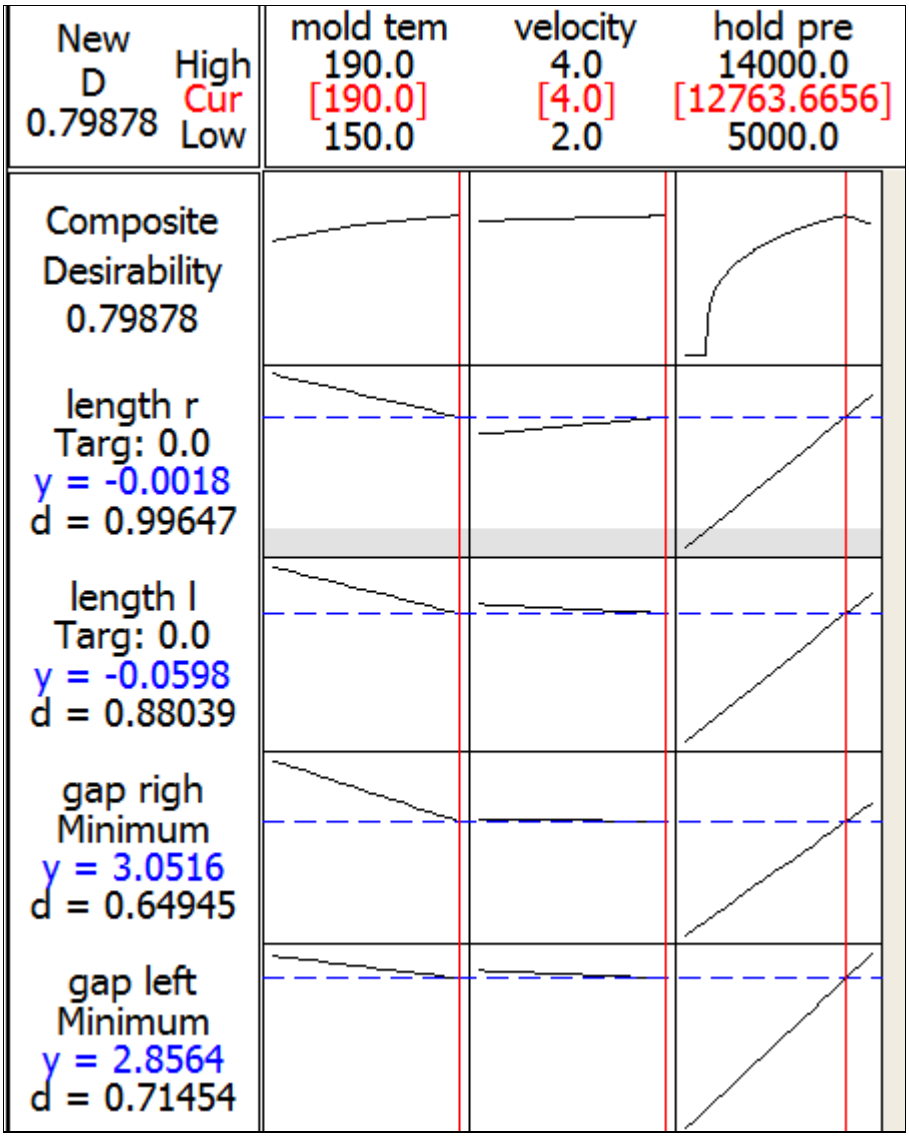
Term	Effect	Coef	SE Coef	T	P
Constant		-0.1625	0.01245	-13.05	0.000
mold temp	-0.1660	-0.0830	0.01245	-6.67	0.000
velocity	0.0120	0.0060	0.01245	0.48	0.633
hold press	0.6270	0.3135	0.01245	25.19	0.000
mold temp*velocity	-0.0090	-0.0045	0.01245	-0.36	0.720
mold temp*hold press	-0.0600	-0.0300	0.01245	-2.41	0.022
velocity*hold press	0.0580	0.0290	0.01245	2.33	0.026
mold temp*velocity*hold press	0.0430	0.0215	0.01245	1.73	0.094

S = 0.0787242 PRESS = 0.309875
R-Sq = 95.59% R-Sq(pred) = 93.11% R-Sq(adj) = 94.62%

R-Sq values for each response were better than 90% indicating that the model fit to each response explains over 90% of the variation witnessed in each response for the experiment.

In order to determine optimal setting for each of the factors so as to achieve the best response for all four responses simultaneously we utilized the “response optimizer” command within Minitab. The

following output was obtained:



The best setting from the above table are:

- Mold temperature = 190 degree F
- Injection velocity = 4.0 (great for process efficiency!) inches/sec
- Hold pressure = 12,763 psi plastic

These setting are predicted to provide mean response values of:

- Length right = -.001
- Length left = -.059
- Gap right = 3.05
- Gap left = 2.85

The next step is to conduct a confirmation trial at the predicted best set point for the input factors (mold temperature, injection velocity, and hold pressure) and see if the prediction from our experiment works. In this case we created an additional 50 shots and measured all parts for the 4 responses of interest. Data and 95% confidence intervals for the population means can be found in Quality Engineering Lab Book RGL 2011-02, pp. 88 and 89. Predicted values obtained above fell within the calculated confidence interval for each of the four responses. Confirmation was successful. Optimal set points were determined. Monte Carlo Simulation was done on the above confirmed prediction equations (details are in Quality Engineering Lab Book RGL 2011-02, pp. 88 and 89). Predicted Cpk values for each response at nominal conditions were:

Response	Predicted Cpk from Monte Carlo
Length right	2.1
Length left	1.7
Gap right	1.5
Gap left	1.4

Additionally 200 shots were made at the optimal set points for our input factors of Mold Temperature, Injection Velocity, and Hold Pressure. Every 5th shot was taken and all responses were measured. Actual Cpk values obtained for these samples were:

Response	Predicted samples taken from 200 shots
Length right	1.9
Length left	1.8
Gap right	1.5
Gap left	1.3

Cpk values obtained from the above samples suggest we have an acceptable process capability at optimal conditions.

In the second part of OQ phase I worst case settings were used on the process to determine if even under worst case conditions the process would be able to provide acceptable capability. Worse case conditions for the process variables are:

Control Factor	Worst case ranges
Mold temperature	180 to 200
Injection Velocity	3.8 to 4.0
Hold Pressure	12060 to 13460

From the main effects plots (above) it appears all responses will tend to be smaller if:

Control Factor	Each response smaller/Each response larger
Mold temperature	200/180
Injection Velocity	3.8/4.0
Hold Pressure	12060/13460

An additional 200 shots were made with mold temperature = 200, injection velocity = 3.8, and hold pressure = 12060 (setting that each response smaller). Every 5th shot was taken and all responses were measured. Actual Cpk values obtained for these samples were:

Response	Cpk calculated for data taken with factor setting that make responses smaller
Length right	1.8
Length left	1.6
Gap right	1.4
Gap left	1.3

An additional 200 shots were made with mold temperature = 180, injection velocity = 4.0, and hold pressure = 13460 (setting that each response larger). Every 5th shot was taken and all responses were measured. Actual Cpk values obtained for these samples were:

Response	Cpk calculated for data taken with factor setting that make responses larger
Length right	1.7
Length left	1.6
Gap right	1.3
Gap left	1.3

Issues/commentary

In summary, during the OQ activity we were able to use a designed experiment to determine optimal input control factor set points. In addition we able to demonstrate with sample data a predicted Cpk better than required for each response. In addition, we were able to determine under extreme process conditions that we would be able to meet or exceed Cpk goals as well.

The molding Operational Qualification was successful.

Role	Name	Pre-Approval Signature	Date	Final Approval Signature	Date
Research and Development	Brian Taylor	Brian Taylor	2/3/12	Brian Taylor	4/17/12
Manufacturing Engineering	Sue Jones	Sue Jones	2/3/12	Sue Jones	4/17/12
Quality Engineering	Mary Curtis	Mary Curtis	2/3/12	Mary Curtis	4/17/12
Manufacturing	Bill Murphy	Bill Murphy	2/3/12	Bill Murphy	4/17/12
Regulatory	Greg Lawson	Greg Lawson	2/3/12	Greg Lawson	4/17/12
Marketing	Mike Gray	Mike Gray	2/3/12	Mike Gray	4/17/12

Performance Qualification Results

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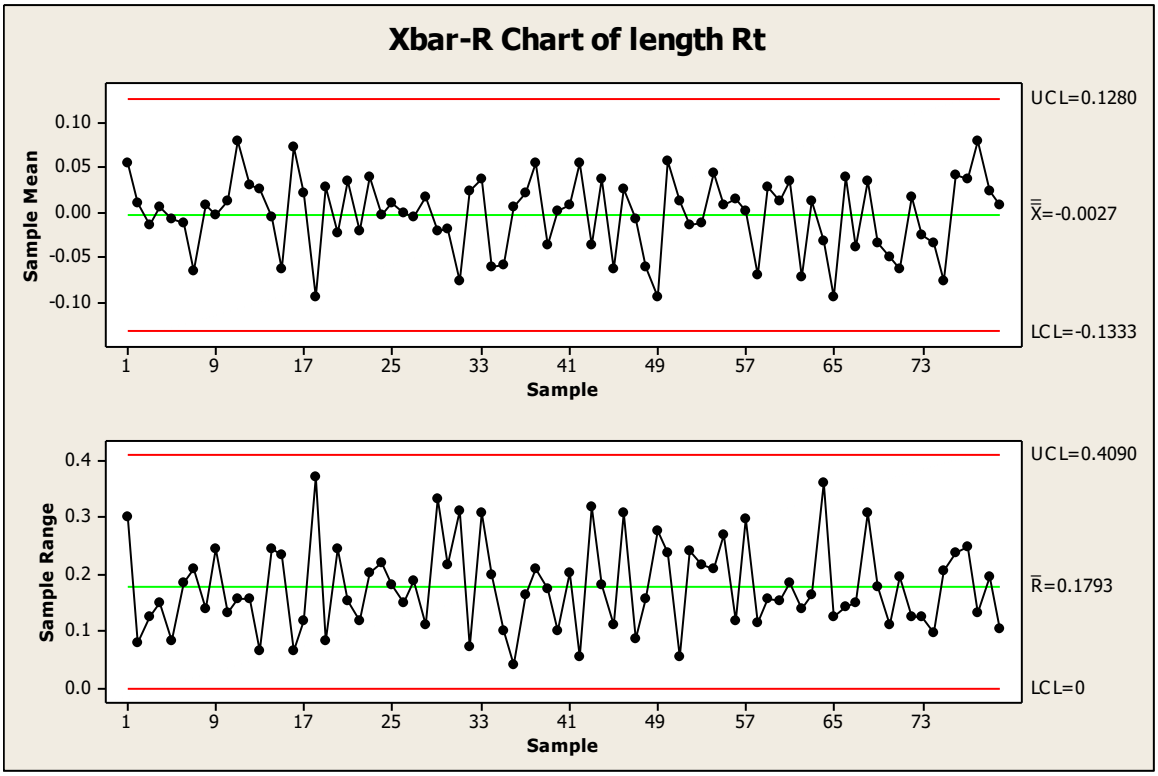
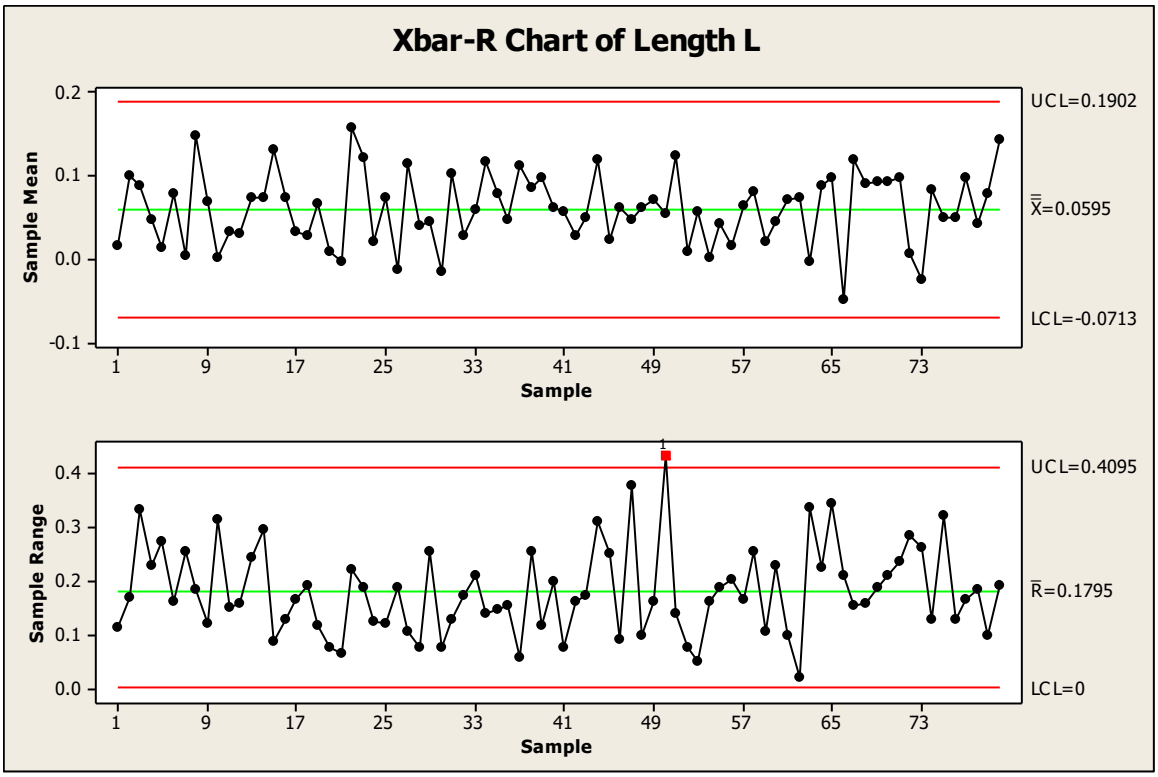
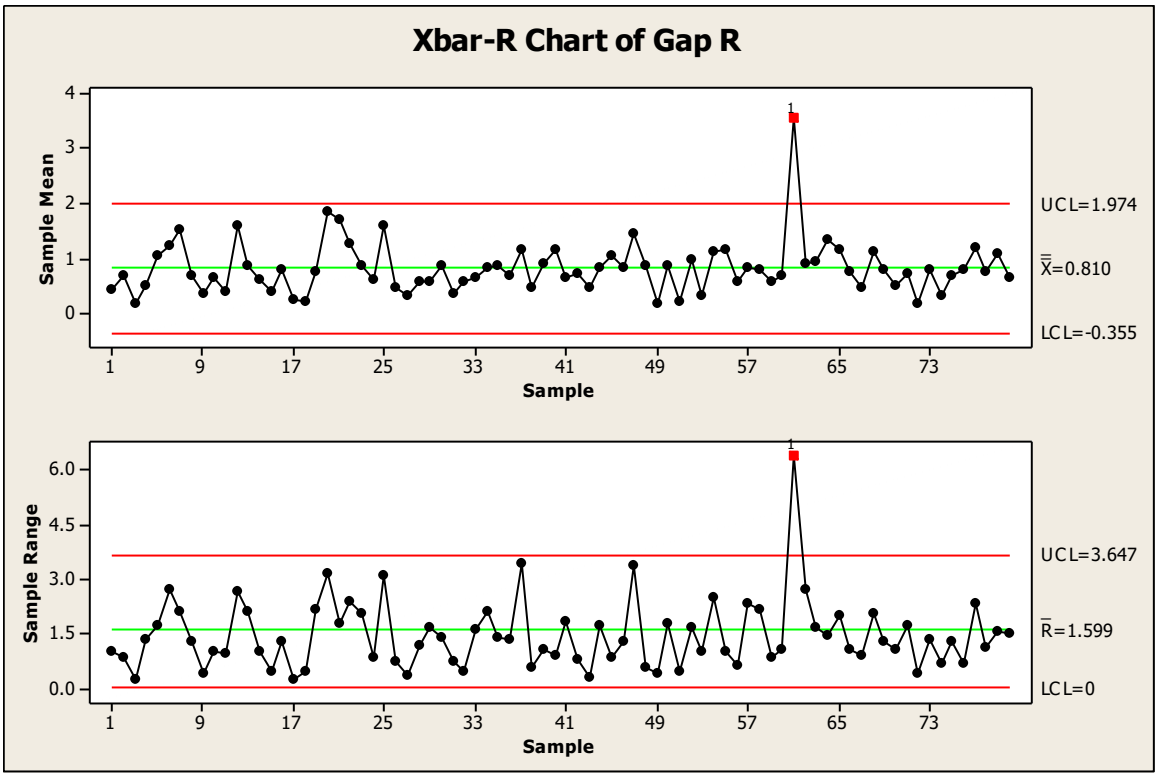
Left and right housings for the Grabow infusion pump were run for one-week (Week of October 24, 2011) under normal production conditions. Four consecutive shots were taken every 30 minutes (per SOP XXX), parts were measured and sample values plotted on X-bar, R charts. Charts obtained were as follows:



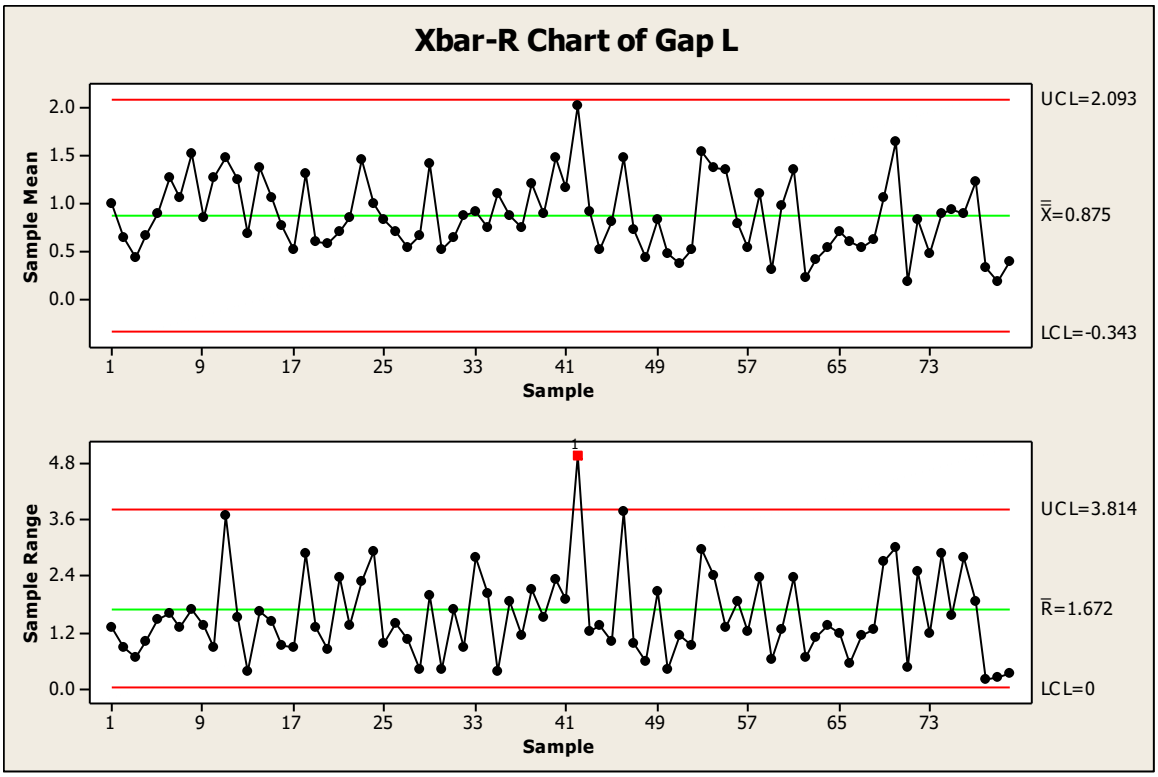
All sample values plotted on above chart display only random patterns of variation. All parts measured were within specifications for the response of Length Right. Calculated Cpk for the week was 1.9.



One point plotted on above chart displayed an out-of-control value (sample 50 on range chart). As soon as this point was plotted the team utilized the section of SOP titled "out-of-control corrective action procedure". No cause could be associated with this event, all parts measured in sample met specification. The process was continued without intervention and as shown in above chart samples continued to fall within statistical control limits.



An out-of-control point occurred at sample number 61 on both the X-bar and R-chart. The team reacted to this flag immediately using the "Out-of control corrective action procedure". It was determined that one part in the subgroup of 4 had a very large value (above specification) recorded. The part was re-measured per SOP and it was determined that the part was actually in specification but the value had been erroneously entered into the analysis software. The correct value was entered into the analysis package and the newly plotted values for both the X-bar and R-chart were now in control.



For the above X-bar and R-chart pair for response Gap L one out-of-control point was witnessed for observations. Using the "out-of-control" corrective action section of the SOP investigation by the team indicated that just before the samples for the subgroup had been taken the machine operator had to stop the machine momentarily to remove a partially stuck part from the left part of the cavity. This allowed for momentary heat loss from the tool. The SOP for operation of the machine indicates that the machine needs to be cycled for three shots (all parts quarantined and sent to MRB). The subgroup in question was created just after the above 3 quarantined shots had been completed. Review of the measurement data for the subgroup indicated that the first part in the subgroup has a relatively large (but in spec.) value. Corrective action was to change the SOP to recycle the machine for 4 shots before initiating production.

The Cpk values for the week were as follows:

Response	Cpk
Length Left	1.9
Length Right	1.7
Gap Left	1.3
Gap Right	1.3

These meet our criteria of 1.1 or greater.

Lab Notebook Reference:

Quality Engineering Lab Notebook, JWS, 98-4, pages 85 – 97.

Issues / Commentary:

None other than the minor discrepancies noted above. SOP has been modified to reflect need for cycling machine for 4 cycles rather than 3 after a process interruption.

The process has demonstrated stability and capability.

The Process Validation Master Plan, PVP 2011-123 has been updated to include machine #MT-001, operating with tool # 005 in the revalidation process.

Role	Name	Pre-Approval Signature	Date	Final Approval Signature	Date
Research and Development	Brian Taylor	Brian Taylor	2/3/12	Brian Taylor	5/10/12
Manufacturing Engineering	Sue Jones	Sue Jones	2/3/12	Sue Jones	5/10/12
Quality Engineering	Mary Curtis	Mary Curtis	2/3/12	Mary Curtis	5/10/12
Manufacturing	Bill Murphy	Bill Murphy	2/3/12	Bill Murphy	5/10/12
Regulatory	Greg Lawson	Greg Lawson	2/3/12	Greg Lawson	5/10/12
Marketing	Mike Gray	Mike Gray	2/3/12	Mike Gray	5/10/12

Final Report
PVP 2011-123

We have reviewed the requirements of the protocol; the IQ, OQ and PQ reports and compared these to the requirements of the reference documents. All requirements have been met and the process is Validated.

Process Validation Team Final Report Approval

Role	Name	Final Approval Signature	Date
Research and Development	Brian Taylor	Brian Taylor	5/22/12
Manufacturing Engineering	Sue Jones	Sue Jones	5/22/12
Quality Engineering	Mary Curtis	Mary Curtis	5/22/12
Manufacturing	Bill Murphy	Bill Murphy	5/22/12
Regulatory	Greg Lawson	Greg Lawson	5/22/12
Marketing	Mike Gray	Mike Gray	5/22/12

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About the Authors

Robert G. Launsby, M.S. Engineering, President of Launsby Consulting. With over 20 years experience in high-tech industries, Bob has held positions as Principle Engineer, Program Manager, and Consulting Engineer. He is co-author of the texts *Straight Talk on Designing Experiments, Understanding Industrial Designed Experiments*, *Design for Six Sigma*, and *Engineering Today's Designed Experiments*. Bob has led over 1,000 applications and trained more than 6,000 people in industrial experimentation, Design Control, Process Validation, and Design for Six Sigma.

Suhas Kulkarni is President of FIMMTECH, a consulting firm that specializes in services related to injection molding. He earned his Masters in Plastic Engineering from the University of Massachusetts, Lowell and a Bachelors in Polymer Engineering from the University of Poona, India. He has 18 years of experience as a process engineer. His main area of expertise is Scientific Processing for Injection Molding. Based on his experience, he has developed a custom software, called Nautilus, that aids the complete process development routine to production release. He also teaches a plastics and molding course at the University of California, San Diego and is a contract faculty at the University of Massachusetts at Lowell.

Jayme P. Lahey has a B.S. in Medical Technology and serves as Technical Director for Launsby Consulting. She has over 20 years experience in high-tech industry and has held positions as Principle Manufacturing Engineer, Quality Engineer and Qualification Engineer. She is co-author of the books *Experimental Design for Injection Molding*, *Process Validation for Business Success* and *Engineering Today's Designed Experiments*. Jayme has consulted domestically and internationally in the areas of statistical process control, design of experiments, and process optimization.

Thomas Oesterle currently works as a Principle New Product Development Engineer for a major medical device manufacturer in the Chicago area. Thomas has outstanding skill and expertise in part and complex system design. Previously, Thomas was Director of Engineering at CEA Technologies in Colorado. CEA specializes in system and part design/manufacturing for the medical device industry. Thomas is a graduate of Fachhochschule Rosenheim – Hochschule fur Technik und Wirtschaft.