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Product Development Insight

Validation Can Make a Product Launch a Sure Thing

When used carefully, process validation is an invaluable tool for manufacturers.

BRYAN CAMPBELL
Mack Molding (Arlington, VT)

We've all heard process validation horror stories. Validations can take years. Creeping elegance can take over. Product launches can be stopped in their tracks. When implemented correctly, however, process validation can improve launch success and minimize product recalls.


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The bottom line for any quality system (QS) is that it must ensure products are manufactured to the OEM's satisfaction. The OEM's requirements, or product specifications, drive process development and define the process parameters. To ensure that the process can be repeated successfully over the long term, it must be validated. This can be simple if the OEM works with its contract manufacturer (CM) to develop and doggedly follow an advanced quality plan, form a cross-functional project team, and provide regular input.

The Importance of Validation

According to FDA's QS regulation, process validation is defined as the establishment of "objective evidence that a process consistently produces a result or product meeting its predetermined specifications."[1]

Apart from meeting regulatory requirements, process validation delivers numerous benefits to both the OEM and CM. It is now expected that the process to make almost any medical component will be validated, regardless of classification. As previously stated, process validation ensures the final product will meet specifications and be of a uniform quality without the need for intensive in-process and finished device testing. Implementing process validation can lead to production efficiency gains as well as a reduction in scrap and an increase in outputs. Rework is eliminated, the cost of quality decreases, and products launch successfully and on time. Ultimately, the OEM will hear fewer complaints and undergo fewer recalls, and it can use process validation data to develop the next generation of products.

Assembling the Right Team

The success or failure of process validation rests squarely on the shoulders of the cross-functional project team. This group should comprise people who specialize in quality and regulatory compliance, design, tooling, procurement, and manufacturing. It should be led by a program manager who clearly understands expectations, articulates them internally, and brings the appropriate people to the table for sign-off at each validation phase.

Contract review sets the stage for all that follows. At this point, the OEM's requirements must be clearly defined and documented. The CM can either acknowledge it has the capability to meet these requirements or it can communicate a different approach, which it will prove out through validation. This is the first of several opportunities for the OEM and CM to work together to develop the most efficient manufacturing approach.

After the OEM has identified all requirements, the project team develops a quality plan outlining how the device will progress through validation and into production. Beyond the stated requirements, this plan must include project deliverables and define the quality standards for each deliverable. It is imperative for the

manufacturer to work with the OEM to jointly establish pass-fail criteria for all critical-to-function requirements.

Developing the Plan

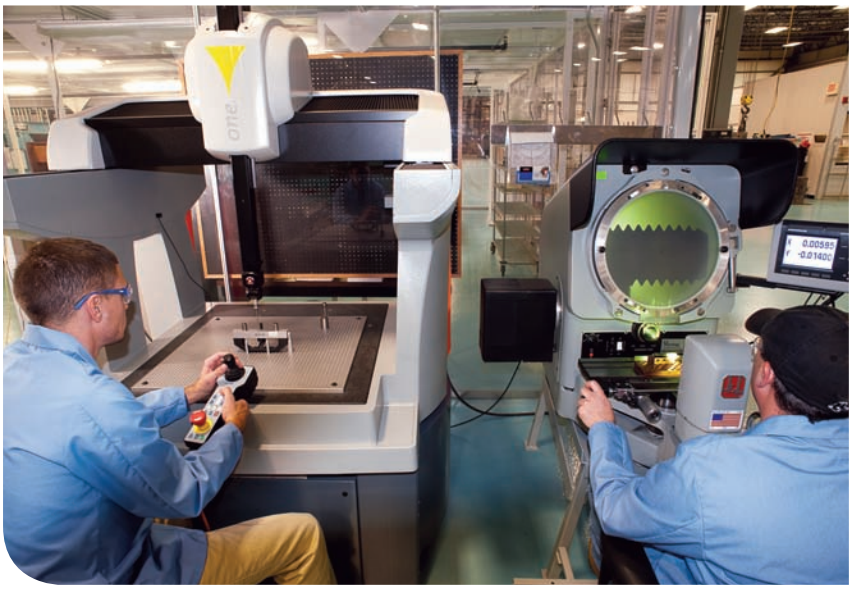
The first step is to identify the device to be produced, as well as potential failure modes and all required outputs. All product attributes must be captured. Suppliers other than the CM must also validate their processes, or the CM can do it for them. Many OEMs are downsizing approved vendor lists. They should be keenly interested in working with suppliers that can handle process validation for themselves and any second- or third-tier suppliers they engage.

Next, the process must be identified. Is it a pure molding project, or does it involve downstream operations? Every process must be clearly defined and captured in the validation.

The criteria for a successful study must be defined so that it doesn't become a moving target. Establish the study duration. How many shifts and operators are needed? Is a 3 × 30 study (consisting of three runs of 30 pieces each) sufficient to gain statistical confidence? Would it be better to do a 3 × 2 study (three runs of two hours each)? There's a fine line between a study that does just enough and one that consumes too much in the way of time, materials, and labor. The CM's challenge is to strike a balance, and the OEM's role is to trust the manufacturer's expertise. CMs should not overdo things, and OEMs should be careful not to overpay.

The CM must identify the equipment that will be used to run the process. If possible, the CM should validate on two or three pieces of the same equipment and at more than one location. This will provide a built-in contingency plan for the OEM and flexibility for the CM. In the event of an equipment failure or location shutdown, alternative equipment and locations will already have been validated. Make note of the utilities that are required to run the validated equipment, and expect the CM to include a preventive maintenance plan in the overall validation.

The validation plan must identify required personnel and necessary qualifications. Personnel should be trained as needed; they must be familiar with both the product requirements and specific work instructions. All training should be documented for each employee.



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Workers perform a process capability study (Cpk). Contract manufacturers should establish methods for measuring process capability and performance.

Process flow must be included. This should cover relevant specifications for products, components, materials, and environmental conditions, such as safety, cleanliness, inspection conditions, and lighting.

The validation controls and conditions should be identified. When, for example, a CM is developing a molding process, the processor must establish the high and low values for time, temperature, and pressure to determine the most desirable process window. During validation planning, the processor must define how to transition from one value to the next. Should the machines run for eight hours on low, shut down for two hours, and then run on high? Should the process be normalized over a 24-hour period, or can it be done in 10 minutes?

The process parameters that will be controlled and monitored must be identified. With regard to plastics molding, for example, more than 100 different parameters establish the final output of the product, but only a handful actually influence the physical part itself. It's critical to clearly define ahead of time the process parameters that are going to be challenged during the validation. With injection molding, the scope narrows to the five or so parameters relating to time, temperature, and pressure that are going to influence the part's geometry, cosmetics, and overall performance.

Once the processor has defined the parameters that will be challenged, it must also precisely outline the monitoring methods that will be used. This should include methods for monitoring various product characteristics as well as the specific measurement techniques. This phase offers another opportunity for the OEM and CM to collaborate regarding acceptable monitoring methods, techniques, and the parameters for defining nonconformance.

Apart from tangible measurements, are there subjective criteria that will be used to evaluate the product? Often, something will be agreed on early in the process and then challenged later when seen by a new set of eyes. For example, it's easy to zero in on the length, width, and height measurements, only to discover that there is a question as to whether the product's surface appearance was correctly classified; does it belong in Class A (highly cosmetic and no defects), B (limited defects), or C (a nonvisible surface)? Don't forget about subjective criteria—they're always there and need to be discussed early on.

Next, expect the CM to establish statistical methods for measuring process

capability and process performance. Is it going to perform a process capability index (Cpk) and a process performance index (Ppk)? What are the acceptable limits within each? Don't lock in on the industry norms (a Cpk of 1.33 or a Ppk of 1.67), or any numbers, for that matter, without first discussing a few crucial factors with the CM, such as the critical nature of the part's function, the role of in-process inspection, and the importance of repeatability. The direction chosen at this crossroad can influence both cost and time-to-market. For example, based on a particular tool, press, and process, it may be possible to yield seven out of 10 critical characteristics with a Cpk of 1.33, while the remaining three have a Cpk of 1.12. How crucial is it that all 10 characteristics have a Cpk of 1.33? Is it important enough for a tooling and process reboot, or is it something that can be addressed through in-process inspection? Save time and money by having this conversation prior to launch.

In this planning phase, it's important to address equipment maintenance and repairs. In addition to the installation qualification, the OEM should work with the CM to develop objective evidence that preventive maintenance and repairs are scheduled and documented for each piece of equipment used in the process.

Make sure the validation defines the conditions that would require a revalidation. For example, if a diameter isn't originally considered a critical characteristic but subsequent fit testing indicates otherwise, that diameter becomes a newly defined output and must be validated.

Finally, the OEM and CM must define the stages during which design review and customer engagement are mandatory. There are many stop signs along the manufacturing continuum where determinations must be made and directions chosen. OEMs can avoid revalidations and save resources by ensuring the right decision-makers are at the table early in the process.

After the cross-functional team develops the data necessary to validate the process, compile the advanced quality plan. This is the hard evidence that demonstrates process capability and performance over the unit's production life. See the sidebar on advanced quality planning on pg. 41, which lists all the documents that must be developed before the first tool is cut.

Installation Qualification

Installation qualification (IQ) focuses on the equipment and facility selected to manufacture the product. The manufacturer must demonstrate that both primary and secondary equipment, along with the facility itself, are being maintained and calibrated according to its quality management system. Has preventive maintenance been scheduled? Have environmental controls been established and documented? Have the workspace and manufacturing line been set up to supply product at a rate that meets the OEM's demand?

IQ should be an ongoing process in the manufacturing facility. It is neither customer- nor part-specific. The manufacturer should have a library of IQs for all existing equipment in its document control system. When needed, providing an IQ is then as simple as exchanging paper.

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After the tool arrives, it's time to execute, beginning with process development. With regard to injection molding, the author recommends performing a short shot study, an in-mold rheology study, a gate-seal analysis, and a pack-pressure study to determine if both the tool and process are performing to specifications. Throughout this short process-development exercise, the OEM and processor should decide on five to seven critical parameters relating to time, temperature, and pressure, and develop a design of experiments (DOE) to define the highs and lows. Through a DOE confirmation run, the processor will determine the process window that will be challenged by the operational qualification (OQ).

Operational Qualification

During OQ, the processor will challenge the established high and low parameters based on the agreed-upon sample size in the quality plan. A 30-piece capability study of both the high and low parameters of the critical-to-function dimensions, plus one full first article inspection (FAI) from each challenge, is sufficient for most applications. The data should be reviewed; nominal shifts or tolerance requirements may have to be considered. The OEM should approve the FAI before process qualification (PQ) begins.

Process Qualification

PQ demonstrates that the process will be stable and dimensionally capable over a long stretch of runs at nominal conditions. The processor should demonstrate this over a minimum of three molding runs of four hours each, with three different resin lots. The critical-to-function dimensions should be measured on sample parts after each run. When executing these runs, both FAI and critical-to-function dimensions should be approved and recorded. Once the processor has established high and low parameters, and has demonstrated the ability to center the process over a long run, it will have established the statistical confidence necessary to demonstrate that the process can meet the OEM's requirements over a long-term production cycle.

Finally, the CM should compile a completion report of all outputs to date, and make that available to the OEM. The report should describe the following information:

- Each activity and who performed it.
- Resulting data from each activity, including a pass or fail determination.
- Mitigation measures for failures.
- Changes made to activities as required by protocol.
- In-process inspection frequency, based on data.
- Red-line prints to support nominal shifts or tolerance adjustments.

Advance Quality Planning Checklist

- Customer-controlled 3-D models and 2-D print.
- Flow chart.
- Failure mode and effects analysis (FMEA).
- Control plan.
- Work instructions.
- Dimensional-visual quality requirements (DVQR; quality-specific work instructions).
- Traveler and line clearance quality record.
- Gauge repeatability and reproducibility.
- Employee training (work instructions and DVQR).
- Material specifications.
- Material certifications (ensure raw materials meet specs).
- Process parameter data sheets.
- Machine installation qualification (IQ).
- List of consumables (manufacturing agents).
- OQ protocol documentation.
- PQ protocol documentation.
- Critical-to-quality (CTQ) capability analysis and XmR summaries.
- First article inspection (FAI) dimensional review.
- Certificates of conformance (for all validated parts).

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In the course of executing an operational qualification (OQ) run, this technician will challenge the high and low parameters that were established in the quality plan.

The OEM should approve the completion report in writing prior to the first production run.

Best Practices

Standardization is as important to the validation plan as it is to the manufacturing process. With that in mind, quality manufacturers should have a validation master plan. This should include the IQ for equipment and facilities, a description of the standard OQ process and recommended sample sizes, and a definition of the PQ process in their facilities. The core of a predefined validation master plan is repeatable for every customer. The OEM's specific requirements make each plan unique.

In terms of protocols, OEMs should always take the following steps:

- Ensure the CM makes contingency plans to qualify similar pieces of equipment.
- Define and establish critical-to-function dimensions during contract review and before the CM executes IQ, OQ, and PQ.
- Clearly establish criteria for success or failure in collaboration with the CM.
- Make sure the CM writes a description of each activity and tests to those activities.

Finally, with demand for validation on the rise, make the process a friend. Learn from the data produced. Beyond the manufacturing efficiencies and the statistical confidence that will result, the validation data can be used by OEMs to develop the next generation of products. And CMs can use the data to improve process efficiency and facilitate smarter decisions in daily operations. Lower overall manufacturing costs will result.

Conclusion

Process validation is standard for almost any medical component, regardless of classification. While we've all heard stories of validations that have run amok, they can result in timely launches, production efficiency gains, reduced scrap, and improved outputs. The key to success rests on a collaborative partnership between the OEM and the CM. Clearly articulated, well-timed, authoritative communication must be the rule, not the exception.

Reference

1. *Medical Device Quality Systems Manual*, updated 6/18/09, FDA, Center for Devices and Radiological Health (CDRH); www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/PostmarketRequirements/QualitySystemsRegulations/MedicalDeviceQualitySystemsManual/ucm122439.htm

Bryan Campbell is headquarters plant manager at Mack Molding (Arlington, VT).