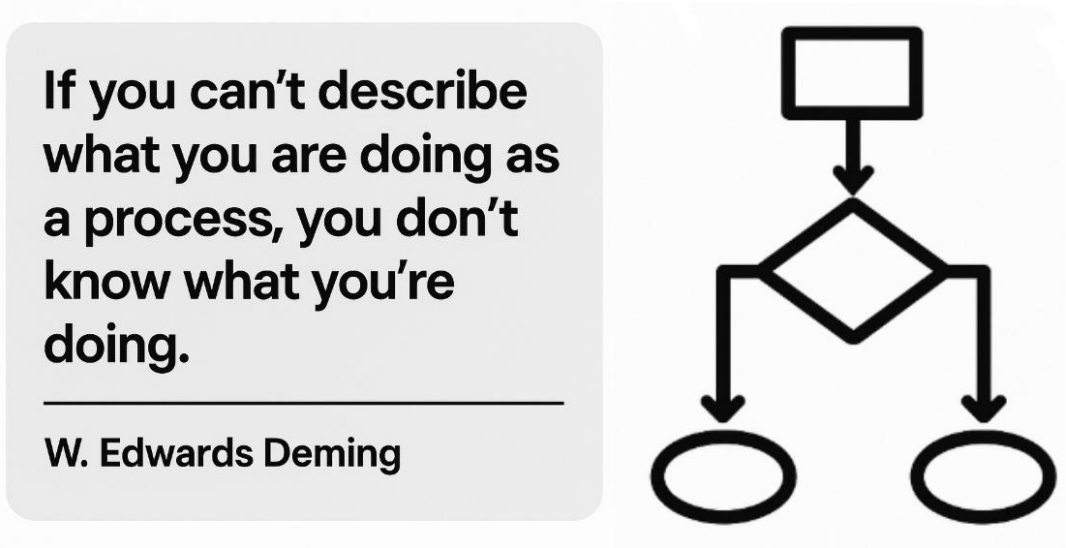
Process Validation in Medical Device Bonding: Controlling Variables

Learn how to validate adhesive bonding processes in medical device manufacturing. Minimise or eliminate variables, ensure ISO/FDA compliance, and improve reliability.

By Kevin Brownsill, Head of Learning and Development, Intertronics

Peter Swanson, MA (Cantab) Founder & Chair, Intertronics

"If you can't describe what you are doing as a process, you don't know what you're doing," said W. Edwards Deming, the man who revolutionised quality control and process improvement in manufacturing in the 1950s and 1960s.



In medical device manufacturing, and particularly in adhesive bonding, this principle is critical. A process is more than a task – it is a defined sequence of controlled steps, with specified inputs, parameters, and outputs. Without this definition, there is no reliable way to measure performance, control variation, or ensure repeatability. Furthermore, when you are establishing the manufacture of a new medical device which involves adhesive bonding, you will be validating that bonding process.

Validating the medical device bonding process

Validation means providing documented, objective evidence that the processes consistently produce products that meet their predetermined specifications and quality attributes. It's not just about proving that assembly procedure can work, but that it will work reliably and repeatably under actual production conditions – that is, with typical operators, equipment, materials, and environmental variables.

Validation is a critical, fundamental and accepted part of getting a device to market because of:

- Patient safety
- Regulatory compliance

ISO 13485:2016 Medical devices – Quality management systems – Requirements for regulatory purposes, Clause 7.5.6 stipulates that "The organization shall validate any processes for production and service provision where the resulting output cannot be verified by subsequent monitoring or measurement." In other words, since testing of adhesive bond strength is invariably destructive, the bonding process must be validated. There is a similar requirement in FDA 21 CFR Part 820: Quality System Regulation (820.75) and EU 2017/756 Medical Device Regulation.

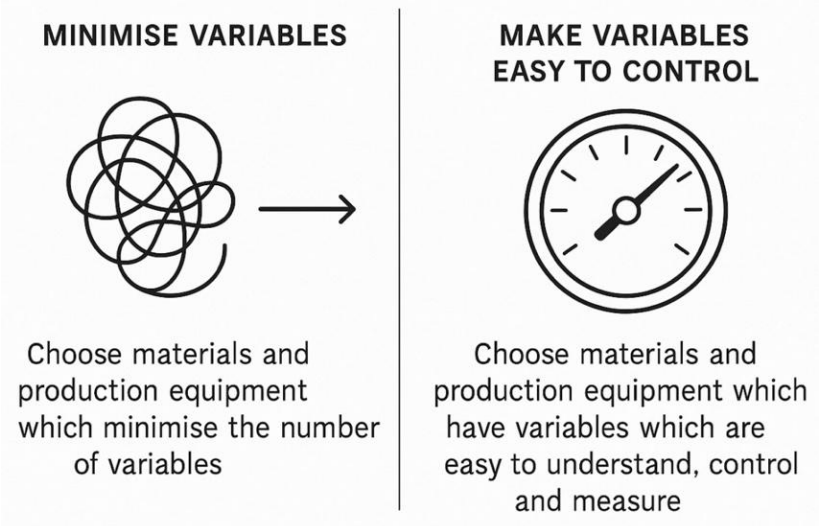
You will have written procedures specifically for the process validation itself. Each validation study needs to be planned, reviewed, and documented in a structured format. And you will have to do it all over again if there are any changes to a material, substrate or piece of production equipment. Revalidation is expensive, so the pressure is on to get it right, and for the long-term. It can be a big ask, with lots of work.

Medical device adhesive process variables

The more variables in the bonding process, the more complex and time-consuming the validation process is. Each variable will generate a validation regime involving evaluations on how to control it, establishing allowable parameters, and performance tests based on the minimum and maximum of the parameter limits. If there is more than one variable in a process (e.g. both curing light intensity and exposure time), then it gets more complicated, as you will look at varying combinations of the variables. You will also want to stress test worst-case scenarios.

In consequence, the product design and assembly process development should have two objectives in mind to help with validation:

- Choose materials and production equipment which minimise the number of variables
- Choose materials and production equipment which have variables which are easy to understand, control and measure



A simple example of the first point would be to choose an adhesive which is single part (1K), rather than two parts (2K). This removes an entire step (mixing) from the process, along with the attendant variables (mix ratio, mix homogeneity).

Assuming you have a design, assembly parts and a specified adhesive, then the bonding process can be broken down into these stages:

- Substrate/surface preparation
- Adhesive preparation
- Application/dispensing
- Assembly/mating
- Cure
- Inspection and testing
- Documentation and traceability

Bonding process characterisation
Once the materials and production equipment has been identified, then you will undertake a process characterisation – the systematic investigation and analysis of the manufacturing process to understand how process variables influence the final product. Variables which are Critical Process Parameters (CPPs) (e.g., mix ratio, dispense pressure, UV light intensity) have a direct and significant impact on the product's quality. These are the variables that must be tightly controlled during production to ensure reliable outcomes. Correspondingly, Critical Quality Attributes (CQAs) are the measurable physical or performance characteristics of a product (such as bond strength or cure completeness) that must remain within predefined limits to ensure product safety and efficacy. The goal of process characterisation is to map the relationships between CPPs and CQAs, enabling robust process control that ensure consistent manufacturing of high-quality, compliant medical devices.

Eliminate or control process variables and CPPs
The balance of this paper looks at examples of medical device adhesive variables and CPPs which can be eliminated or tightly controlled. It is by no means exhaustive.

Adhesive preparation – mixing
Mixing a multi-part adhesive, paste, or solution can be a significantly variable process. Mixing by hand is inherently inconsistent. Poor wetting of powders or dispersion can lead to over-mixing or mixing for longer periods to overcome these issues. Over-mixing can impact the compound in terms of causing stress, adding heat through friction, and extended times could reduce the usable life of an adhesive that needs to be applied.

One solution is to use a non-contact "planetary" mixer, which uses a combination of rotation and revolution to mix liquids, pastes, powders and fillers. This includes engineering compounds and pharmaceutical or cosmetic formulations and dispersions. They mix, disperse and degas materials in seconds to minutes in a sealed or lid-less container such as a jar, beaker, syringe tube or cartridge. The non-contact mixing principle makes it possible to combine compounds from very small amounts such as 0.5ml to large production scales. There are models which include software and connectivity options to control, monitor, and record mixes and mixing parameters.

Figure 1 – A **Thinky ARE-312** *industrial non-contact "planetary" mixer homogenously mixes liquids, pastes and powders in a completely replicable way*

These machines are programmable with process variables like speed and time. Once a "recipe" has been established as producing a fully homogenous mix, then it will replicate that mix every time.

Application/dispensing – quantity

The accuracy of a dispensing process can be disrupted by minor changes in the rheology of the adhesive. Fluctuations in viscosity caused by batch-to-batch variation (within acceptable limits) or ambient temperature changes can pose problems for some dispensing techniques, such as pneumatic time/pressure – a fluid dispensing method where compressed air pressure is applied to a syringe or reservoir, forcing the adhesive out through a dispensing needle. Non-Newtonian liquids, like most adhesives, will increase in viscosity (thicken) in colder conditions and lower in viscosity (thin) in warmer ambient conditions, perhaps observed between stores and production line unless a period of conditioning is observed. Another issue is the variability in dispensed quantity as the syringe barrel empties. The amount of compressible air in the system increases accordingly, which means that the same pulse of compressed air from the dispensing controller has a lesser, delayed impact on the liquid, resulting in smaller deposits.

A basic time/pressure dispensing process is unable to dynamically alter the time or pressure settings to overcome a change in viscosity or other effects. If the parameters are left unchanged, more or less material could be dispensed. It can therefore become incumbent on the production operator to conduct regular checks and make necessary adjustments to keep the line within acceptable limits. This is another significant process variable, which is difficult to predict and control.

An application that demands tight dispensing tolerances should consider a viscosity independent volumetric dispensing pump. The preeflow range of **eco-PENs for single**

component and eco-DUOs for two-component materials provide dial-in shot size and flow rate capability with an accuracy of ±1%, >99% of the time. The system can be easily calibrated and operated via an intuitive touchscreen interface, with PLC integration capability and options for inbound and outbound material pressure monitoring for even more process control.

Figure 2 – The preeflow ecoPEN XS 180 can dispense adhesives accurately down to 0.00025 ml using volumetric positive displacement

Materials are dispensed through a sealed stator with a motorised rotor, meaning that even very low viscosity materials can be easily controlled. The progressive cavity "Endless Piston" principle ensures material is extruded stress-free and consistently without pulsing, with shot sizes as low as 0.25µl (250nl) and flow rates up to 60ml/minute.

Application/dispensing – positioning

Positioning your deposit of adhesive in a repeatable manner is an important factor in creating a consistent manufacturing process. Adopting a robot for dispensing processes removes operator variation whilst significantly increasing accuracy and throughput. Deskilling repetitive tasks releases skilled operators to work on more valuable assignments.

Automation doesn't have to break the bank. Three- and four-axis benchtop and gantry dispensing robots are readily available and costs can be less than £10,000. They are easy to program via a teach pendant or PC using an intuitive camera positioning and alignment option. Accurate movement over areas from 200mm x 200mm to over 1m are available, with a repeatability as low as 8µm in each axis. The robot's payload capability means that any

dispensing systems can be attached and gives potential to add further equipment such as UV light curing depending on the application.

*Figure 3 – **Fisnar dispensing robots** enable the accurate and repeatable application of materials during production*

Adhesive cure – thermal

For heat-cured systems (e.g. some epoxy chemistries), temperature uniformity, ramp rates, dwell times, and cool-down profiles are all critical process parameters (CPPs). Variations of just a few degrees can change reaction rates, alter crosslink density, or induce residual stress in the adhesive joint. The challenges include oven calibration and uniformity—ensuring all parts experience the target temperature profile, even with varying part geometries or load sizes. The energy dose (total heat energy delivered, i.e. temperature x time) must be validated to ensure complete cure without thermal degradation. Even minor process drift can lead to under-cure (poor strength, chemical resistance) or over-cure (brittleness, reduced toughness).

Adhesive cure – moisture

Systems that cure through reaction with moisture in the air or on surfaces (e.g. cyanoacrylate adhesives, silicones) will require a sufficient and stable ambient relative humidity (RH); fluctuations can alter cure rates and depth of cure. These adhesives are sensitive to uncontrolled environmental changes— even seasonal variations in the factory's environmental control system can introduce inconsistency. Sometimes the environment in a cleanroom will have insufficient RH to effect cure. RH is a CPP with these adhesive types.

Adhesive cure – UV/visible curing light

Successful UV light curing is dependent on the correct wavelength(s) of light and the dose of energy. Similarly to heat curing, the minimum energy dose (total light energy delivered, i.e. light intensity x time) must be established and validated and is a CPP. Broad-spectrum lamps (mercury arc lamps) have been used in UV light adhesive curing applications for decades. The degradation of the power output of the bulb over time/use is well-understood, albeit not necessarily predictable. This is a significant process variable, which can require a lot of resource to manage. Processes using broad-spectrum lamps are typically validated with a margin of safety, which aims to maximise the life of the bulb and understand where the lower limits are in order to change the bulb at appropriate intervals.

A radiometer is a measurement device for the UV output of a light source and should be used for initial setup, process validation, and at regular points during manufacture. The measuring sensor is placed either directly at the output of the lamp or positioned at the bond line to measure the intensity of UV light that the adhesive will receive for curing.

*Figure 4 – A **UV radiometer** designed for measuring the intensity of the curing light is essential for process control and data collection*

Adhesive cure – LED UV curing

Since the late-2000s, LED-based UV curing lamps have emerged onto the market. While initial intensities and illumination areas were modest, the process variability reduction potential was immediately evident. LEDs don't have to warm up, so they can be turned on and off instantly, whereas broad spectrum lamps need time to warm up and typically stay lit for a whole shift/day - wasting energy and bulb life. The output of LEDs remains stable for many thousands or tens of thousands of hours compared to one or two thousand hours of a broad-spectrum lamp. LED-curing adhesive chemistry and curing equipment has now developed to a point where LED is the default first choice for new applications.

*Figure 5 – **modern LED-based curing lamps** combine high intensity LED UV light with a consistent, uniform output over a large area (in this example, up to 2,100 mW/cm² over 127 mm x 127 mm)*

Adhesive cure – distance from UV light source

One of the key variables to control, in addition to any light degradation, whether that be through aging or lens contamination, is the distance between the light source and the adhesive. Keeping the bond line at the same distance from the lamp is imperative to achieving consistency – something that is very difficult to achieve in a handheld application, for example.

The intensity of UV light reduces by the inverse square rule. The inverse square rule simply means that as the distance from the UV lamp increases, the intensity of UV light decreases proportionally to the square of that distance. I.e. if you double the distance, the intensity becomes a quarter of its original strength. It is therefore essential that an appropriate light source is used to achieve the appropriate dose over the desired area.

Once a lamp has been selected, it should be mounted in such a manner as to allow air flow to avoid overheating, at an appropriate distance from the adhesive being cured. The part on which the adhesive is dispensed should be held in tooling designed for the purpose of achieving the same distance and position under the lamp in a repeatable manner. Tooling can take many forms, including CNC machined aluminium or PTFE jigs or 3d printed versions. Care should be taken in the design of jigs to ensure the light path to the bond line is not obscured or shadowed.

Adhesive cure – control

Are you really in control of the cure without measured energy? When curing is driven by a measured energy input (heat, UV and/or visible light), the total dose delivered can be defined, monitored, and validated. In contrast, when relying solely on ambient conditions, the cure is at the mercy of environmental variability unless those conditions are tightly measured and actively controlled. It isn't always easy to determine the cure state of a two-part epoxy adhesive which is mixed at the point of dispense and left at ambient temperature to cure; it takes some days to achieve enough cross linking to allow validation testing.

For regulated medical device manufacturing, the burden is to prove – through validation data – that all cure variables are consistently maintained within defined limits, regardless of whether the cure comes a controlled source of energy or from environmental conditions.

Inspection and testing - visual aids

Ensuring correct adhesive application in a medical device bondline can be challenging, especially when both the adhesive and the substrates are transparent. To overcome this, many medical device adhesives are formulated with fluorescent indicators, which make the adhesive visible under a UV-A inspection lamp (black light). This fluorescence can also be detected by optical sensors, enabling automated adhesive inspection directly on the production line. In high-volume medical device assembly, this approach provides a fast, reliable go/no-go check that improves quality control and reduces the risk of undetected adhesive gaps.

Traditional chemistry produces a blue fluorescence; however, this lacks contrast with some medical plastics which also naturally fluoresce blue, making it hard to visually or automatically detect the adhesive “glow” at the point of inspection. Ultra-Red fluorescing adhesives fluoresce bright red providing a vivid contrast that permits accurate bond-line inspection. The red fluorescence does not absorb the same light energy wavelengths as those used to cure the adhesive, resulting in faster and deeper light cures when compared with the same adhesives containing blue fluorescence.

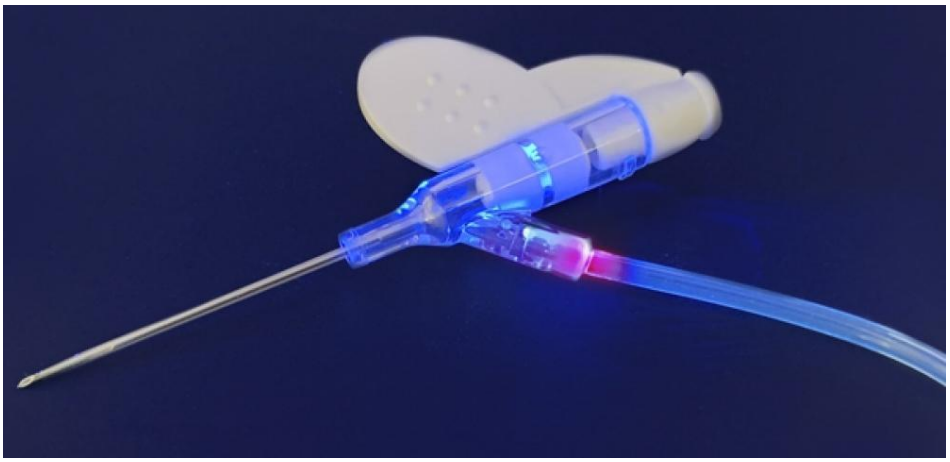


*Figure 6 – **Dymax Ultra-Red adhesives** fluoresce bright red when exposed to low-intensity “black” light at 365 nm facilitating visual inspection*

Documentation and traceability

It goes without saying that adhesive batch codes or lot codes must be both highly visible and easy to find and recorded against manufacturing batches. Many pieces of production equipment now have I/O capability which will allow you to automatically record process events or parameters, as Industry 4.0 turns the bonding process from variable-prone into a fully monitored, traceable, and auditable operation.

Conclusion

In adhesive bonding for medical device manufacture, process validation is not just a regulatory formality, it's a fundamental risk mitigation strategy. Each stage of the adhesive process, from mixing through dispensing to cure, contains variables that, if uncontrolled, could lead to failure modes that are difficult or impossible to detect through final inspection. By proactively eliminating variables where possible, and tightly controlling those that remain, manufacturers can dramatically reduce the scope and cost of validation while increasing long-term process reliability.

The key to success lies in deliberate process design: selecting adhesives and equipment that minimise complexity, building in automation to reduce operator variability, and designing fixtures and tooling that enforce repeatability. Technologies like robotic dispensing, volumetric dispensing and LED UV curing aren't just productivity enhancers - they're enablers of compliance, product quality, and patient safety. An investment in these technologies early in process development pays dividends when it comes to validation efficiency, process robustness, and speed to market.

About the authors

Kevin Brownsill is Intertronics' Head of Learning and Development. He has over 25 years in adhesives, including experience in formulation and manufacturing, quality, sales, and technical support. He is a CIPD accredited educator and drives our learning strategy.

Peter Swanson is the Founder and Executive Chair of Intertronics, with over 40 years of hands-on experience in supplying the technology manufacturing sector. An award-winning technical author, he has written extensively about adhesives, and the application and curing of them – including dispensing, robotics and UV light curing.

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INTERTRONICS
Station Field Industrial Estate
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Oxfordshire
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England
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www.intertronics.co.uk

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