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Compliance Corner: These Are The 6 Top Process Validation Mistakes Made By Firms, According To An FDA Investigator

by Shawn M. Schmitt

US FDA investigator Ben Dastoli sees medical device manufacturers making the same process validation mistakes over and over. Here are the top six validation problems he sees.

When US Food and Drug Administration investigator Ben Dastoli inspects a medical device company, he typically sees firms making the same process validation mistakes over and over.

"There are six process validation issues that have been common this year – they just continuously seem to happen," said Dastoli, who is based in Division 1 within the Office of Medical Devices and Radiological Health Operations (*OMDRHO*), within the FDA's Office of Regulatory Affairs.

At MedCon 2019 in Cincinnati, OH, Dastoli listed those issues and commented on each. He said manufacturers fail to:

1. Identify all processes that require validation. "As we as investigators are doing our facility walk-through, we're reviewing manufacturing instructions and we're looking at different processes that may require validation. Processes that seem to be commonly missed are gluing, layer-crimping and reagent-mixing. And keep in mind that if *destructive testing* is the only way to verify that specifications are met, then it's most likely a process that requires validation.

"So, I always encourage all the managers at a company to walk the entire manufacturing floor – it's a good way to identify these processes. A lot of times when investigators are pointing out these problems, I think the quality manager is just as surprised to see some of the stuff that is going on with their products.

"Another process where we see process validation issues is in the manufacture of automated soldering PC boards. When we ask if the process has been validated, the common response is, 'We 100% verify, therefore, there's no need to validate.' Verification activities usually include visual inspections, *burn-in*, X-ray and point-of-connection testing. But none of these are testing the solder connection. So, what else do you need to consider?

"Did you identify the risk of solder failure during design? Can the soldering joints withstand operating conditions such as vibration, heat, expansion and contraction? And are your inspections designed to capture failure modes, such as loose connections?

"So, does your automated soldering process need to be validated? The answer is, probably."

2. Identify all process variables. "Recently I was inspecting a firm that had an automated printing process. The equipment used various dyes depending on the wire gauge terminal connections. The dyes had different dials on them that could be adjusted by the operator, from one to 10, and that determined the crimp life – which also affects the crimp strength.

"Yet the firm did not consider this variable at all during validation studies. Therefore, they're inadequate validation studies. That whole situation was no good."

3. Select statistically based sample sizes. "This activity must be commensurate with the risk level associated with the failure. For example, selecting a plan allowing for one failure out of 35 for a sterile packaging operation is probably not acceptable.

"But what would be acceptable? Well, that's always the question. We're always evaluating this during an inspection.

"The validation method must ensure that predetermined specifications are consistently met, and the challenge is to repeat it enough times to ensure that the results are meaningful and consistent. Keep that in mind."

4. Identify and consider worst-case conditions. "For example, your vat size during a validation process – such as clean-treating or heat-treating – should be considering the term 'maximum load size' for processing. So, if you're validating an ultrasonic clean process and it was validated using a load size of 30, we as investigators wouldn't expect to see large load sizes during the manufacturing process, which could pose additional challenges to a

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05 Jun 2017

process.

"Another example I recently encountered was an automated soldering operation of a PC board. The process was validated using a single-sided PC board. Well, the firm also manufactured double-sided boards in the same system – which means it had to undergo the process twice, so they didn't really challenge it. So, it wasn't the worst-case scenario anymore.

"And remember: Consider density, proximity and complexity when validating a soldering operation."

This is Compliance 360°, a podcast series from *Medtech Insight* on US FDA compliance and enforcement issues. In this ninth installment, we interview former FDA investigations branch director Ricki Chase, who explains why your device firm needs to be on the ball when it comes to process validation activities and offers tips for best practices.

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5. Identify variations in raw materials, components and equipment. "Let's say you're validating an ultrasonic welding operation for a company that uses lid seals. You should identify the variability and the fitness of the cups and the lids to understand the *tolerance stack-up* and evaluate accordingly.

"Additionally, you need to determine your gauge, reliability and repeatability to fully understand your worst-case stack-up conditions. For example, if a measuring tool has a 5% variability, this should be considered when establishing your acceptance criteria."

6. Address failures found during validation. "As investigators, we often come across problems that are simply dismissed for reasons such as operator error. Well, did you really investigate and determine that operator error is the root cause? And, has your sample criteria really been met now that you can eliminate certain samples? And, if you dismiss your results, do you need to make corrective actions or possibly need to revalidate?

"Those are questions you need to ask yourself."