Monitoring Validated Processes

The Context
Device manufacturers, as part of operating a validated process in §820.75(b), monitor the process input parameters to ensure they remain within the limits set during process validation. When the process input parameters change values, the monitoring allows the operator to bring them back into the limits. By monitoring and controlling the input parameters, the operator ensures the validated process produces only conforming product.

The Warning Letter
FDA sent this February 18, 2016 Warning Letter to C World KSG Corporation, a manufacturer of contact lenses, located in Carmona, Philippines. The Warning Letter resulted from an FDA inspection.

The Issue Cited
The Warning Letter includes a citation about operating a validated process. Because the FDA redacts some of the specific details, the citation is a paraphrase. The Warning Letter says the company validated a process and defined three process parameters. "However, the required process parameters are not met for [redacted] lots of contact lenses manufactured in [redacted] and shipped to U.S. customers."

The firm responded and FDA said, "The response also indicated that your firm will conduct a review of the [redacted] test and other methods to ensure adequate validation, as well as conduct personnel training. However, the response did not provide this updated validation documentation for review. Additionally, your response did not include a risk assessment for product manufactured outside of specified validation parameters."

The FDA said that the response did not include a risk assessment of the product manufactured when the process parameters were outside the specified limits. This is very important, since the basis of a validated process is that when the input parameters are within limits the process produces only conforming product. However, when the input parameters are outside of their limits the process no longer offers a high degree of assurance of conforming product. In this case, the company may have shipped contact lens that are out of specification.

The Warning Letter includes the statement, "Given the serious nature of the violations of the Act, contact lenses manufactured by your firm are subject to refusal of admission under section 801(a) of the Act, 21 USC §381(a), in that they appear to be adulterated. As a result, FDA is taking steps to refuse entry of these devices into the United States, known as 'detention without physical examination', until these violations are corrected."

The Requirement
The Quality System Regulation requires, in §820.75(b), "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". In addition, §820.75(b)(2), requires, "For validated processes, the monitoring and control methods and data, the date performed, and,

where appropriate, the individual(s) performing the process or the major equipment used shall be documented".

Recommendations

The first recommendation prevents the QMS problem by ensuring the procedures have the necessary contents.

- The process validation procedure includes a requirement to identify the process parameters, their limits, and their action levels. [820.75(b)]
- The process validation procedure requires that this information (parameters, limits, and action levels) be included in the work instruction for operating the validated process. [820.75(b)]
- The work instruction for operating the validated process explains how to monitor the parameters, states the monitoring interval & frequency, explains how to control the parameters, and describes how to record the data.

The second recommendation ensures data review as part of the Device History Record, DHR.

- §820.184(d) requires the acceptance records demonstrating device manufacture in accordance with the DMR.
- §820.80(d)(2) requires review of the documentation and data before its inclusion in the DHR.

The third recommendation uses the internal quality audit program to detect any issues. Check a sample of the validated process operation records to ensure they are complete, correct, and legible.

- The monitoring and control methods
- The monitoring and control data
- The performance date of the validated process
- The name of the individual performing the process
- The record demonstrating that the individual who performed the process was qualified
- The major equipment used to operate the process