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1 Regulatory Basics of Process and Design Validation

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Introduction

Countless US Food and Drug Administration (FDA) warning letters and inspectional observation forms are issued by the agency each year, with many citing a failure to ensure that processes were validated or revalidated. While it is true that corrective and preventive action (CAPA), complaint handling, production and process controls, and design controls are also violations cited frequently by the FDA, process validation is the most challenging to address.[1]

Process validation was sixth on the list of reasons for issuing FDA Form 483s. Inadequate process validation was cited 86 times in 2022, or three out of the 10 most-cited violations.[2] The problem may lie in the definition of "validation" in the agency's Quality System Regulation (QSR), 21 CFR Part 820. Section 820.75 of that rule explains that validation is confirmation by examining and providing objective evidence that the requirements for a specific intended use can be consistently fulfilled. The QSR also divides process validation and design validation into two separate entities: "Process validation means establishing by objective evidence that a process consistently produces a result or product meeting its predetermined specifications."[3] The rule further says that "design validation means establishing by objective evidence that device specifications conform with user needs and intended use(s)."[4]

The definitions lack specificity, and companies must interpret the regulation independently. Even more head-scratching is that "process validation" is defined differently in a 2011 FDA guidance document as the "collection and evaluation of data, from the process design stage through the commercial production, which establishes scientific evidence that a process is capable of consistently delivering a quality product."[5]

The FDA's 2011 guidance updated a 1987 process validation guidance from the agency. Thus, the 2011 document replaces the 1987 version, but only for human drugs, veterinary drugs, biological and biotechnology products, finished products and active pharmaceutical ingredients (APIs or drug substances), and the drug constituent of a combination product. The 2011 guidance does not cover medical devices; rather, guidance for devices was provided in cooperation with the Global Harmonization Task Force (GHTF), the precursor to the International Medical Device Regulators Form (IMDRF).[6]