Production and Process Controls

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Hello, my name is Vidya Gopal, and I'm a Consumer Safety Officer in the Division of Industry and Consumer Education at FDA's Center for Devices and Radiological Health. In this presentation, I'll discuss the topic of Production and Process Controls. I have experience in developing processes and the controls associated with them when I worked as an engineer in industry. I have also worked as a compliance officer at the FDA and understand the importance of production and process controls in producing a quality product. I hope to bring a balanced perspective from both sides to my discussion on production and process controls.

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Production and process controls are a key part of the Quality System for medical device manufacturing. They help ensure that you manufacture products that meet pre-determined specifications and build the products you said you were going to build.

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Here are the learning objectives for this module. By the time we are finished, I will (1) explain how production and process controls relate to the overall Quality System, (2) describe the general aspects of production and process controls, (3) describe the aspects of inspection, measuring, and testing equipment, and (4) define the concept of process validation.

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Let us start at this diagram of the Quality System. This shows the 7 major subsystems of the quality system, with management at the center of it all. Today's talk will focus on the Production and Process Controls subsystem.

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Under the production and process control subsystem, we will cover production and process controls; inspection, measuring and test equipment; and process validation.

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Let's begin with the topic of production and process controls, which is outlined in the Code of Federal Regulation under 21 CFR 820.70.

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Manufacturers need to develop, conduct, control, and monitor production processes to ensure that a device conforms to its specifications.

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Let us consider an example of a common process - package sealing. In order for the package to be sealed correctly, the criteria for temperature, pressure and time must be established. And this process then has to be monitored to make sure it is functioning correctly.

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If deviations from device specifications could occur as a result of the manufacturing process, there are 5 things you are required to do.

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One, have instructions, standard operating procedures or SOPs, and methods that define and control the production. Two, include how the process will be monitored and controlled during production. Three, include the reference standards or codes against which to compare the process. Four, approve processes and equipment for the specific purpose. And finally, define the criteria for workmanship. This may be samples or photos of acceptable and unacceptable product.

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In dealing with production and process changes, manufacturers should establish procedures for changes to a specification, method, process or procedure. You should verify, or where appropriate, validate these changes before implementation. And these changes need to be approved. Document change control addresses the administrative aspects of a change. Design and production and process change controls involve the technical work associated with the change, mainly proving with objective evidence that the change will not affect the ability to produce a device that meets user needs and intended uses consistently. The main intent is to maintain control throughout.

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We are going to talk about environmental controls next. If environmental conditions have an adverse effect on product quality, then you need to have environmental controls. The type of controls or the changes to these controls are based on risk.

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Typical environmental conditions that may require control are: particles, humidity, air pressure, flow, filtration, and ionization, temperature, lighting, sound and vibration.

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Let us consider a Rinsing process. If you are going to be using water to rinse the product, then you need to know the source of that water, to help you determine the type of controls required to make sure there are no harmful residues left behind.

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Periodically inspect environmental control systems to verify that the system, including equipment, is adequate and functioning properly. Inspection of the control systems allows manufacturers to detect issues before substantial product impact can occur. These environmental control activities need to be documented and reviewed.

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For example, review the humidity charts in the facility to make sure they are within the operating window. Check the electrostatic discharge, or ESD, station grounding daily to prevent inadvertent ESD damage.

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Next, we're going to talk about Personnel. Manufacturers need to establish and maintain requirements for the health, cleanliness, personnel practices, and clothing of personnel. This is especially important if contact between people and product or work environment could have an adverse effect on the quality of the device.

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Companies typically have clothing restrictions or require the use of uniforms, especially with respect to cleanrooms or electronic products. Examples of appropriate clothing are hair nets and smocks. Most manufacturing facilities will have their employees use hair nets and smocks, so that no contaminant gets onto the product. Another common requirement is to not permit food or drink in manufacturing areas.

And finally, companies often have procedures on how to address illnesses while at work, such as respiratory illness or skin conditions. The point to note here is that FDA is interested in how you protect your medical device during manufacturing. The protection of the employees is under the purview of another government agency, the Occupational Safety and Health Administration, or OSHA.

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Before going forward, I want to provide a short background on the preamble to the Quality System Regulation. When proposed rules are published, stakeholders have an opportunity to comment and ask questions. FDA then responds to those comments and questions in the preamble to the regulation. The preamble is very important as it explains the intent of FDA at the time the rule was published. For more information about the preamble to the quality system regulation, please watch the CDRH Learn module on the Quality System Overview.

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Preamble Comment #129, contains some clarification regarding personnel. It says that the requirements will not permit unclean or inappropriately clothed employees, or employees with medical conditions, to work with devices where these conditions could have an adverse effect on product quality. It re-iterates that the procedures must also address acceptable clothing, hygiene, and personnel practices, if contact between personnel and product or environment could have an adverse effect on product quality.

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There needs to be procedures that address maintenance and other personnel who are required to work temporarily under special environmental conditions. They need to be appropriately trained or supervised by a trained individual.

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For example, when maintenance workers or janitorial staff enter a cleanroom, we need to make sure that they follow the procedures of the cleanroom like gowning and entering, bringing in materials and such.

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Next is Contamination Control. Establish and maintain procedures to prevent contamination of equipment or product by substances that could have an adverse effect on product quality.

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One of the examples that comes up often is cardboard boxes in cleanrooms. If you deem that the particulate from the cardboard boxes is going to contaminate your product, then you should not have cardboard boxes in the cleanroom. You make the determination of what affects your product and have steps to mitigate it.

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The preamble provides some more clarification on cleaning. Contamination control must include establishing and maintaining adequate cleaning procedures and schedules. It makes the connection between Production and Process Controls and Personnel in 820.25. Personnel requires that employees should have a thorough understanding of their job functions including cleanliness and sanitation procedures.

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21 CFR 820.70(f) addresses Buildings. Buildings should be of suitable design and contain sufficient space to perform necessary operations, prevent mix ups, and assure orderly handling.

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Next is Equipment. Equipment is the broad category of items necessary to produce a product. All equipment used in the manufacturing process must meet specified requirements and be appropriately designed, constructed, placed and installed to facilitate maintenance, adjustment, cleaning and use. This means that all equipment is subject to an installation qualification. The extent of the installation effort can be based on Risk.

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You need to establish and maintain schedules for the adjustment, cleaning and other maintenance of equipment to ensure that manufacturing specifications are met. A good place to start is with the equipment manufacturer's instructions for maintenance activities and intervals, and then tailor it to your specific operation. These maintenance activities should be documented including the date and individuals performing the maintenance activities.

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Once you establish the maintenance schedules, then conduct periodic inspections to ensure adherence to the maintenance schedules and document inspections including the date and individuals conducting the inspections.

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Post any inherent limitations or allowable tolerances visibly on or near the equipment requiring periodic adjustments or make this information readily available to the persons performing the adjustments. This requirement emphasizes that personnel using the equipment need to know what is and is not allowable. Every equipment dial doesn't necessarily have to be used to its full range.

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We will next talk about manufacturing material. Let's first review the definition. Manufacturing material is defined as any material or substance used in or used to facilitate the manufacturing process, a concomitant or byproduct material produced during manufacturing that was not the design or intent of the manufacturer.

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Comment 26 in the Preamble helps to clarify this definition. "Concomitant material" refers to those material or substances that naturally occur as part of the material or during the manufacturing process which are intended to be removed or reduced in the finished device.

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If the manufacturing material is expected to have an adverse effect on product quality, then establish and maintain procedures to remove the manufacturing material.

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For example, the allergenic or adverse proteins that occur in natural rubber latex components of medical devices are concomitant materials. These must be reduced or removed from the finished devices.

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The Use and Removal of Manufacturing Material may be part of another procedure. For example, in a coating process, Use may be part of a mixing procedure. Procedures should have an associated data form for recording values. And finally, SOPs, data forms and purchasing requirements are part of the device master record.

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We will next talk about Automated Process. If a computer software is used as part of production or the Quality System, then you should validate it for its intended use. This means if a system is capable of doing 100 different functions, you do not need to validate all 100 of them.

Validate for your intended use and according to an established protocol. Software changes must be validated before approval and issuance. This requirement is difficult to meet if systems are set up to automatically download updates from vendors. Another common mistake is equipment maintenance suppliers that update software during their preventive maintenance visits. Finally, document your validation activities and results.

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This slide lists several examples of automated processes. These include: an injection molding process, statistical process control software, complaint tracking software, inventory tracking, and document control.

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In the next section, we will talk about Inspection, Measuring and Test Equipment as outlined in 21 CFR 820.72.

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Ensure all inspection, measuring, and test equipment is suitable for intended purposes and capable of producing valid results.

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Why do we need to control equipment? Inspection, measuring and test equipment is used to evaluate whether product is conforming or nonconforming during design, process validation and routine production. The equipment must provide valid results if the evaluation is to be meaningful.

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We need to make sure equipment is routinely inspected, checked, maintained and calibrated. These procedures should also address equipment handling, preservation, storage. These activities need to be

documented. One thing to keep in mind is that when using an electronic system to track calibration status, that system is subject to 820.70(i) - automated process validation, as discussed earlier.

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Calibration is further addressed in the regulation. A manufacturer is required to establish procedures, including specific directions and limits for accuracy and precision. To produce valid results, the equipment should be accurate and precise. Accurate means how close the measured value is to the actual value. Precise means the proximity of multiple measurements to each other - for example, how close they are to each other. There are different ways to establish equipment capability. "Gage Repeatability and Reproducibility", or Gage R&R, is one of the ways to do it. It evaluates variability between people and between equipment to understand typical performance.

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The procedures must include provisions for remedial action to reestablish the limits and evaluate for adverse effect on device quality. When you are evaluating for adverse effects, consider all usage since last known good condition. Records also need to include "as found" condition when submitted for calibration in order to recognize need for remedial action.

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Calibration is always performed against a known physical reference also known as the calibration standard. Calibration standards must be traceable to national standards, international standards, or independent reproducible standards. Independent reproducible standards apply if the manufacturer of the equipment provides a standard for calibration purposes.

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Calibration records must include equipment identification, calibration dates, individuals performing each calibration, and the next calibration date. These Records must be posted on or near equipment. Proximity of records facilitates operator verification that equipment is in calibration and ok to use.

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The next section is Process Validation covered by 21 CFR 820.75.

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Process validation means establishing by objective evidence that a process consistently produces a result or product meeting its predetermined specifications.

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Since process validation is a vast subject and a very important one, we have an entire module dedicated to that. Please visit our CDRH Learn Module on process validation for more information.

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Additional information on the Quality System, its Preamble, and the FDA Inspection Guide may be found at the links on this slide.

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Let's summarize this module. First, we showed the relationship of production and process control to the overall Quality System. We then discussed the general aspects of Production and Process Controls

and described the aspects of inspection, measuring, and testing equipment. And finally, we introduced the concept of Process Validation.

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In concluding this presentation, I now ask you to take on the following Call to Action:
Establish your Production and Process Controls so you may manufacture products that meet your specifications.

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This presentation and other helpful videos and educational resources may be found at CDRH Learn. We encourage you to use these and other industry education resources we've developed especially for you, as shown on this slide. Of note, for comprehensive regulatory information, please contact CDRH's Division of Industry and Consumer Education. We look forward to helping you. Thank you for watching this program.

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