

Production and Process Controls, Part Two

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Hello, my name is Vidya Gopal, and I am a Consumer Safety Officer in the Division of Industry and Consumer Education. This presentation, Production and Process Controls, Part 2, will address the topics of Acceptance Activities, Handling, Storage, Distribution, and Installation. When I worked in the cardiovascular industry, I developed processes and the controls associated with them. I also worked in FDA's compliance group for medical devices and understand the importance of process controls in producing product. I hope to bring a balanced perspective from both sides to my discussion on production and process controls.

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I encourage you to view the companion CDRH Learn module, Production and Process Controls. A link to this module is listed on this slide.

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The learning objectives for this module are to review the purpose of production and process controls subsystem and to describe the aspects of Acceptance Activities, Handling, Storage, Distribution, and Installation. Throughout this presentation, for each topic, we will first discuss the regulatory requirement, then discuss implementation strategies, and then conclude with some examples.

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As mentioned in the previous module, Production and Process Controls, subsystem is a key part of the Quality System for medical device manufacturing. This subsystem helps ensure that you manufacture products that meet specifications and build the products you said you were going to build. Manufacturers need to develop, conduct, control and monitor production processes. They also need to validate or fully verify processes to ensure that a device conforms to its specifications. Manufacturers must also control the product and its environment throughout handling, storage, distribution, and installation.

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The previous module covered the basics of production and process controls from Subpart G that included production and process controls, inspection, measuring and test equipment as well as a brief introduction to Process validation. In this module, we will focus on Subparts H and L. The table on this slide shows the titles and regulation numbers that we will review in this presentation.

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We will start with subpart H, which includes acceptance activities as outlined in Title 21 CFR 820.80. First, let's discuss the requirements for general Acceptance Activities. The manufacturer must have procedures for acceptance activities, which include inspections, tests and any other verification activities that are necessary.

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Receiving acceptance activities are outlined in 21 CFR 820.80 b. This section provides for acceptance of incoming product which may involve some form of testing or inspection. The manufacturer must establish and maintain procedures for acceptance of incoming product. Make sure to use a risk-based approach and strike a balance between the purchasing controls and acceptance activities for controlling

supplied product and service. You must keep documentation of the acceptance or rejection of incoming components. Often, FDA investigators will note rejects during an inspection and will follow up to find out what happened to the rejects, and possibly follow up on vendor notification and Corrective and Preventive actions, or CAPA, as applicable.

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Next, as product is made and it moves through the manufacturing process, we will deal with In-process acceptance activities. Requirements for In-process acceptance activities are outlined in 21 CFR 820.80 (c). This section provides for testing or inspection of in-process-devices to make sure they meet specifications. The manufacturer must establish and maintain procedures for in process product. This calls for work in-process, or W-I-P, devices to be controlled. That means not routed for further manufacturing until all acceptance activities have been completed. Usually the earlier you identify a problem, the easier it is to correct and the less it will cost. If you identify a problem in the initial steps of manufacturing, it is easier and cheaper to rectify than if you catch the same problem at final inspection.

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Next are Final acceptance activities as the product moves to the end of the manufacturing process. Requirements for Final acceptance activities are outlined in 21 CFR 820.80 (d). This section provides for testing or inspection of finished devices before they can be released for distribution. Procedures must ensure that each production run, lot or batch meets acceptance criteria. Devices must be controlled until they have been released for distribution.

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Before releasing finished devices for distribution, make sure that all manufacturing, testing and inspection steps required by the Device Master Record, or DMR, have been completed and documented by reviewing the Device History Record, or DHR. Also, make sure that the person designated to release product for distribution authorizes the release, and that the release is documented with the designated person's signature and date.

As stated before, the FDA investigators may note rejects during an inspection and will follow up to see what happened to those rejects. It is essential to keep careful documentation and be able to account for rejects, whether they are reworked or destroyed or scrapped.

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Let's move on to some ways on how you can implement these regulations. We talked about risk-based approach before and what that means is you use risk to determine the frequency of testing and how much testing is required. Low risk components may require less testing or sampling than a high-risk one. Make sure when sampling that the sampling methods used are statistically based, as required by 21 CFR 820.250(b).

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The quality system or the QS regulation is not prescriptive and allows the manufacturer the flexibility on how to implement the requirements. You can have a Kanban system if that suits your operation, or a full-blown electronic system where every item is bar coded with its status, or any other system that suits your needs. It is up to you, as the manufacturer, to choose the amount of controls that are required and what works for your company.

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Let's look at some examples. Most of the examples I am going to give here are from the cardiovascular industry, but these translate to any type of device. An example for receiving inspection is verifying extruded tubing from an extrusion supplier. Now using the risk-based approach, the testing that is required for balloon tubing is much different and more vigorous than testing for tubing that is used for in-process packaging.

An example of an in-process inspection is bond strength testing for various joints during a catheter manufacturing process. These bond strength testing processes have to be validated, and a sample of the joints tested as part of the in-process acceptance testing.

Finally, an example of final acceptance testing is leak testing of catheters.

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The regulation outlines Acceptance records in 21 CFR 820.80 (e). You must document the following Acceptance activities: acceptance activities performed, dates performed, results obtained, signature of individual(s) conducting the activities, and equipment used, where appropriate. These records shall be part of the DHR.

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The preamble makes the connection between acceptance records and another part of the QS regulation: Nonconforming product. It states that when a product fails to pass acceptance activities, the procedures for control of nonconforming product must be implemented. This is also a good place to mention that there are many modules in our CDRH Learn library that deal with the various aspects of the Quality system regulation and the link between these requirements. I encourage you to watch these modules.

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Now I will discuss Acceptance Status that is outlined in 21 CFR 820.86. Very simplistically, Acceptance status is "Do I know with certainty whether this product meets my specifications?"

A manufacturer must identify acceptance status of product to indicate conformance or nonconformance with acceptance criteria. Manufacturers must also maintain acceptance status identification throughout manufacturing, packaging, labelling, installation, and servicing to ensure that only product which has passed required acceptance activities is distributed, used, or installed.

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Now that we have covered Subpart H, let's transition to Subpart L, that deals with handling, storage, distribution and installation.

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We will begin with Handling as outlined in 21 CFR 820.140. Manufacturers must establish and maintain handling procedures to prevent mix-ups, damage, deterioration, contamination, and other adverse effects to product.

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There are a variety of controls to protect product during handling that can be implemented, including the use of anti-static measures, gloves, holding fixtures, piping, and conveyors.

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Some examples of preventing mix ups are the use of bins, carts, and/or trays to move product. Another example is the use of electrostatic discharge, or ESD, protective containers or packages and hoods, to prevent deterioration especially for ESD sensitive products.

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We can link handling requirements to the acceptance status requirements. Make sure that the Acceptance Status of parts is clearly notated when moving from station to station, or start to finish.

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We will now move on to Storage requirements per 21 CFR 820.150. Similar to handling requirements, manufacturers must establish and maintain storage procedures to prevent mix-ups, damage, deterioration, contamination, and any other adverse effects to product. Temporary product staging areas in production and inspection work areas are also considered as storage areas. For environmentally sensitive product, storage may also include refrigerators or freezers.

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Continuing with Storage requirements, you must establish and maintain procedures to ensure that no product is used or distributed if obsolete, rejected, or deteriorated. Also, product should be stored in such a way to facilitate stock rotation if quality of product deteriorates over time. One of the Common stock rotation schemes is First In, First out, or FIFO.

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Manufacturers are also required to establish and maintain storage procedures that describe the various methods for authorizing receipt of product from the storage areas and stock rooms.

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You can implement this regulation by making sure that the storage area is contained, product is accounted for, acceptance status is notated, and ensuring that who can add or remove product is designated and controlled.

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Examples of controls for storage areas that may be considered for implementation include limited access as a Security control; regulation of temperature, humidity, UV light as Environmental controls; and dust free conditions as Contamination control. This also includes cleanliness conditions for Personnel controls and packaging and handling controls for fragile products.

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Some examples of implementing storage and handling requirements are the use of cages, red tag and green tag designation, an electronic system, and segregation or a clearly labeled product.

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Next, let's review the Distribution requirement as required by 21 CFR 820.160. Manufacturers must establish and maintain procedures to ensure: that only devices approved for release are distributed; that purchase orders are reviewed to ensure ambiguities and errors are resolved before release for

distribution; and that expired or deteriorated devices are not distributed. This requirement is a confirmation that the product is released per 820.80(d), and that it is done before any of the product is shipped.

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Manufacturers must maintain distribution records which include or refer to the location of the name and address of the initial consignee, the identification and quantity of devices shipped, the date shipped, and any control numbers used. These records are essential in supporting a recall investigation. Written agreements are established with distributors to maintain product traceability that will be useful in conducting a recall.

Written procedures address the selection of finished devices for shipping, the recording of shipment details on a pick list, the invoice or other record, and the retention of hard and/or electronic copy shipment records.

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One of the questions we often get asked in DICE is - when is the device considered to be “in distribution”, especially in the context of recalls? Is it when all the forms are signed, when the product leaves the building; or when it is in a distribution warehouse?

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The answer is, “when it leaves the building”. This is when the product is considered no longer under your control.

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Next, we move on to Installation requirements as outlined in 21 CFR 820.170. If installation is required, then manufacturers will have procedures to ensure proper installation. These include adequate installation instructions, inspection instructions, and test procedures, where appropriate, and ensuring that instructions and procedures are available to the person(s) installing the device. These procedures and instructions are part of the DMR, per 820.181(e).

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The person installing the device shall ensure that installation, inspection, and testing are performed in accordance with the instructions and procedures. They should also document the inspection and test results and demonstrate proper installation.

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An example of implementing these requirements is, if installation is included as part of the device design, then installation instructions need to be provided, and training is performed by qualified individuals.

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Additional information on the Quality System regulation, its Preamble, and the FDA Guide to Inspections of Quality System can be found at the links on this slide.

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In summary, we reviewed the purpose of the production and process controls subsystem, which helps ensure that you manufacture products that meet specifications. And second, we described the different aspects of Acceptance Activities, Handling, Storage, Distribution, and Installation with implementation strategies and examples.

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This presentation and other helpful videos and educational resources can be found at CDRH Learn. For text-based information on premarket and post market topics, including how to bring a medical device to market, please visit Device Advice. For additional information on these or any other medical device regulatory topics, feel free to contact us at the Division of Industry and Consumer Education. Links to these resources are included on this slide.

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In concluding this presentation, I now ask you to take on the following Call to Action. First, make sure you document acceptance activities and the status of product. And second, ensure that product is controlled throughout handling, storage, distribution, and installation. Thank you for watching this module.
