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Corrective and Preventive Action Subsystem

Cultivating Compliance Conference

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Discussion Topics

- Related Regulatory Requirements Under 21 CFR 820
- Precedent Rationale to Substantiate Regulatory Requirements
- Applicable Standards and Regulatory Requirements
- FDA Inspection Approach
- Questions

Regulatory Requirements Under 21 CFR 820

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21 CFR 820.100 (a)(1)

Establish (define, document and implement) and maintain procedures for implementing corrective and preventive action.

- Analysis of processes, work operations, concessions, quality audit reports, quality records, service records, complaints, returned product, **and other sources of quality data to identify existing and potential causes of nonconforming product, or other quality problems.** Appropriate statistical methodology shall be employed as needed to detect recurring quality problems.

Regulatory Requirements Under 21 CFR 820 (cont.)

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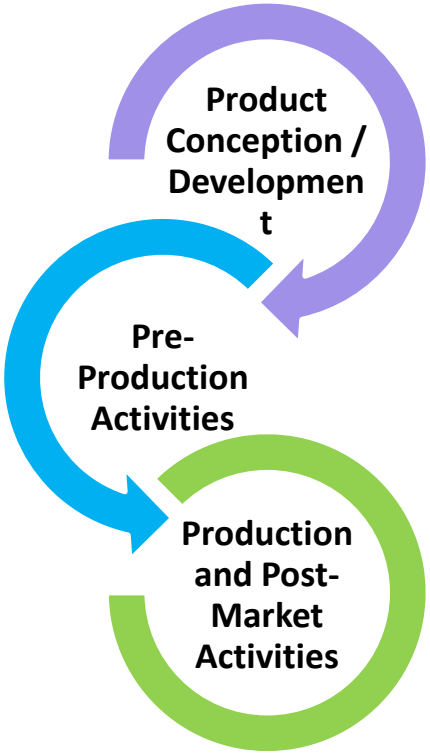
What is a non-conforming product?

21 CFR 820.3(q) *Nonconformity* means the nonfulfillment of a specified requirement.

21 CFR 820.3(r) *Product* means components, manufacturing materials, in- process devices, finished devices, and returned devices.



Regulatory Requirements Under 21 CFR 820 (cont.)

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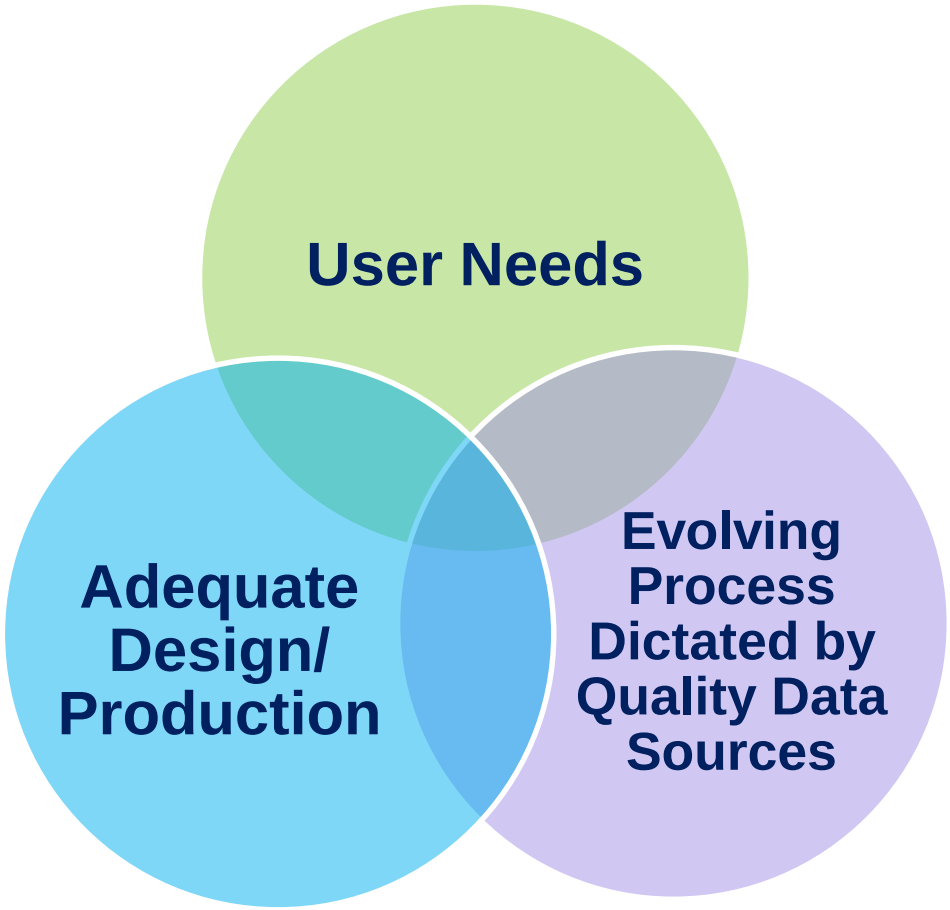
What Is Quality?

- 21 CFR 820.3(s) "*Quality* means the totality of features and characteristics that bear on the ability of a device to satisfy fitness-for-use, including safety and performance."



Regulatory Requirements Under 21 CFR 820 (cont.)

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21 CFR 820(a)

(2) Investigating the cause of nonconformities relating to product, processes, and the quality system;

(3) Identifying the action(s) needed to correct and prevent recurrence of nonconforming product and other quality problems;

(4) Verifying or validating the corrective and preventive action to ensure that such action is effective and does not adversely affect the finished device;

(5) Implementing and recording changes in methods and procedures needed to correct and prevent identified quality problems;

(6) Ensuring that information related to quality problems or nonconforming product is disseminated to those directly responsible for assuring the quality of such product or the prevention of such problems; and

(7) Submitting relevant information on identified quality problems, as corrective and preventive actions, for management review.

Regulatory Requirements Under 21 CFR 820 (cont.)

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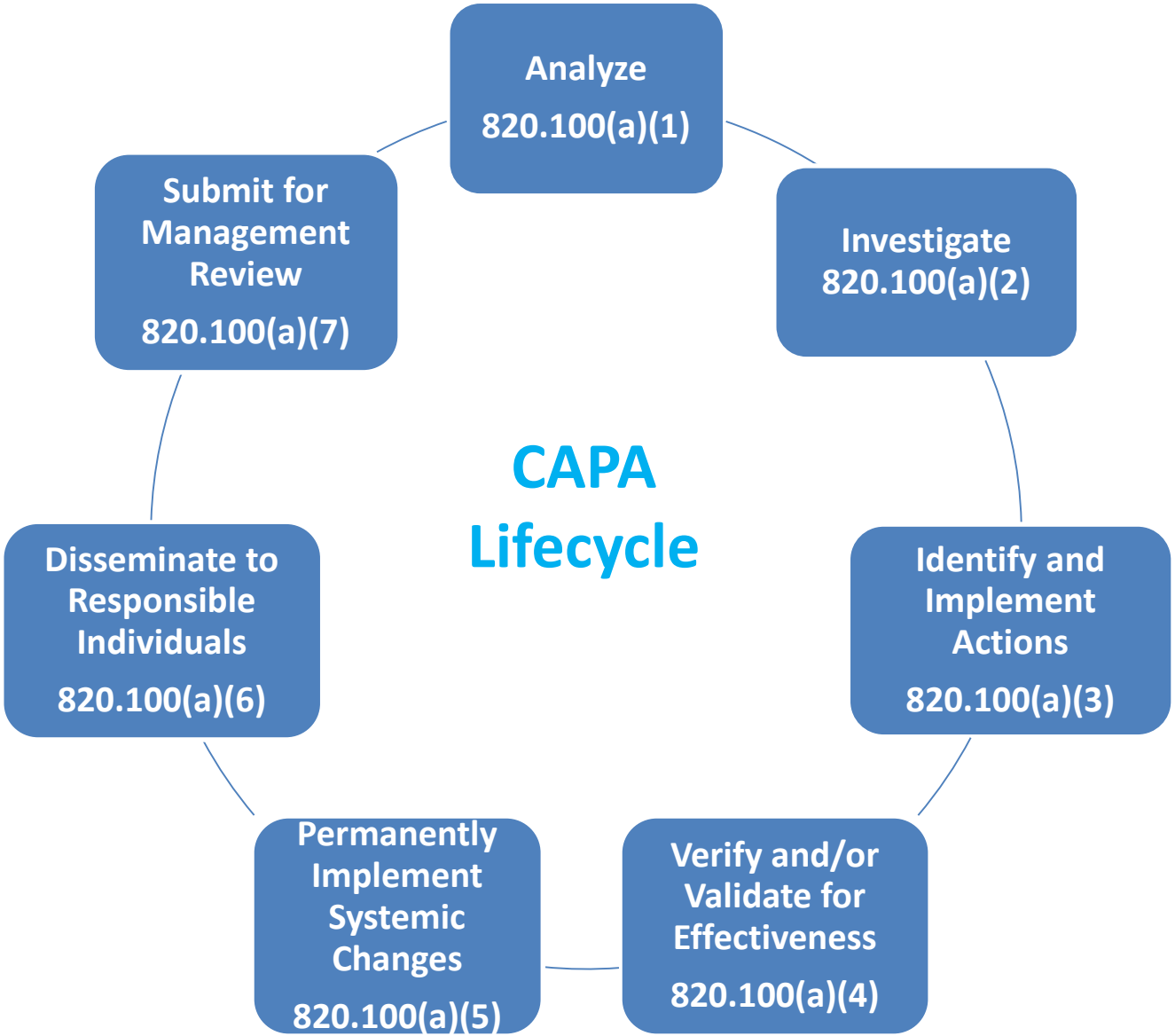

Regulatory Requirements Under 21 CFR 820 (cont.)

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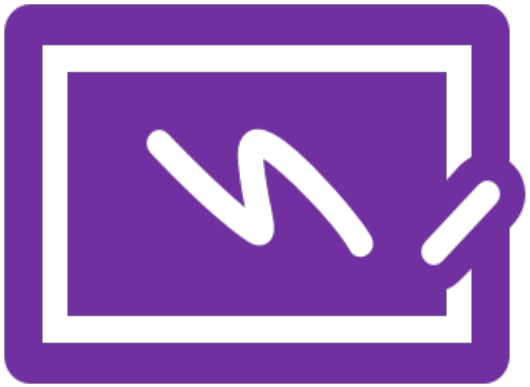
21 CFR 820.100(b)

- Requires that all activities to be conducted be documented.



Other Related Regulatory Requirements

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Satellites concerning the CAPA Subsystem

Medical Device Reporting 21 CFR 803

- Requires to establish procedures for evaluating events that can be considered as reportable under the MDR requirements.

Corrections and Removals 21 CFR 806

- Requires to report to FDA, within a specific timeframe, actions taken to address corrections made to products after being distributed.
- Market withdrawal, product correction in the field, retrieval of product from user facility, product returns amongst others.
- Requires that for actions which were not reported to FDA, a rationale is to be documented.

Medical Device Tracking 21 CFR 821

- Requires to adopt a method of tracking a class II or class III device, if the device meets following criteria; and FDA issues an order to the manufacturer.

Precedent Rationale to Substantiate Regulatory Requirements

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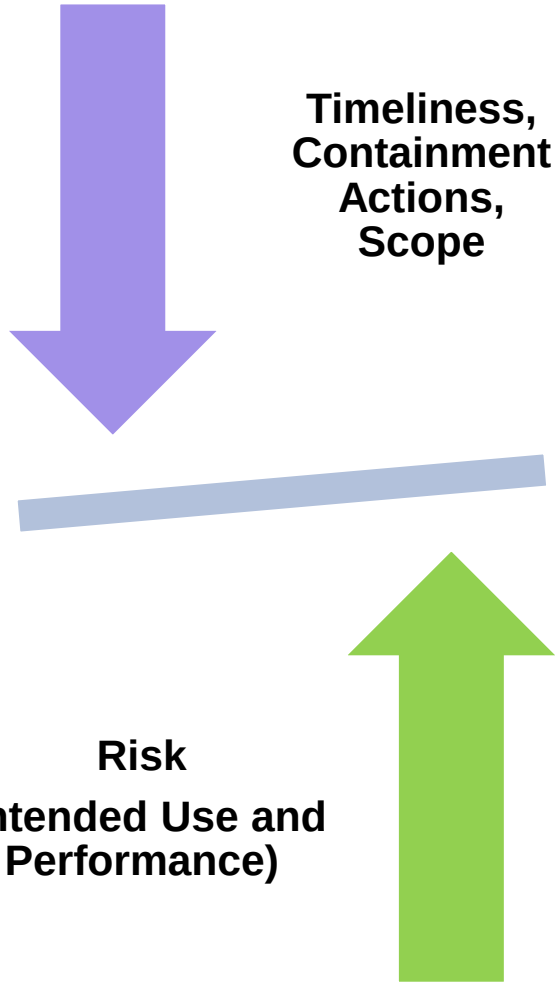
Quality System Regulation Preamble

Comment 159

- "FDA agrees that the degree of corrective and preventive action taken to eliminate or minimize actual or potential nonconformities must be appropriate to the magnitude of the problem and commensurate with the risks encountered."
- Relevant when establishing proactiveness, scope, and adequacy of actions implemented to prevent recurrence.



Precedent Rationale to Substantiate Regulatory Requirements (cont.)

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Comment 160

- "FDA wants to make it clear that corrective and preventive actions, to include the documentation of these activities, which result from internal audits and management reviews are not covered under Sec. 820.180(c)."
- **It is within FDA's authority to review CAPA's that result from these activities and these are be contemplated within the firm's CAPA procedures and established CAPA subsystem.**

The exception under 820.180(c) FDA excludes the following:

- Reports required by 820.20(c) Management review, 820.22 Quality audits, and supplier audit reports used to meet the requirements of 820.50(a) Evaluation of suppliers, contractors, and consultants..."
- Procedures for management reviews, internal audits and purchasing controls are also not contemplated within the exception.

Precedent Rationale to Substantiate Regulatory Requirements (cont.)

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Comment 160

- "FDA emphasizes that the appropriate statistical tools must be employed when it is necessary to utilize statistical methodology. FDA has seen far too often the misuse of statistics by manufacturers in an effort to minimize instead of address the problem. Such misuse of statistics would be a violation of this section."

- Statistics are not to justify the exclusion of additional actions, or inaction, in terms of corrective and preventive actions, specifically when controls to address recurrence of reported problems were non-existent.

Precedent Rationale to Substantiate Regulatory Requirements (cont.)

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Comment 166

- "Two comments stated that the records required under Sec. 820.100(b) should be treated as part of the internal audit. FDA disagrees with these comments because this information is directly relevant to the safety and effectiveness of finished medical devices. FDA has the authority to review such records and the obligation to do so to protect the public health."

- CAPA activities are to be commensurate with risk; are required to be documented; and FDA is entitled to review these. This further substantiates comments 159 and 160.

Applicable Standards and Regulatory Requirements

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Recognized Consensus Standards

- Are non-binding in respect to requirements under the regulation and adherence to these is voluntary.

- Manufacturers may submit a Declaration of Conformity to applicable Consensus Standards that apply to their device and/or processes.

Statutory Requirement meant to be adaptable. May exceed standard requirements.

Specific to a process, device, environment, or operation. Not mandated by law. May exclude or exceed regulatory requirements.

Applicable Standards and Regulatory Requirements (cont.)

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- During inspections, FDA may routinely audit the data or information that supports the firm's conformity to the standard.
- Commonly used standards include:
  - ISO 13485-2019 "Medical devices—Quality Management Systems-Requirements for Regulatory Purposes"
  - ISO 14971-2019 "Medical Devices-Application of Risk Management to Medical Devices"

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FDA Inspection Approach

Procedural direction form managing CAPA's and related activities.

- Are these comprehensive ?
  - Did procedures address all potential quality data sources for evaluation and escalation to CAPA's as needed ?
- Are theses consistently implemented ?
  - Are these followed ?

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FDA Inspection Approach-Cont'd

Comprehensive approach to root cause determination and subsequent corrective actions implemented.

- Were all contributing factors and common denominators evaluated ?
- Processes, products, acceptance activities, components, workforce, environment, design, etc.

FDA Inspection Approach (cont.)

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Comprehensive approach for implemented corrective actions.

- Were all affected product, processes, components, instructions amongst others impacted by corrective actions implemented ?

Adequacy of related investigations.

- Risk
- Impact on product performance
- Where lack of controls to prevent recurrence adequately identified ?

FDA Inspection Approach (cont.)

Proportionality of corrective actions implemented to related risk and product impact.

- Timeliness
- Product scope
- Containment actions
- Additional controls

Adequacy of effectiveness evaluations.

- Is effectiveness quantifiable ?
- Are timeframes to measure effectiveness adequately established.
- Are the quality data sources selected to measure effectiveness adequate to detect recurrence ?

FDA Inspection Approach (cont.)

- Effectiveness to prevent recurrence.
  - Are there repetitive instances documented on subsequent and/or separate CAPA's or related quality data sources ?
- Documented CAPA activities
  - Are investigations, actions, verification and/or validation adequately documented to include objective evidence ?