Surviving an FDA Inspection: An Industry Perspective

Ben Khosravi
Executive Vice President Quality,
Leads Development & Operations
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Quality System Regulation

820.180 General Requirements

- Maintain all required records at manufacturing establishment, or other reasonably accessible location.
- Make records readily available for review and copying for FDA employees.

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820.180 General Requirements

- Ensure records are legible and stored to minimize deterioration and prevent loss.
- Back up records stored in automated data processing systems.

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General Requirements

820.180 (b) Records Retention Period

- Retain for a period of time equivalent to the design and expected life of the device, but in no case less than 2 years from the date of release for commercial distribution by the manufacturer.

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820.100 (a)(1) & (2) Corrective & Preventive Action

Establish procedures, including requirements for

- Analyzing sources of quality data to identify existing and potential causes of nonconforming product or other quality problems.
- Investigating the cause of nonconformities.

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820.100 (a)(1) Corrective & Preventive Action

Potential sources of quality data

- Purchased Components Incoming Inspections
- Work Operations
- Returned Products
- Manufacturing Non-conformances
- Internal Audits
- Management Reviews

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820.100 (a)(2),(3) & (4) Corrective & Preventive Action

Establish procedures, including requirements for

- Investigating the cause of nonconformities.
- Identifying the action(s) needed to correct and prevent recurrence of nonconformities.
- Verifying or validating that the corrective and preventive action is effective.

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820.100 (a) Corrective & Preventive Action

Establish procedures, including requirements for

- Implementing and recording changes in methods and procedures needed to correct and prevent identified quality problems.
- Ensuring information related to quality problems or nonconforming product is disseminated to appropriate personnel.
- Submitting relevant information for management review.
- Documenting all related activities and results.

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820.198 (a) Complaint Files

All manufacturers must

- Maintain complaint files.
- Designate a formal complaint handling unit.
- Establish and maintain procedures for receiving, reviewing, and evaluating complaints.

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820.198 (a) Complaint Files

Procedures must ensure that

- All complaints are processed in a uniform and timely manner.
- Oral complaints are documented upon receipt.
- Complaints are evaluated to determine whether the complaint represents a MDR (21 CFR 803).

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820.198 Complaint Files

Records of investigations

- To be maintained by the formally designated unit, including
  - Any corrective action taken
  - Any reply to the complainant

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820.198 (d) Complaint Files

MDRs

- Promptly review, evaluate, and investigate any complaint that represents an MDR.
- Maintain any complaint that represents an MDR in a separate portion of the complaint files or otherwise clearly identify the complaint.

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Definition

803.3 (r) MDR Reportable Event

- An event about which user facilities become aware of information that reasonably suggests that a device has or may have caused or contributed to a death or serious injury; or
- An event about which manufacturers or importers have received or become aware of information that reasonably suggests that one of their marketed devices.
  - May have caused or contributed to a death or serious injury; or
  - Has malfunctioned and that the device or a similar device marketed by the manufacturer or importer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

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Definition

803.3 Serious Injury

- An injury or illness that
  - Is life-threatening;
  - Results in permanent impairment of a body function or permanent damage to a body structure; or
  - Necessitates medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure.

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Definition

803.3 Permanent Injury

- Irreversible impairment or damage to a body structure or function, excluding trivial impairment or damage.

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MDR Reporting Times

- Reporting time for normal MDRs is 30 days
- Reporting time for MDRs requiring remedial action is 5 days

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820.198 Complaint Files

Foreign manufacturers

- **Required records must be reasonably accessible in the United States at either**
  - **Location in the United States where the manufacturer's records are regularly kept**
  - **Location of the initial distributor**

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Introduction

820.30 Design Controls

- The design control requirements are not intended to apply to development of concepts and feasibility studies.
- FDA will evaluate the process, the methods, and the procedures that a manufacturer has established to implement the requirements for design controls.

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Introduction

820.30 Design Controls

- The FDA has amended the IDE regulation, reaffirming that an IDE device is exempted from complying with the GMP's "….with the exception of Sec. 820.30 "Design Controls."

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Introduction

820.30 Design Controls

FDA will evaluate the adequacy of manufacturers' compliance with design control requirements in routine inspections of Quality System regulation compliance, including pre-approval inspections for pre-market approval applications (PMAs).

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Objectives

820.30 Design Controls

- Explain what is meant by “interfaces with different groups of activities”
- Describe a process for risk assessment for device safety.
- Briefly describe the requirements for software validation/verification during design.

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Objectives

820.30 Design Controls

State the requirements for, and where applicable, what is necessary to document

- Design and development planning
- Design input
- Design output
- Design review

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Objectives

820.30 Design Controls

State the requirements of, and where applicable, what is necessary to document

- Design verification
- Design validation
- Design transfer

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Definitions

820.3 (g) Design Output

- Design output means the results of a design effort at each design phase and at the end of the total design effort. The finished design output is the basis for the device master record. The total finished design output consists of the device, its packaging and labeling, and the device master record.

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820.30 Design Controls

Design output

- Results of design effort at each phase and the end of the total design effort.
- Finished design output is basis for the DMR.

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820.30 Design Controls

Total finished design output consists of

- Device
- Packaging
- Labeling
- DMR

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Definitions

820.3 (h) Design Review

- Design review means a documented, comprehensive, systematic examination of a design to evaluate the adequacy of the design requirements, to evaluate the capability of the design to meet these requirements, and to identify problems.

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Design Controls

820.3 (e) Design Review

- Ensure that formal reviews of design results are planned and conducted at appropriate stages.

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Design Controls

820.3 (e) Design Review

- Ensure participants include representatives of all functions concerned with design stage being reviewed.
- Individual(s) who do not have direct responsibility.
- Document results in the DHF.

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820.3 Design Controls

Design changes

- All design changes made after the design review that approves the initial design inputs for incorporation into the design, and those changes made to correct design deficiencies once the design has been released to production, must be documented. The evaluation and documentation should be indirect proportion to the significance at the change.

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820.3 Design Controls

Design changes

- The safety and effectiveness of devices cannot be proven by final inspection of testing. Quality can only be ensured if change is controlled in the development process, as well as the production process.
- Each manufacturer must establish criteria for evaluating changes to ensure that changes are appropriate for its design.

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820.3 Design Controls

Design changes

- Where a design change cannot be verified by subsequent inspection and test, it must be validated.

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GHTF
Process Validation Guidance

Validation Steps

- Define/develop product and process
- Install equipment (IQ)
- Operational Qualification (OQ)
  - •Prequalification Studies
  - •Understand Variables
  - •Characterize Process Limits
- Conduct PQ at nominal conditions
- Approve process = release

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Objectives

820.72 Inspection, Measuring and Test Equipment

- State the types of manufacturing equipment that must be controlled under a calibration system.
- List the elements that should be included in a calibration system.

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Inspection, Measuring, and Test Equipment

820.72 (a) Control of inspection, measuring, and test equipment

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

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Inspection, Measuring, and Test Equipment

820.72 (a) Control of inspection, measuring, and test equipment

- Establish procedures to ensure equipment is routinely inspected, checked, maintained and calibrated.
- Document activities.

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Objectives

820.70 Production and Process Controls

- Explain the differences and interrelationships between production and process changes, document changes, and design changes.
- Describe when environmental controls or contamination controls are necessary.

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Objectives

820.70 Production and Process Controls

- Explain a manufacturer's responsibilities for the health, cleanliness, personal practices, and clothing of personnel.

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Production and Process Controls
820.70 (a) General

Develop, conduct, control, and monitor production processes to ensure devices confirm to specifications.

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Production and Process Controls

820.70 (c) Environmental control

- Establish procedures to adequately control environmental conditions.
- Inspect control system(s) to verify adequacy and proper functioning.
- Document and review these activities.

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Production and Process Controls

820.70 (d) Personnel

- Establish and maintain requirements for the health, cleanliness, personal practices, and clothing of personnel.
- Ensure maintenance and other temporary personnel are appropriately trained or supervised.

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Production and Process Controls

820.70 (g) Equipment

- Equipment must meet specified requirements and be appropriately.
  - •Designed
  - •Constructed
  - •Placed
  - •Installed

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Objectives

820.90 Nonconforming Product

- Describe the controls and investigations requirements for nonconforming product.
- Discuss the requirements for reworked product, including retest and reevaluation requirements.

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Objectives

Definitions

820.3 (x) Rework

- Rework means actions taken on a nonconforming product so that it will fulfill the specified DMR requirements before it is released for distribution.

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Nonconforming Product

820.90 (b)(1) Nonconformity review and disposition

- Establish and maintain procedures defining the responsibility for review and the authority for the disposition, including the review and disposition process.

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Nonconforming Product

820.90 (b)(2) Nonconformity review and disposition

- Establish and maintain procedures for rework, including retesting and reevaluation.
- Document rework and reevaluation activities in the DHR.
- Including a determination of any adverse effect on the product.

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Definitions

820.3 (j) Device Master Record

- Device master record (DMR) means a compilation of records containing the procedures and specifications for a finished device.

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820.181 Device Master Record

Establish and maintain DMR for each type of device, including

- Device specifications
- Product process specifications
- QA procedures and specifications
- Packaging and labeling specifications
- Installation, maintenance, and servicing procedures and methods.

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Definitions

820.3 (i) Device History Record

- Device history record (DHR) means a compilation of records containing the production history of a finished device.

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Definitions

820.3 (m) Lot or Batch

- Lot or batch means one or more components or finished devices that consist of a single type, model class, size, composition, or software version that are manufactured under essentially the same conditions and that are intended to have uniform characteristics and within specified limits.

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Document Controls

820.40 (a) Document Approval and Distribution

- Establish and maintain procedures to control all required documents.
- Designate individual(s) to review documents for adequacy and approve prior to issuance.

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Document Controls

820.40 (a) Document Approval and Distribution

- Make documents available at designated locations.
- Remove obsolete documents from all points of use/prevent from unitended use.

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Document Controls

820.40 (b) Document Changes

- Review/approval changes by individual(s) in the same function/organization as original review and approval.
- Communicate approved changes to appropriate personnel.

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Document Controls

820.40 (b) Document Changes

- Maintain records of changes, including
  - Description of the change
  - Identification of the affected documents
  - Signature of the approaching individual(s)
  - Approval date
  - When change becomes effective

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Definitions

820.3 (t) Quality Audit

- Quality audit means a systematic, independent examination of a manufacturer's quality system that is performed at defined intervals and at sufficient frequency to determine whether both quality system activities and the results of such activities comply with quality system procedures, that these procedures are implemented effectively, and that these procedures are suitable to achieve quality system objectives.

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820.22 Quality Audit

Describe the quality audit requirements for manufacturers, including

- Auditor qualifications and independence
- Review of results
- How follow-up to corrective actions should be handled

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820.22 Quality Audit

- Establish procedures for quality audits.
- Conduct audits to assure compliance by individuals not having direct responsibility for areas audited.

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820.22 Quality Audit

- Perform corrective action(s), including re-audit of deficiencies.
- Generate a written report of audit results for management review.

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820.25 Personnel

- Describe the general training requirements for personnel.
- Describe the general training requirements for contract and temporary personnel.
- Briefly discuss the “identification of training needs”

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820.25 (a) & (b) Personnel

- Employ sufficient personnel with necessary education, background, training, and experience.
- Establish procedures for identifying training needs and to ensure personnel are adequately trained.
- Document training.

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Purchasing Controls

820.50 (a) Evaluation of suppliers, contractors, and consultants

- Establish and maintain requirements, including quality requirements, to be met by suppliers, contractors, and consultants.

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Purchasing Controls

820.50 (a)(1) Evaluation of suppliers, contractors, and consultants

- Evaluate and select suppliers, contractors, and consultants based on their ability to meet specified requirements.

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Purchasing Controls

820.50 Evaluation of suppliers, contractors, and consultants.

- Maintain records of the evaluation results.
- Define the type and extent of control to be exercised based on the evaluation results.
- Maintain records of acceptable suppliers.

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820.65 Traceability

- Describe when traceability is necessary.
- Describe the extent to which traceability is required for finished devices.
- Describe when and how traceability could be applied to components.

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Definitions

820.3 (d) Control Number

- The control number is the means by which the history of the device, from purchase of components and materials through distribution, may be traced, where traceability is required.

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820.65 Traceability

Examples of Control Numbers

- Lot Numbers
- Batch Numbers
- Serial Numbers

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Receiving, In-Process, & Finished Device Acceptance

820.80 (a) General

- Establish and maintain procedures for acceptance activities, including inspections, tests, or other verification activities.

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Receiving, In-Process, & Finished Device Acceptance

820.80 (c) In process acceptance activities

- Control in-process product until appropriate acceptance activities are completed and documented.

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Receiving, In-Process, & Finished Device Acceptance

820.80 (d) Final acceptance activities

- Establish and maintain procedures for finished device acceptance to ensure each production run, lot, or batch meets acceptance criteria.

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Objectives

820.250 Statistical Techniques

Describe when statistical techniques are appropriate.

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820.250 (b) Statistical Techniques

- Write and base sampling plans on valid statistical rationale.
- Establish and maintain procedures to ensure that sampling methods are adequate for their intended use.

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Questions?

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