

Guidance for Industry and/or for FDA Staff

# **Guidance on Quality System Regulation Information for Various PreMarket Submissions**

*Draft Guidance – Not for Implementation*

**This guidance document is being distributed for comment purposes  
only.**

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**U.S. Department of Health and Human Services  
Food and Drug Administration  
Center for Devices and Radiological Health**

**Office of the Director  
Division of Enforcement III  
Office of Compliance**

# Preface

## **Public Comment:**

For 90 days following the date of publication in the Federal Register of the notice announcing the availability of this guidance, comments and suggestions regarding this document should be submitted to the Docket No. assigned to that notice, Dockets Management Branch, Division of Management Systems and Policy, Office of Human Resources and Management Services, Food and Drug Administration, 5630 Fishers Lane, Room 1061, (HFA-305), Rockville, MD 20852.

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# **GUIDANCE<sup>1</sup> ON QUALITY SYSTEM REGULATION INFORMATION REQUIRED FOR VARIOUS PRE-MARKET SUBMISSIONS**

## **INTRODUCTION**

This document discusses information required by the Quality System (QS) regulation (21 CFR part 820) that applicants should include in their premarket approval applications (PMA) and product development protocols (PDP). This document also describes the information that should be maintained at the manufacturing facility for premarket notifications (510(k)s).<sup>2</sup> The information required by the QS regulation covers two basic categories: design controls and manufacturing. Design control requirements help to ensure that the device's design will meet its approved specifications when released to production and meet the users' needs. The manufacturing requirements cover a number of inter-related elements that include the following: management responsibilities; quality assurance and personnel; records; production and process controls; acceptance activities; supplier/purchasing controls; corrective and preventive action procedures; and related problem solving activities.

PMA and PDP submissions should include a complete description of design controls and manufacturing information required by the QS regulation. This information should be included in standard PMA's, modular PMA's, streamlined PMA's, and PMA supplements. Without this information, the premarket review process for these devices cannot be completed.

## **INFORMATION REQUIREMENTS**

### **BACKGROUND**

The preamble to the Quality System regulation preamble states that:

- "Since early 1984, FDA has identified lack of design controls as one of the major causes of device recalls. The intrinsic quality of devices, including their safety and effectiveness, is established during the design phase."
- "Unsafe and ineffective devices are often the result of informal development that does not ensure the proper establishment and assessment of design requirements which are necessary to develop a medical device that is safe and effective for the intended use of the device and that meets the needs of the user."

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<sup>1</sup> This document is intended to provide guidance. It represents the Agency's current thinking on the above. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both.

<sup>2</sup> Refer to 21 CFR 820.30(a)(2)(ii) for a list of class I devices subject to design controls. For Special 510(k) Device Modification Submissions, refer to Attachment 2 of the guidance entitled, "The 510(k) Paradigm: Alternate Approaches to Demonstrating Substantial Equivalence in Premarket Notifications" for the type of design control information to submit, if requested by FDA after market clearance to verify design controls. The design dossier for a Special 510(k) must be readily available at the manufacturing site for inspection.

FDA must balance the need for design controls with the need for product innovation. Accordingly, the agency does not intend to apply design control requirements to the early research stage of product development. However, once a manufacturer decides to develop a design, the QS regulation requires the use of design controls to ensure that the design specifications released to production meet the approved design requirements.

***The following information required under the QS regulation should be submitted with PMA and PDP submissions and readily available, when requested by FDA, for a device subject to 510(k) requirements.***

## **DESIGN CONTROL DOSSIER**

### *820.30(a) General*

1. An explanation of the stage in the design and development effort when design controls apply.
2. A description of how risk management or risk analysis will be used throughout the design and development of the device. A summary of the methods used and at what stages of design and development they were and will be employed.

### *820.30(b) Design and Development planning*

3. The design and development plan or a summary of the plan.
  - The plan should describe or reference, and assign responsibility for the implementation of each of the following:
    - a) Risk Analysis
    - b) Design Input
    - c) Design Output
    - d) Design Review
    - e) Design Verification
    - f) Design Validation
    - g) Design Transfer
    - h) Design Changes
    - i) Interfaces (departments, individuals(s), etc.)
  - The submitted plan or summary should have provisions for the review, update, and approval of the plan as design and development evolves.

- The plan should include information on the chronology of the development strategy (e.g., Gantt Chart) and outline the timing strategy, i.e., initiation, completion, and analysis, for all testing, with specification and justification of data needed prior to subsequent studies contained or referenced in the plan. The plan should contain specific deliverables of each stage and criteria for initiation and completion. The plan should identify critical milestones that must be completed before initiation of subsequent tasks.

820.30(c) Design Input

4. A copy of the written procedures for the identification and control of design input.
  - The following relevant aspects should be addressed:
    - a) intended use
    - b) user/patient/clinical (interfaces and inputs)
    - c) performance characteristics
    - d) safety characteristics
    - e) limits and tolerances for safety and performance parameters
    - f) risk analysis
    - g) toxicity and bio-compatibility
    - h) electromagnetic compatibility (EMC)
    - i) compatibility with accessories/auxiliary devices
    - j) compatibility with the environment of intended use
    - k) human factors
    - l) physical/chemical characteristics
    - m) labeling/packaging
    - n) reliability
    - o) statutory and regulatory requirements
    - p) voluntary standards
    - q) manufacturing processes
    - r) sterility
    - s) MDRs/complaints/failures and other historical data
    - t) past design history files (DHF's)
    - u) year 2000 problems for computerized devices and computerized interfaces
  - The procedures should describe the process or mechanism for addressing incomplete, ambiguous, or conflicting requirements.
  - The procedures should explain how design inputs are documented, reviewed and approved.
5. A summary of how user interface and other human factor issues are considered and addressed in the design input.

6. For electrically powered devices, an explanation of how EMC issues are considered and addressed in the design inputs.

#### 820.30(d) Design Output

7. A copy of the written procedures used to define and document design output in terms that allow an adequate and measurable evaluation of conformance to design input requirements.
  - The procedure should contain or make reference to acceptance criteria.
  - The procedure should contain or make reference to the process or mechanism used to identify the design outputs considered essential for the proper functioning of the device.

#### 820.30(e) Design Review

8. A written copy of the written procedures that define and control the following design review elements:
  - The procedure should describe how formal design reviews are planned and how the appropriate stages of the device's design development are defined for the purpose of conducting formal design reviews.
  - The procedure should contain or make reference to the processes or mechanisms that ensure that formal design reviews are comprehensive, systematic, and that participants at each design review include representatives of all functions concerned with the design stage being reviewed. (Note, this information should be consistent with the information submitted under Design Input – Interfaces above.)
  - The procedure should contain or make reference to the process or mechanism by which the manufacturer ensures that an individual(s) who does not have direct responsibility for the design stage being reviewed, as well as any specialists needed, are included in the formal design reviews.
  - The procedure should include provisions for the results of design reviews to be documented in the design history file, along with the date, and the individual(s) involved.

#### 820.30(f) Design Verification

9. A copy of the written procedures used to verify the device design.
  - The procedure should have provisions for the documentation of the results of design verification, including identification of the design, methods(s), date, and individuals(s) performing the verification.
  - The procedure should contain or make reference to a process for resolving any discrepancy between design output and design input requirements.

10. A summary of the method or mechanism used to trace and confirm that the design output meets the design input requirements.

820.30(g) Design Validation

11. A copy of the written procedures used to validate the device design activities.
  - The procedures should address the documentation of design validation results, including the identification of the design, methods used, date, and individuals performing the validation.
12. If validation activities will be performed or were performed on non-production devices, a summary of the process or scientific method that will be used or was used to prove equivalence to production devices.
13. A summary of how the clinical evaluations planned will ensure that the design of the device meets user needs and the intended uses.
14. If the device is automated with computer software, a description of how the software validation will be completed when the overall design validation is finished.
15. A summary of the risk management program. Describe how and when risk analysis was and will be performed. Include how the results of the risk management process will be documented, used, and updated.

820.30(h) Design Transfer

16. A copy of the written procedures used to transfer the design output from design and development to manufacturing.
  - The procedures should include provisions that ensure the final review and approval of design and development activities, e.g., the approval of the device master record and its transfer to manufacturing.

820.30(i) Design Changes

17. A copy of the written procedures for design change control.

- The procedure must clearly define when in the design control process design change control begins. Some degree of design change control begins in the early stages of development. At a minimum, change control must exist after the design inputs have been approved.
  - The procedure should describe when verification of changes is sufficient in lieu of validation of changes and how this will be documented. The procedure should not simply state, “validation or where appropriate verification.” “Where appropriate” should be clearly defined or the procedure should provide a process for such decision making.
  - The procedures should ensure that changes are validated or, where appropriate, verified, reviewed, and approved prior to implementation of the design change.
18. A description, reference, or summary of how design changes to the device or the manufacturing process (including methodology) will be handled after the device has been transferred to manufacturing.

820.30(j) Design History File (DHF)

19. Written procedures for maintaining the contents of the DHF, or a summary of such procedures.
- If more than one device shares a common DHF, the procedure should describe how the manufacturer identifies each device within the family or group having common design characteristics.

**MANUFACTURING DOSSIER**

1. A copy of the quality manual, or equivalent documentation, for the manufacturing facility that will be responsible for manufacturing the device. The quality manual should be consistent with ISO 10013-1195 “Guidelines for Developing Quality Manuals.” A quality manual should include the following information:
- a) title, scope, and field of application
  - b) table of contents
  - c) a definitions section, if appropriate
  - d) introductory pages about the organization concerned and an outline of the structure of the quality manual or quality system documentation
  - e) the quality policy and objectives of the organization
  - f) a description of the organizational structure, responsibilities, and authorities
  - g) a description of the elements of the quality system and any references to documented quality system procedures
  - h) a guide to the quality manual, if appropriate
  - i) an appendix for supportive data, if appropriate

- The QS regulation states, “Each manufacturer shall establish quality system procedures and instructions. An outline of the structure of the documentation used in the quality system shall be established where appropriate.” (21 CFR 820.20(e)) An outline is appropriate for most devices subject to PMA or PDP approval. The development of a quality manual that includes the above-referenced elements would satisfy the quality system requirement.
2. A description or flow diagram that identifies the steps involved in the manufacturing process for the device or family of devices involved in the submission.
  3. A copy of the validation master plan or a description of which manufacturing processes have been or will be validated. A validation master plan is a convenient method of quality planning for process validations required in the manufacturing of the device. (21 CFR 820.20(d)). Identify any processes that will be validated, especially when the manufacturer has not performed a similar type of validation at the particular manufacturing.

For example, a manufacturer may need to perform a sterilization validation for a device subject to PDP approval. If the design specifications call for ethylene oxide (ETO) sterilization and the manufacturer has never performed sterilization validation or has only performed a different type of sterilization validation, such as gamma sterilization, then the manufacturer’s lack of experience with this new process should be noted in the submission. If a manufacturer has performed similar ETO sterilization validations for other products, then the sterilization validation does not need any special notation.

- The manufacturer must validate processes where the results of a process cannot be fully verified by subsequent inspection and test. (21 CFR 820.75) If the manufacturer chooses to validate a process that can be fully verified by subsequent inspection and test, then the manufacturer voluntarily subjects these processes to the process validation requirements of 21 CFR 820.75.
4. A copy of the validation procedures or individual validation plans for each process that will be validated.
    - Validation procedures should contain or refer to objective and measurable acceptance criteria.
    - Appropriate statistical methodology for data collection and analysis should be employed. The validation procedures should define or reference the statistical methodology.
    - The validation procedures should also contain the criteria for revalidation.
  5. A copy of the general Acceptance Activities procedure(s) (to include receiving, in-process and final inspection and test procedures), required under 21 CFR

- 820.80 for the device or a summary of how the acceptance activities will be carried out.
6. A copy of the general purchasing control procedures or a summary of how the evaluation of suppliers will be handled. In particular, if contract designers or contract manufacturers have been or will be used, the controls applicable to these suppliers should be specified.
  7. A copy of the corrective and preventive action (CAPA) procedures, as required by 21 CFR 820.100. If the CAPA includes the following elements required under separate sections of the QS regulation, then reference where these elements are found in the CAPA procedures:
    - Non-conforming product procedures (21 CFR 820.90)
    - Service reports, if appropriate. (21 CFR 820.200)
    - Complaint handling procedures (21 CFR 820.198), which include medical device reporting procedures. (21 CFR 803)