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FDA's Design Control Requirements for Medical Devices

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Design controls are a mechanism for bringing the design of certain class I and all class II and class III investigational devices under the umbrella of the good manufacturing practices (GMPs) of a corporate quality system. In 1996, the GMP requirements were revised to include the area of design control and have become a part of the Quality System Regulations (QSR) with which all medical device manufacturers must comply. It is incumbent on the manufacturer to demonstrate compliance with the QSR and, as of 1996, with design control requirements as well. Once the product definition and regulatory strategy have been prepared, medical device developers must work to comply with the design control provisions of the QSR as the device development process moves forward. The QSR is the medical device equivalent of the pharmaceutical current good manufacturing practices (cGMPs). The QSR, unlike cGMPs, also regulates the device development process via its design control provisions (21 CFR 820.30) which describes the device developer's requirements under the design control provisions of the QSR. Design controls are an integrated set of management practices (policies, processes and procedures) which are applied to control design activities while assessing quality and correcting errors through a reiterative device process control. Once management has determined that the device is feasible and the decision has been made to transition from research to clinical applications, the design control process begins. As such, the device application becomes part of corporate quality system.

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Medical Device Design

FDA requires the consideration of human factors during the development of medical devices. In 1996 FDA issued guidance, “Do It By Design—An Introduction to Human Factors in Medical Devices”, which established design requirements to avoid so-called user errors (1). Most recently the agency introduced those concepts of human reliability to drug and biotechnology manufacturers. To elaborate this concept by frequency and by significance, one must differentiate between error (mistakes) and defects (also known as nonconformance). It is difficult for regulated firms to recall products because there were human errors during the manufacturing process. In some situations, the firm’s quality system is unable to detect the human error and the non-conformed device distribution becomes an adulterated item. Human error can be defined as a departure from acceptable or desirable practices on the part of an individual which results in unacceptable or undesirable outcome. Human factors include designing machines, operations, and work environments to match human capabilities, limitations, and needs. In those situations where an operator does not properly execute a manufacturing step, human error can be avoided by using risk management tools described in ISO 14971—Application of Risk Management to Medical Devices (Hazard and Operability Study (HAZOP) and Hazard Analysis and Critical Control Point (HACCP)). HACCP for medical devices is designed to prevent and/or control device safety and performance. A trained HACCP team is helpful for monitoring the device production processes from raw materials, components receiving, manufacturing controls, distribution, and use by the customer. Since HACCP focuses primarily on the production process, it is also assumed that the design is complete and the manufacturing system is already in place; however HACCP, and/or the corrective and preventive action plan, may indicate the need to revise the design and/or the manufacturing process, subject to compliance with change control provisions of the QSR (2).

Medical Device Quality Systems and GMPs

The QSR regulates both the device development and the manufacturing process for all class II and class III devices from the beginning of the design engineering development phase until commercial use and post-marketing surveillance. The Medical Device Life Cycle (MDLC) interconnects all developmental aspects, manufacturing and commercial use of devices along with quality monitoring via design control requirements. The QSR also covers the manufacturing process for many class I devices. The goal of the QSR is to create a self-correcting system that reliably produces robust device designs and production methods, ensuring that devices perform in a manner consistent with their intended use. Much of the information that is included in a 510(k) or PMA is taken from the Design History File (DHF), prepared as a result of the design control requirements of the QSR. Once a device is marketed,



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the corrective and preventive action (CAPA) provisions of the QSR are closely related to compliance with the MDR regulation. An additional feature of the QSR is that it follows the basic principles of the international medical device standard, ISO 13485, which is advantageous to enable device firms to sell their devices internationally to maintain quality system commonalities for most design and production-related activities. In most cases, the QSR system requires more extensive documentation than ISO 13485. The system requires specific activities and documentation beginning during the development process. The manufacturing and quality processes also require specific evaluations and procedures, all of which must be documented. Frequently, the FDA investigators will follow the quality system inspection technique (QSIT) when inspecting a medical device facility. This process breaks the QSR compliance into four main modules and four satellite modules, some of which may not be applicable to all device firms. Generally, the FDA investigator will choose a subset of those modules and determine the device specific compliance with QSR. This means that not every system's modules are reviewed during a QSIT inspection; however this approach does yield a general assessment of the QSR compliance. Many device firms rely on various customer-oriented feedback loops and accountability of the process. This approach can be useful by reducing time to market and by reducing the number of field corrections and recalls contributing to increasing customer satisfaction and device safety and effectiveness. The FDA's guide to Inspections of quality systems provides instructions for conducting medical device QSIT/GMP inspections.

Device Design Control Components

The essential components of design controls stretch from planning through design transfer (from development, manufacturing, to end user). Also, it is essential to maintain existing designs. These controls apply to all class II and class III medical devices and a small number of class I devices. The main purpose of the design control components are to establish and maintain procedures to control the design of the device and maintain the intrinsic quality of the device in order to ensure that specified design requirements will meet user needs, the device's intended uses, its specifications, safety and effectiveness, and reduction in recalls. These design components are developed in a reasonable manner in compliance with the firm's existing design control standard operating procedures (SOPs). Design controls are closely linked to many other QSR components and the entire quality system must work together to build and maintain the intrinsic quality of the device. The device firms must prepare and follow SOPs that comply with the regulations and that fully describe how the firm will meet all relevant regulatory requirements. All the relevant activities must be fully documented in the firm's design history file (DHF).



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Essential Elements of Design Control Requirements

The design control regulations require each manufacturer to establish and maintain procedures for the following:

- Design and development planning
- Design input
- Design output
- Design review
- Design verification and validation
- Design transfer
- Design changes
- Design history file

Additionally, risk analysis must be conducted for the majority of medical devices subject to design control requirements. Each element listed above is interconnected for creating an integrative device development process that will be compatible with the management and organizational structure of the device manufacturer in compliance with the FDA requirements. The organizational structure is responsible to ensure administrative, technical, and human factors affecting the safety and effectiveness of the device. The design control functions involve incoming materials, process controls, software, hardware associated with the finished device for the end-user. All such functions should be contributing to reduction, elimination, or corrective and preventive aspects of design control conformance. The organizational structure responsible for design control compliance is determined in part by the type of device produced, the manufacturer's organizational goals, and the needs and expectations of the customers.

FDA's design control regulations require that medical device manufacturers establish a design and develop a plan that describes the activities that are necessary for the specific device design and the responsibility for its implementation. As part of the regulations, the manufacturer must assign responsibilities for its implementation to identified individuals or departments, and to ensure that there is sufficient regulatory supervision and that each device conforms to the intended design specifications and functions to achieve clinical benefits for its intended patient population. The design records should be reviewed and updated in the design history file (DHF). The design control procedures and records play a key role both during FDA inspections and during reviews of PMA manufacturing sections.

Design input establishes the requirements that the device will meet the needs of the intended users. This includes all of the steps necessary to ensure that the design



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requirements for a specific device technology are appropriate for and address the intended use of the device, and meet the needs of both the user and the patient. The information for design input is gathered about the performance requirements, and preliminary specifications for elements such as design characteristics, form and configuration, along with the materials needed. The design input requirements should be documented, reviewed, and approved by a designated individual.

Design output describes procedures for the device and process documentation. This information is needed to transform the product idea into a prototype or finished device. This requirement must include the test plans, procedures, and reports that will verify that the device meets the design input requirements and specifications. Design output is documented, reviewed, and approved before release. These documents apply to all stages of the design process that are included in the Design History File (DHF). Design output includes the detailed documentation covering all functional aspects of the device needed to produce and maintain the device features throughout the device's total product life cycle (TPLC).

Design review consists of comprehensive and systematic evaluation of the device in terms of adequacy of the design requirements and capability of the design to meet those requirements. Design reviews are conducted over the course of the device development and manufacturing cycle to assure that the design extends beyond user-stated requirements and that safety and effectiveness and PMA's performance goals are met. Design reviews are formal meetings, pronounced, conducted by agenda, and documented with minutes of the meeting, and/or project status reports. These documents are included in the DHF. The main purpose of the design review process is to ensure that the design of the device during development and manufacturing conforms to the established criteria and to identify device design deficiencies or defects for CAPA provisions of the QSR

Design verification and validation refers to a series of ongoing procedures that ensure that the device design output meets its design input and the device conforms to defined user needs and intended uses. Design verification covers the design and conduct of testing to establish performance characteristics, safety, and effectiveness of the device. For example, biocompatibility testing of materials, bioburden testing of sterile devices, clinical studies in humans to establish safety or feasibility are considered as verification tests. Generally, testing of prototype or production units takes place both under defined test conditions and under actual or simulated use conditions. The design verification step is conducted to demonstrate that the actual device design is consistent with the device the firm intended to build. This step verifies that the device was built correctly according to specifications of the design and how the firm tested prototype and manufactured devices in order to ensure that the device design matches the manufacturer's input requirements. Design validation follows successful verification



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and is performed under defined operating conditions on initial production units, lots, or batches, or their equivalents. Design validation ensures that devices conform to defined user needs and intended uses that include testing of production units under actual or simulated use conditions. Design validation includes software validation and risk analysis, where appropriate. The results of the design verification and validation must be documented in the DHF.

Design transfer ensures that the design specifications of the device are accurately translated into production specifications, which means confirming that production devices are the same as the pilot plant devices on which tests such as hazard analysis, failure analysis, preclinical and clinical testing were conducted. This involves transferring all of the documentation from the design process to manufacturing. The design transfer is a critical step of the QSR's design control which requires that firms have SOPs in place to ensure that the device design is correctly translated into product specifications with acceptance activities at the operational level. As manufacturing proceeds, it becomes apparent that some design changes may occur (design changes do take place for various reasons). A change control procedure may be needed to identify, document, verify, validate, review, and approve any design changes before their implementation.

Design history file (DHF) is a compilation of records or reference to records that describes the design history of a finished device. Under QSR, the manufacturer establishes and maintains a DHF for each type of device technology. This requirement is necessary to demonstrate that the design of a specific type of device was developed in accordance with the approved design plan. Manufacturers are free to develop and define the details of their own specific design control systems; however, they must meet the general requirements of the device GMP regulations.

FDA Quality System Inspection Technique (QSIT)

FDA's QSIT approach to inspection is derived from seven sub-systems described in the QSR (21 CFR, Part 820). Four primary areas are main focus of inspection: management controls, design controls, corrective and preventive actions (CAPA), and production and process controls. The remaining three subsystems are covered via "linkages" within the QSIT inspection subsystems. The QSIT review includes both a broad review of whether the firm has procedures in place and appears to meet the general QSR requirements, and a closer detailed review of specific device technology applications and records to verify that the requirements have been implemented in actual production, design, and daily quality assurance situations described in the premarket applications (510(k) or PMA).



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Summary

- Risk and hazard analysis activities are required as part of total product life cycle (TPLC)
- The standard for the application of risk management (ISO 14971) for Medical devices) is part of TPLC
- The risk management process covers risk analysis, risk evaluation, and risk controls through CAPA and design control requirements
- Design control requirements described in this publication play a key role from device design prototype, manufacturing process controls and the finished device for user needs.
- The extent of testing and evaluation is proportional to the level of risks associated with the device technology and intended clinical use
- FDA reviews the “safety and effectiveness” of the device and it is essential that any risks and hazards are mitigated to “acceptable” levels.

Conclusion

FDA reviewers and field investigators evaluate the design control requirements and processes and make recommendations based on whether the manufacturer has the required checks and balances in place, verify and validate implementation of the design control requirements in support of the sponsor’s 510(k) or PMA.

References

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