“Device Validation Forum” discusses regulatory requirements, scientific principles, strategies, and approaches associated with medical device validation that are useful to practitioners. We intend this column to be a valuable resource for daily work applications. The key objective for this column: Useful information.

Reader comments, questions, and suggestions are needed to help us fulfill our objective for this column. Case studies illustrating principles associated with medical devices submitted by readers are most welcome. Please send your comments and suggestions to column coordinator John E. Lincoln at jel@jelincoln.com or to journal coordinating editor Susan Haigney at shaigney@advanstar.com.

KEY POINTS

The following key points are discussed in this article:

• Medical device research and development under the US Food and Drug Administration’s design control requirements is discussed
• The majority of serious device problems are introduced during the design and change phases of development
• Design control and design history file (DHF) requirements of the good manufacturing practice (GMP) guidelines were initiated by FDA in 1996-1997
• Medical device design control begins somewhere between research and development when senior management makes a medical device research effort a formal project and begins to budget or make major expenditures for commercialization
• Key elements of device design control are discussed
• A suggested new or changed product project checklist (or DHF table of contents) is proposed
• Formal control of the design and development process facilitates project management and gating and is good business practice.

INTRODUCTION

This issue of “Medical Device Forum” discusses medical device research and development under the US Food and Drug Administration’s design control requirements. FDA recognizes that with devices, the majority of serious problems are introduced during the design or change phases of development of new or changed products. Changes to existing products have been addressed under “Change Control, Engineering Change Orders” (1), and similar required current good manufacturing practice (CGMP) procedures (1). Recognition that the design of new product or major changes and line extensions to existing products were not well controlled was addressed in the mid 1990s (2). In fact, in many companies, such development was not controlled at all, with research and development (R&D) departments allowed free rein in a key process and determinant of device quality.

The formal design control and design history file (DHF) requirements of the GMPs were initiated by the FDA in 1996-1997 (2). Progressive companies were already enacting these requirements, and many had recognized the value to the retention of their intellectual property (IP) by proper documentation of development and changes, as well as a record of false starts, blind alleys, and similar development “dead ends.”
DESIGN CONTROL “START” DATE
Figure 1 indicates FDA’s expectation that the start of formal medical device design control begins somewhere between research and development, in the region indicated in blue (3). A repeatable system for many companies is usually to designate the “start” of formal design control as the time when senior management makes a medical device research effort a formal project and begins to budget for or make major expenditures to commercialize it internally or with the idea of selling off the technology.

KEY ELEMENTS AND STEPS IN DEVICE DESIGN CONTROL
The following key elements of device design control are detailed in FDA’s Design Control Guidance for Medical Device Manufacturers (4), with each element defined by the company’s standard operating procedures (SOPs):

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

The following sections are derived and adapted from the FDA Design Control Guidance for Medical Device Manufacturers (4). Note: Section A: General.

Section B. Design and Development Planning
Plans are to be initiated and maintained that describe or reference the design and development activities and define responsibility for implementation. Often this may consist of Gantt Charts, which define milestones, tasks, timelines, and responsibilities, and are updated periodically.

DESIGN PLANS should identify and describe the interfaces with different groups or activities that provide, or result in, input to the design and development process. The plans should then be reviewed, updated, and approved as design and development evolves.

Section C. Design Input
Product developers are responsible to establish and maintain procedures to ensure that the design requirements relating to a device are appropriate and address the intended use of the device. This includes meeting the needs of the user and clinician and patient, as well as meeting the requirements of any applicable standards mandated in the markets in which the product will be sold. Procedures should include a mechanism for addressing incomplete, ambiguous, or conflicting requirements.

These design input requirements should be documented, reviewed, and approved by designated individuals who are qualified for the activity or document element that they are reviewing or approving. The approval, including the date and signature of the individuals approving the requirements, needs to be documented.

Section D. Design Output
The developer is also responsible to establish and maintain procedures for defining and documenting design output in terms that allow an adequate evaluation of conformance to design input requirements. Design output procedures must contain or make reference to acceptance criteria and should ensure that design outputs essential for the proper functioning of the device are identified. The developer should document, review, and approve the design output before release. The approval, including the date and signature of the individuals approving the output, must be documented.

Section E. Design Review
The developer or company must further establish and maintain procedures to ensure that formal documented reviews of the design results are planned and conducted at appropriate stages of the device’s design development (see suggested milestones). The procedures must ensure that participants at each design review include representatives of all functions concerned with the design stage being
reviewed. Any specialists needed would also comprise the relevant review team. Also required is an individual who does not have direct responsibility for the design stage being reviewed to provide an independent ‘voice.’ The make-up of such review teams may change through the design and development process as review needs progress.

In a small company, complete independence is very difficult to obtain. Within the context of formal design reviews, the practical solution is simply to ensure a fresh perspective, based on the principle that those who are too close to the design may overlook design errors. Thus, reviewers will often be from the same organization as the developers, but they should not have been significantly involved in the activities under review. The expectation of formal design review teams and their activities is to provide a major role in assuring independent and objective reviews.

The results of a design review, including identification of the design, the date, and the individuals performing each review, are documented in the design history file (DHF).

Section F. Design Verification
SOPs must be established and maintained for verifying, testing, and/or inspecting the device design to confirm that the design output meets the design input requirements (see Figure 2). The results of the design verification, including identification of the design, method(s), the date, and the individuals performing the verification shall also be documented in the DHF.

Section G. Design Validation
SOPs for device design validation are to be established and maintained. Design validation should be performed under defined operating conditions on initial production units, lots, or batches, or their equivalents (use of early stage prototypes are to be avoided). The purpose of design validation activities is to ensure that devices conform to defined user needs, intended uses, and applicable standards. Such validation includes testing of production units under actual or simulated use conditions, with such products having been built in a production environment using production or test equipment, and production personnel (see Figure 2). Carelessness in these requirements has often resulted in future product recalls.

Design validation should include software validation where appropriate and device risk analysis (re: ISO 14971:2007 and ICH Q9). The results of the design validation, including identification of the design, method(s), the date, and the individual(s) performing the validation, should be documented in the DHF.

Section H. Design Transfer
Each manufacturer should establish and maintain procedures to ensure that the device design is correctly translated into production specifications. Production specifications must ensure that manufactured devices are repeatedly and reliably produced within product and process capabilities. If a manufactured device deviates outside those capabilities, performance may be compromised. Thus, the process of encapsulating knowledge about the device into production specifications is critical to device quality.

Section I. Design Changes
Procedures must be established and maintained for the identification, documentation, validation, or where appropriate, verification, review, and approval of design changes before their implementation. In “design control” the two principal administrative elements and activities involved in controlling design changes are document control and change control, as follows:

• **Document control.** Document control involves the enumeration of design documents and the tracking of their status and revision history. Documents refer to all design documents, drawings, and other items of design input or output which characterize the design or some aspect of it.

• **Change control.** Change control involves the enumeration of deficiencies and corrective actions arising from verification and review of the design at its various stages after “start,” and the tracking of their resolution prior to design transfer.

Section J. The Design History File
The DHF is to be compiled for each type of device. The DHF contains or references the records necessary to demonstrate that the design was developed in accordance with the approved design plan and the requirements of the FDA’s design control. The design and development history, maintained in documentation such as laboratory notebooks and/
or similar files and documents, are to remain the property of the manufacturer and not the individual. Separate notebooks are to be maintained for each project, and surrendered to the document control center or engineering librarian at the conclusion of an engineer's active participation in the project. Laboratory notebooks are to be surrendered if the employee leaves the company. Product development supervisors shall review employees' laboratory notebooks at specified intervals to ensure that records are complete, accurate, and legible. Such documentation is to be properly witnessed, and may also serve in supporting patent claims.

**Figure 2**: Medical device verification and validation “waterfall” (4).
There are no requirements on the location or organization of the DHF. For simple designs, the designer may choose to assemble and maintain the entire DHF. For larger projects, a document control system will likely be established for design documents. These files will likely be maintained in some central location, usually within the product development department. However, the system utilized is to be defined by SOP.

Based on the structure (or lack thereof) of the product development organization, more or less extensive controls will be required. For example, company policy should state unequivocally that all design history documentation is the property of the manufacturer, and not the employee or contractor. Design and development contracts should explicitly specify the manufacturer’s right to design information, as well as define and establish standards for the form and content of design documentation. This would include custom software as well. Finally, certain basic design information may be maintained in a single project file in a specified location. This may include the following:

- Detailed design and development plan specifying design tasks and deliverables
- Copies of approved design input documents and design output documents
- Documentation of design reviews
- Verification and validation documentation
- Copies of controlled design documents and change control rationale and records, when applicable.

**NEW AND CHANGED PRODUCT PROJECT**

With these requirements in mind, this section presents a suggested new or changed product project checklist (or DHF table of contents). While by no means presented as definitive, it is for the purpose of stimulating evaluation of a company’s R&D and design control requirements and new or changed medical device project management milestones and tasks. The author initially developed this in the early 1980s to assist engineers at a large device manufacturer in bringing a new product to market. It was then expanded in the 1990s to include the FDA’s newly defined elements of design control.

**Possible/Suggested Milestones**

Use the following as appropriate for project; sequence as necessary. FDA design control elements are listed in bold:

- New product concept, line extension, product changes:
  - Feasibility
  - Written scope/objective
  - Patent search/considerations/application
- Marketing:
  - Specification
  - Sales forecast
- Competitive analysis (product, market share):
  - Foreign and/or domestic considerations
- Feasibility study:
  - Manufacturability
  - Cost estimates; rough cut time frame
- Design input: initial product performance specification (in engineering terms and/or “TBD”)
- Initial design and development plan (including Gantt/PERT/CPM)
- Initial risk analysis (e.g., ISO 14971, FTA, FMEA, or...)
- Project approval (design review)—From senior management:
  - Start design control
  - Begin compilation of DHF
- Regulatory affairs:
  - 510(K) - Vendor-supplied, or internal/company-initiated; or IDE; or PMA
  - Written rationale for not submitting
  - Perform written analysis
  - Foreign submission requirements
- Preliminary drawings
- Prototyping
- Bench testing (protocol or lab book documented; as required):
  - Failure analysis
  - Bench/lab studies
  - Animal studies
  - Safety/efficacy
  - Materials selection
  - Sterilization data
  - Environmental/age testing
  - EMC, UL, etc.
  - Other relevant standards (domestic or foreign)
  - Packaging/labeling instructions
  - Clinical, marketing trials
  - MDD/CE requirements
- Volume planning (capacity/resources/constraints):
  - In-house production capability
  - Inventory (levels, lead times)
  - Vendors, contract services
  - Samples (sales/samples)
  - Foreign/domestic requirements

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• Design review
• Design output (manufacturing engineering):
  • Formal product performance specifications
  • ID vendors (w/ purchasing)
  • Obtain/assign catalog/item number(s)
  • Obtain/assign part number(s) (P/Ns)
  • Write raw material/component specs, finished
    prints (QC test attributes, sampling plan, developed
    by QS and added to specs)
  • Product cost development
  • Mold tooling
  • Draft SOPs (w/ QS)
  • Labeling—P/Ns, copy/blue lines (w/ QS)
• Marketing literature
• Product labels
• Instructions
• Pouch, packaging, inner carton (chipboard; if
  required)
• Shipper
• Packaging
• BOMs
• Current inventory on-hand
•Obsolete inventory NCMR’d/scraped
• Initiate formal product testing:
  • Shake drop
  • Environmental/accelerated aging
  • Sterility (w/ QS)
  • 3X sterilization cycle
  • Functional
  • Pkg integrity
• Manufacturing process definition:
  • Equipment acquisition (specs, POs, documenta-
    tion, including drawings, software
    algorithm/code, buy-off data)
  • Fixturing
  • Equipment/tool numbers assigned; drawings
  • Facilities lay-out
  • Utilities hook-up
  • PM program development
  • Instrumentation calibration/NCI (non-cal-
    brated instrument)
  • Equipment installation qualification (IQ)
    checklist initiated
• Design review (include DI = DO)
• QS/RA (w/ Mktg. and Mfg. Eng.):
  • Biocompatibility, Tripartite / ISO 10993
  • QC inspection attributes, methods
  • Sampling plan, AQL/DPM, SPC/control charts
  • Pre-production QS analysis (FEMA, etc.)
  • Clinicals, if additional required
  • Train production personnel; document
• Design verification(s) and design validation(s)
  (QAE/Eng.):
  • Installation qualification (IQ; checklist)
  • Operational qualification (OQ; process param-
    eter challenge)
  • Performance qualification (PQ; consistent pro-
    duction of acceptable product)
  • Continuous process monitoring
    systems/procedures
  • Design output compared to design input
  • Design transfer complete
  • Design changes tracked, documented, V&V’d,
    implemented
• Design review (include final DO = DI; project
  release)
• First lot to stock (production—to inventory)
  build
• FQA release
• Product roll-out
• Design (project) history file (DHF) completion:
  • Compilation completed; supplemental narra-
    tives written
  • Routed for signatures
  • Archived in document center
    Note: For CE-marking a “snapshot in time”
    Technical File (MDD Class I and IIa / IIb), or
    Design Dossier (MDD Class III) would also
    be required.
• Post-market surveillance.

VALUE
Irrespective of the regulatory requirements that
are extremely important, it should be evident that
design control is synonymous with formal control
of the design and development process. Periodic
reviews of the process should be at appropriate
points for “gating” the project (i.e., allowing for the
successful conclusion of a previous activity and the
initiation and funding of the next activity), usually
with design reviews as the “gate.” Many points
outlined in the FDA’s guidance for design control
parallel management techniques for “fast cycle”
product development.
Such documented design control requirements also
serve to do the following:
• Protect a company’s investments in R&D
• Facilitate additional related research and failure
  investigation
• Training of new or replacement technicians, engi-
  neers, and scientists
• Protect the resulting IP.
Hence, in addition to the regulatory mandate, a strong business case can be made for the FDA's requirements for medical device design control.

REFERENCES
2. After an extensive effort, the part 820 revision was published on October 7, 1996 with 820.30, Design Control, and went into effect June 1, 1997. http://www.fda.gov/medicaldevices/deviceregulationandguidance/default.htm.
4. FDA, Design Control Guidance for Medical Device Manufacturers, March 11, 1997. JVT

ARTICLE ACRONYM LISTING
AQL  Acceptable Quality Level
CFR  Code of Federal Regulations
CGMP  Current Good Manufacturing Practice
DHF  Design History File
DI  Design Input
DO  Design Output
DQ  Design Qualification
DPM  Defects per Million
EMC  Electromagnetic Compatibility
FDA  US Food and Drug Administration
FMEA  Failure Modes, Effects Analysis
FTA  Fault Tree Analysis
GMP  Good Manufacturing Practice
ICH  International Conference on Harmonization
IDE  Investigational Device Exemption
IP  Intellectual Property
IQ  Installation Qualification
ISO  International Organization for Standardization
MDD  Medical Device Directive (EU)
NCI  Non [or Not] Calibrated Instrument
NCMR  Non-conforming Material Report
OQ  Operational Qualification
PMA  Pre-Market Approval
P/N  Part Number
PQ  Performance Qualification
QAE  Quality Assurance Engineer
QS  Quality System(s)
R&D  Research and Development
SOP  Standard Operating Procedure
SPC  Statistical Process Control
TBD  To Be Decided
UL  Underwriters Laboratories
V&V  Verification and Validation