Rocky Mountain Regulatory Affairs Society

Elements of and Maintenance/Remediation of the Design History File (DHF)

March 15, 2017

RMRAS
REGULATORY, EDUCATION, NETWORKING

DOHMEN
LIFE SCIENCE SERVICES

dsi
design solutions, inc.

Design History File

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Presentation Topics

1. What is the Design History File?
2. Why is an effective DHF good for business?
3. DHF / DMR Checklists
4. FDA Critical DHF assessment area
5. Common DHF Deficiencies
6. When / Why is a DHF gap analysis warranted

What is the Design History File?

Definition

Design History File (DHF) Definition:

- A compilation of records which describes the design history of a finished product.
- It should provide objective evidence that design controls were followed.
- The DHF is a living file that is constantly updated throughout the entire design life cycle.

What the DHF is not!

Device Master Record (DMR)

- Compilation of all the instructions, drawings and other records, that must be used to produce a product.
- Processes, bill of materials, assembly drawings, gerber files, etc.

Device History Record (DHR)

- **FDA requirement:** Each manufacturer shall establish and maintain procedures to ensure that DHR's for each batch, lot, or unit are maintained to demonstrate that the device is manufactured in accordance with the DMR.
- Dates of mfg, quantity mfg, acceptance records, identifiers, etc.

Why is an effective DHF good for business?

Why is an effective DHF good for business?

1. **It is required by the FDA!!!**
2. Shows the FDA proof that you have a followed a structured product development process.
3. Common way to organize the design.
4. Keeps track of design decisions that helps assess impacts of design changes.
5. Helps to prevents design mistakes, prevents organization from repeating effort that has already been tried in past.
6. Helps to bring new resources up to speed on a project.
7. Protection of intellectual property.

Design History File (DHF)Checklist

Regulation:
21 CFR 820
Design Controls => Sec 820.30

Design Control Sections

- Design and Development Planning
- Design Input
- Design Output
- Design Review
- Design Verification
- Design Validation
- Design Transfer
- Design Changes
- Design History File

DHF Checklist - Planning

- ✓System Development Plan
- ✓Schedule
- ✓Budget
- ✓Design Verification Plan
- ✓Software Development Plan
- ✓Risk Management Plan
- ✓Manufacturing Plan
- ✓Design Transfer Checklist
- ✓Statements of work

DHF Checklist - Requirements

- ✓Same as Design Inputs
- ✓System Requirements
- ✓Software Requirements
- ✓Usability / Human Factors Requirements

DHF Checklist – Risk Management

- ✓System Risk Analysis
- ✓System FMEA
- ✓Software FMEA
- ✓Process FMEA
- ✓Fault Tree Analysis
- ✓Feed into Design Inputs (Requirements)

DHF Checklist – Design Specifications

- ✓Same as Design Outputs
- ✓System Design Specification
- ✓Software Design Specification
- ✓User Interface Design Specification
- ✓Wiring Diagram
- ✓PCBA CAD Database
- ✓Software Source Code
- ✓Mechanical CAD Database

DHF Checklist – Verification & Validation

- ✓Verification Test Protocols
- ✓Validation Test Protocols
- ✓Usability Test Protocols
- ✓Clear and Stated Pass/Fail Criteria upfront
- ✓Software Test Protocols (All levels)
- ✓Test Method Validation
- ✓All Test Protocols & Matching Reports

Verification vs Validation

- ✓Verification : Did I make it right?
- ✓Met all Design Requirements

- ✓Validation: Did I make the right product?
- ✓Do only with representative users of the product

DHF Checklist – Prototypes

- ✓Alpha Prototypes
- ✓Beta Prototypes
- ✓What will you use the Prototypes for?
- ✓User Interface Prototype
- ✓Mechanical Models
- ✓Simulations
- ✓ID Concepts and Models
- ✓V&V on production equivalent product

DHF Checklist – Reviews

- ✓ Program / Phase Reviews
- ✓ Requirements Reviews (Design Inputs)
- ✓ Specification Reviews (Design Outputs)
- ✓ Risk Reviews
- ✓ Test Protocol Reviews
- ✓ Schematic / Layout Reviews
- ✓ Mechanical Design Reviews
- ✓ S/W Code Reviews
- ✓ First Article Inspections
- ✓ DFM/DFT Review
- ✓ Production Readiness Reviews

Device Master Record (DMR) Checklist

DMR Checklist – Bill of materials

- ✓ Recipe for build the product
- ✓ Assembly drawings
- ✓ Individual component specifications
- ✓ Electronic Files (3D Models & PCB files)
- ✓ S/W Executable Files
- ✓ Assembly Procedures
- ✓ Assembly and Test Fixture specifications
- ✓ Test Procedures
- ✓ Record of everything you need to build it

How does the DHR fit in? (Device History Record)

- ✓ All the output records from the manufacturing process
- ✓ Objective Evidence that you followed the DMR
- ✓ One DHR for each device/Lot manufactured
- ✓ DHF – How the product was designed
- ✓ DMR – How to make the product
- ✓ DHR – What went into shipped device

Maintaining and managing a DHF

GENERAL

- What Are Design Controls?
  - Set of policies and practices intended to ensure consistent translation of input requirements into a physical product that meets those requirements.
- Where Are They Defined For Medical Devices?
  - 21 CFR 820.30 + other ancillary requirements (i.e. - statistical techniques)
  - FDA Design Control Guidance for Medical Device Manufacturers (1997)
  - ISO 13485 – Section 7.3
- When Should I Start Design Controls?
  - To be most effective, they should be applied at the time you move from general research to product development.

General (CONT.)

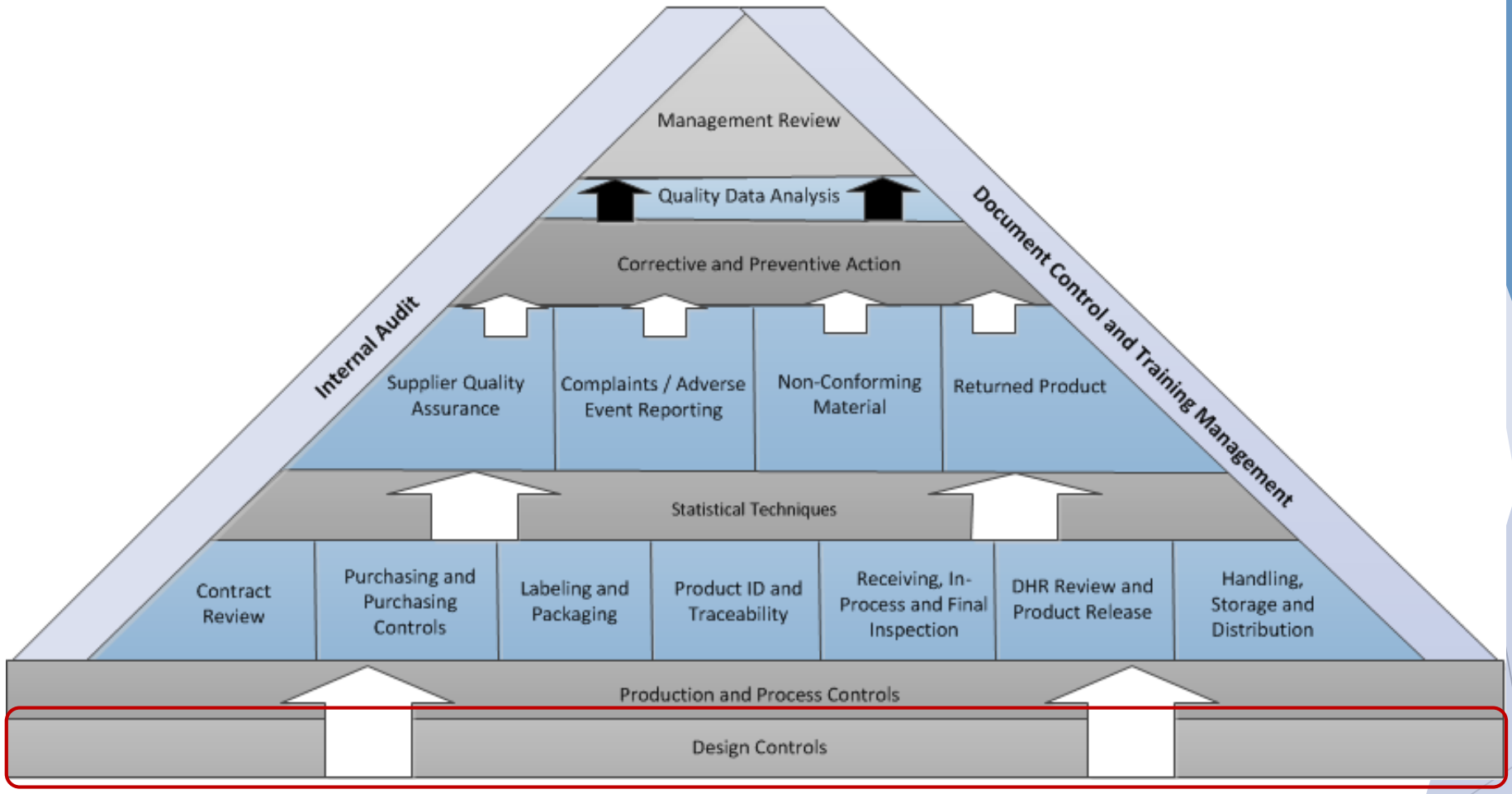
- The Design History File (DHF) is a complete history of the development of new and modified products and processes.
- Once a DHF is created for a product, subsequent changes to the product must complement or update the past documentation whenever reasonable.
- Changes to the DHF as a result of design changes or new information must be reviewed and approved prior to implementation.
- Generally, changes to DHF documents are processed through the CO system

Strategic Advantages

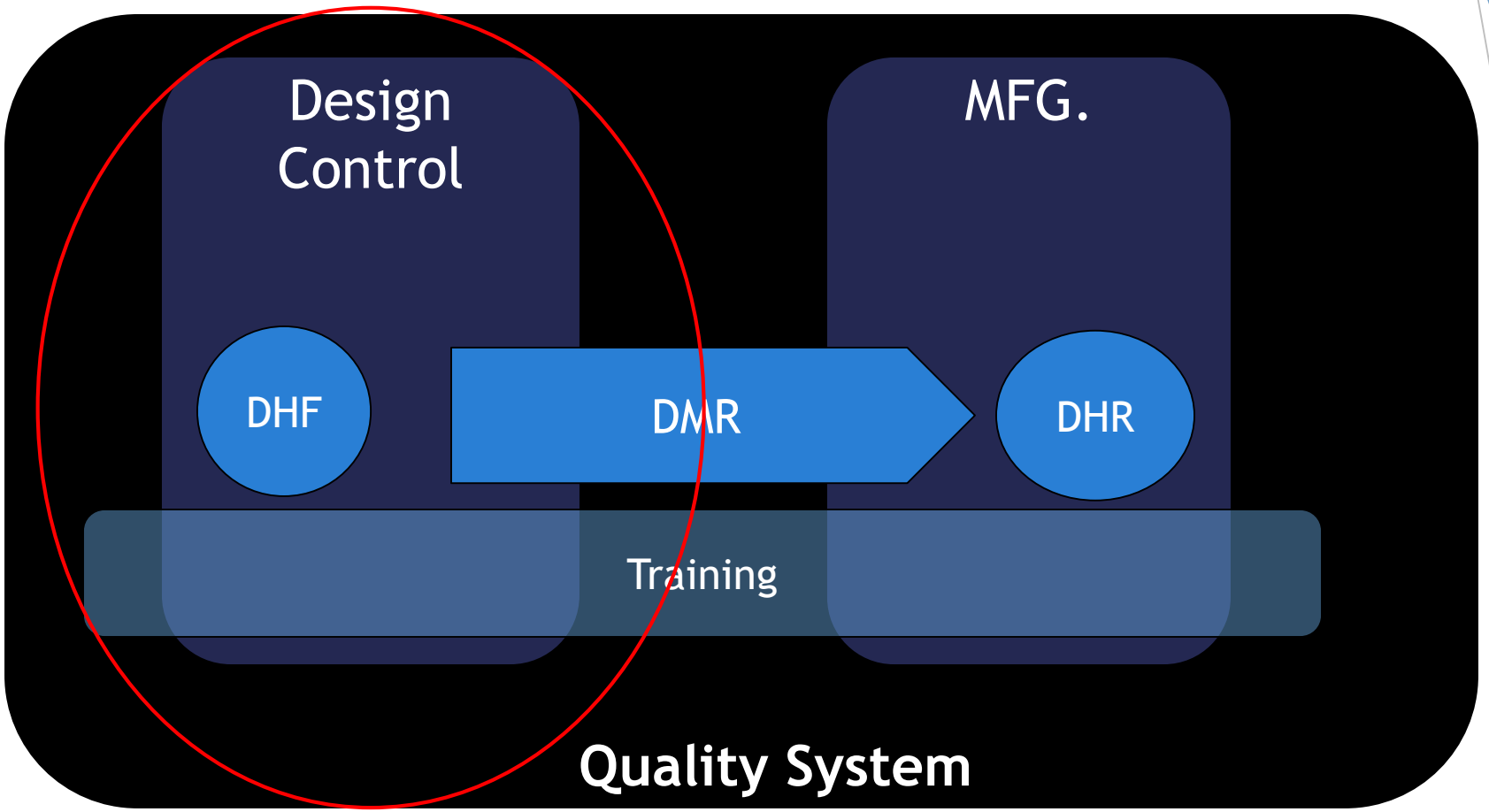
- What Should I Expect To Gain From Application of Design Controls?
  - Safe and Effective Product
    - Can significantly reduce the number of complaints and potential for recalls
  - Documentation Supporting Pre-Market Submissions
    - Forms basis for all Regulatory Submissions
    - Greater ability to make performance claims
    - Reduce potential for restriction of future clearances / approvals
  - Well Documented Design Specifications and Characteristics
  - Building Blocks of the Device Master Record (DMR)
  - Documented Product Configuration Allowing Controlled Changes in the Future
    - Less complex and costly
  - Regulatory Compliance
    - Key element in Regulatory Inspections (QSIT)
    - Retrospective Remediation (2x – 10x cost to do it correctly)
    - Reduce likelihood of 483 / Warning Letter (damage to company reputation / market)
  - Less Problems During Due Diligence / Acquisition
  - Lower Total Cost / Time to Market

DHF Content	510(k) Section(s)
Design Inputs	Intended Use / Indications for Use, Device Description
Design Outputs (specifications)	Device Description, Substantial Equivalence Comparison, Software, Labeling
Risk Analysis	Software Section
Design Verification	Performance Testing (Bench)
Design Validation	Performance Testing (Bench), Performance Testing (Animal), Performance Testing (Clinical), Biocompatibility, Sterilization, Electrical Safety and EMC, Shelf-Life, Declarations of Conformity
Traceability	Software Section

Taking the mystery out of how a DHF integrates with a QMS



QMS Structural view



Where Design Control fits

DESIGN CONTROLS: DESIGN CONTROL

Embodiment

- Design Control SOP
  - Should define the requirements and processes for Design and Development of new products, and changes to existing products
  - Should also include process for auditing of DHF prior to release of product for sale

Evidence/Requirements

- Evidence
  - N/A – Slides below
- Document Requirements
  - N/A – Slides below

DESIGN CONTROLS: DESIGN AND DEVELOPMENT PLANNING

Embodiment

- Design and Development Planning SOP
  - Should define the requirements and processes for Design and Development Planning
  - Process should be the vehicle for approving Design and Development projects.
  - May utilize subcontractors to perform some of the Design and Development activities defined in this procedure.

Evidence/Requirements

- Evidence
  - Design and Development Plan
    - Must include definition of responsibilities, including those which are sub-contracted
- Document Requirements
  - Formal Approval and Control
  - Revision control after initial approval
  - Utilizes the CO system

DESIGN CONTROLS: DESIGN INPUT

Embodiment

- Design Input SOP
  - Should define the process for collecting user requirements, reviewing and approving those requirements
  - Should contain a process for resolving incomplete, ambiguous or conflicting requirements

Evidence/Requirements

- Evidence
  - Product Requirements Document
    - All requirements consolidated into a single, unified requirements specification for the product
    - Forms the basis for product development (specifications) and verification and validation
- Document Requirements
  - Formal Approval and Control
  - Revision control after initial approval
  - Utilizes the CO system

Embodiment

- Risk Management and Risk Analysis SOPs
  - Should defines the requirements and processes for the application of Risk Management throughout the product lifecycle
  - Should defines the requirements and processes for execution of Risk Analysis (FMEA, FTA, etc.)

Evidence/Requirements

- Evidence
  - Hazard Analysis
  - DFMEA
  - UFMEA/AFMEA
- Document Requirements
  - Formal Approval and Control
  - Revision control after initial approval
  - Utilizes the CO system

DESIGN CONTROLS:
DESIGN Input/design output

DESIGN CONTROLS: DESIGN OUTPUT

Embodiment

- Design Output SOP
  - Should define the process for converting the requirements into physical manifestation of the design (design specifications).
  - Should contain a process for resolving incomplete, ambiguous or conflicting specifications

Evidence/Requirements

- Evidence
  - Product Specification Document
    - Defines the comprehensive set of verifiable product and performance specifications
  - Detailed Design Specifications
  - Risk Analyses
  - Traceability Matrices
- Document Requirements
  - Formal Approval and Control
  - Revision control after initial approval
  - Utilizes the CO system

Embodiment

- Design Verification and Validation SOP
  - Should define the basic requirements and process for Design Verification and Validation of new products, and changes to existing products

Evidence/Requirements

- Evidence
  - Design Verification and Validation Plan
  - Design Verification and Validation Protocols
  - Original test data
  - Design Verification and Validation Reports
- Document Requirements
  - Suggested format, but changes acceptable if key sections included
  - Formal Approval and Control
  - Protocols Pre-Approved Prior to Execution
  - Deviations to acceptance criteria not allowed
  - Revision control after initial approval
  - Utilizes the CO system

DESIGN CONTROLS: DESIGN Verification and Validation

DESIGN CONTROLS: DESIGN review

Embodiment

- Design Review SOP
  - Should defines the requirements and process of collecting peer input at various points in the development process
  - Should define the minimum functional representation required based on documentation being reviewed e.g.:
    - Regulatory Affairs (safety and clinical)
    - Independent Reviewer

Evidence/Requirements

- Evidence
  - Design Review Meeting Minutes
- Document Requirements
  - Minutes kept at each review
  - Configuration reviewed
  - Attendees
  - Date
  - Action Items

DESIGN CONTROLS: DESIGN Transfer

Embodiment

- Design Transfer SOP
  - Should define the requirements and processes for planning and execution of the transfer of the design to manufacturing

Evidence/Requirements

- Evidence
  - Design Transfer Plan
- Document Requirements
  - Formal Approval and Control
  - Revision control after initial approval
  - Utilizes the CO system

OTHER QMS ELEMENTS:
Quality system/management responsibility

Embodiment

- Quality Manual (Policy)
  - Should define the company specific interpretation of the regulations and applicability and non-applicability to the company
  - Should define Management Responsibilities
- Management Review SOP
  - Should defines the requirements and process in order to execute Management Reviews

Evidence/Requirements

- Evidence
  - Management Review Meeting Minutes
- Document Requirements
  - Minutes kept at each review
  - QMS Elements/Data reviewed
  - Attendees
  - Date
  - Action Items
  - State of Quality System

OTHER QMS ELEMENTS: DOCUMENT CONTROLs

Embodiment

- Document Origination and Change Control SOP
  - Should define the requirements and processes for origination, change and maintenance of documents within the Quality Management System (policies, procedures, design and DHF and DHF documentation, etc.)

Evidence/Requirements

- Evidence
  - Policies
  - SOPs
  - DHF
- Document Requirements
  - N/A

OTHER QMS ELEMENTS: personnel

Embodiment

- Employee Training SOP
  - Should define the requirements and process for the definition, execution, and maintenance of employee training within the Quality Management System

Evidence/Requirements

- Evidence
  - Job Descriptions
  - Training Plans
  - Training Records
- Document Requirements
  - N/A

OTHER QMS ELEMENTS: PURCHASING CONTROLS

Embodiment

- Supplier Quality Assurance SOP
  - Should define the requirements and processes for the evaluation and qualification of suppliers (including consultants and sub-contractors)
    - FDA expects that qualification of external resources working on design control activities be documented, reviewed and approved.
- Purchasing of R&D Materials SOP
  - Should define the requirements and processes for the purchase of development materials, including transfer of these materials to manufacturing under certain conditions.

Evidence/Requirements

- Evidence
  - Approved Supplier List
  - Supplier Qualification Documentation
  - Purchasing Records and Specifications
- Document Requirements
  - N/A

Embodiment

- Equipment Maintenance and Calibration SOP
  - Should define the requirements and process for the maintenance and calibration of equipment utilized within execution of Design Verification and Validation

Evidence/Requirements

- Evidence
  - Equipment Maintenance Requirements and Records
  - Equipment Calibration Requirements and Records
- Document Requirements
  - N/A

OTHER QMS ELEMENTS:
Inspection, measuring, and test equipment

OTHER QMS ELEMENTS: Process validation

Embodiment

- Process Validation SOP
  - Should define the requirements and processes for validation of equipment utilized in the manufacture of units for formal Design Verification and Validation
  - At a minimum, Installation Qualification (IQ)

Evidence/Requirements

- Evidence
  - Installation Qualification Protocols
  - Original test data
  - Installation Qualification Reports
- Document Requirements
  - Suggested format, but changes acceptable if key sections included
  - Formal Approval and Control
  - Protocols Pre-Approved Prior to Execution
  - Deviations to acceptance criteria not allowed
  - Revision control after initial approval
  - Utilizes the CO system N/A

OTHER QMS ELEMENTS: Statistical techniques

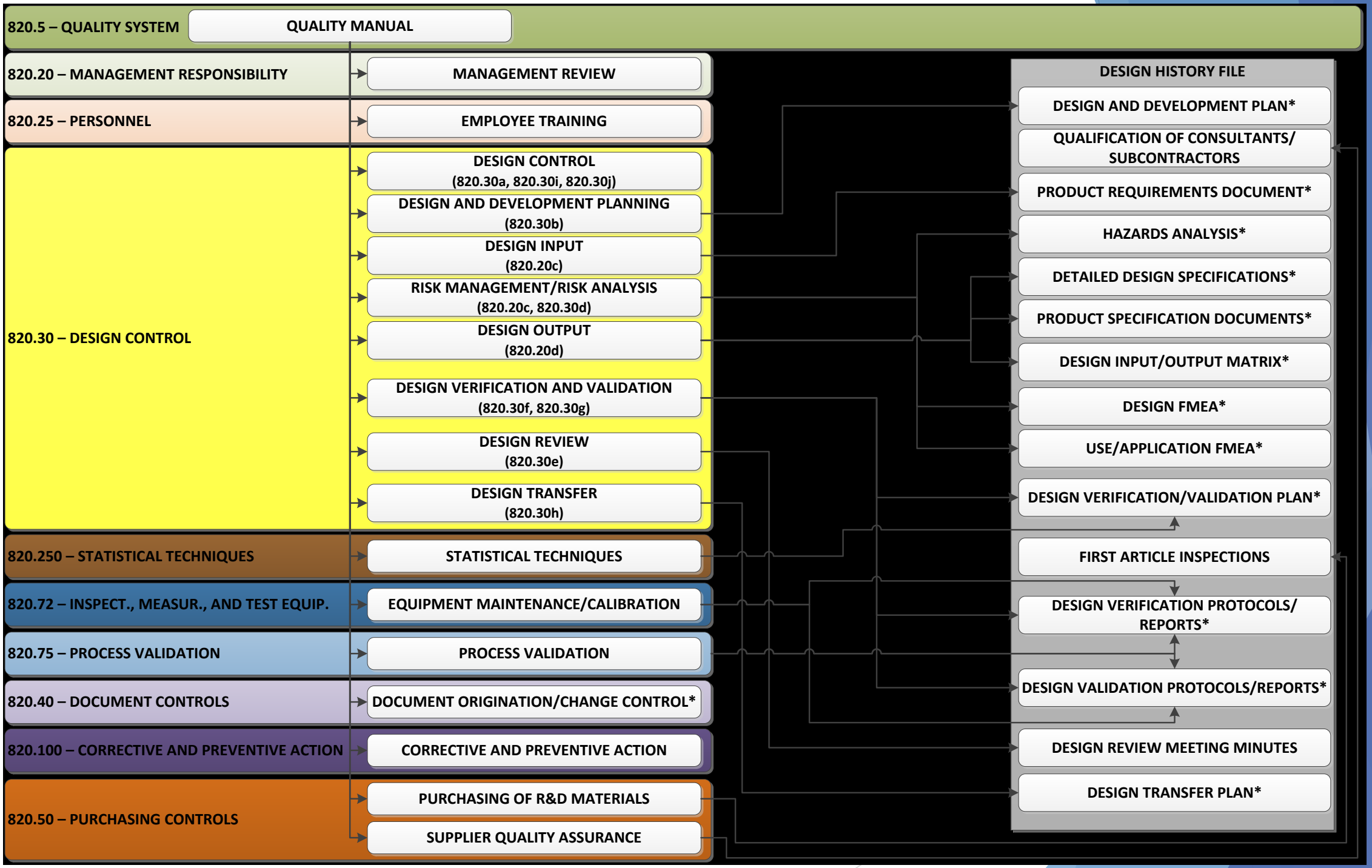
Embodiment

- Statistical Techniques SOP
  - Should define the requirements and process for the application of Statistical Techniques within Design Verification and Validation
  - Should define the minimum statistical requirements based on risk for Design Verification and Validation

Evidence/Requirements

- Evidence
  - N/A
- Document Requirements
  - N/A

Example QMS integration and dhf interaction diagram (21 cfr part 820)


820.5 – QUALITY SYSTEM
QUALITY MANUAL
820.20 – MANAGEMENT RESPONSIBILITY
MANAGEMENT REVIEW
820.25 – PERSONNEL
EMPLOYEE TRAINING
820.30 – DESIGN CONTROL
DESIGN CONTROL (820.30a, 820.30i, 820.30j)
DESIGN AND DEVELOPMENT PLANNING (820.30b)
DESIGN INPUT (820.20c)
RISK MANAGEMENT/RISK ANALYSIS (820.20c, 820.30d)
DESIGN OUTPUT (820.20d)
DESIGN VERIFICATION AND VALIDATION (820.30f, 820.30g)
DESIGN REVIEW (820.30e)
DESIGN TRANSFER (820.30h)
820.250 – STATISTICAL TECHNIQUES
STATISTICAL TECHNIQUES
820.72 – INSPECT., MEASUR., AND TEST EQUIP.
EQUIPMENT MAINTENANCE/CALIBRATION
820.75 – PROCESS VALIDATION
PROCESS VALIDATION
820.40 – DOCUMENT CONTROLS
DOCUMENT ORIGINATION/CHANGE CONTROL*
820.100 – CORRECTIVE AND PREVENTIVE ACTION
CORRECTIVE AND PREVENTIVE ACTION
820.50 – PURCHASING CONTROLS
PURCHASING OF R&D MATERIALS
SUPPLIER QUALITY ASSURANCE
DESIGN HISTORY FILE
DESIGN AND DEVELOPMENT PLAN*
QUALIFICATION OF CONSULTANTS/ SUBCONTRACTORS
PRODUCT REQUIREMENTS DOCUMENT*
HAZARDS ANALYSIS*
DETAILED DESIGN SPECIFICATIONS*
PRODUCT SPECIFICATION DOCUMENTS*
DESIGN INPUT/OUTPUT MATRIX*
DESIGN FMEA*
USE/APPLICATION FMEA*
DESIGN VERIFICATION/VALIDATION PLAN*
FIRST ARTICLE INSPECTIONS
DESIGN VERIFICATION PROTOCOLS/ REPORTS*
DESIGN VALIDATION PROTOCOLS/REPORTS*
DESIGN REVIEW MEETING MINUTES
DESIGN TRANSFER PLAN*

Case study

CASE Study #1:
NO QMS or DHF when 510(k) was submitted

- Summary
  - Small start-up company with biliary stent/catheter device
  - Submitted 510(k) with no QMS or DHF in place
    - Limited documentation of configuration/device
    - Insufficient performance testing (bench)
- Impacts
  - 510(k) on hold due to significant requests for additional information
- Conclusion
  - Significant delay in regulatory approval (>9mo)
  - Significant cost in order to implement QMS and remediate DHF

CASE STUDY #2: Remediation of DHF due to 483

- Summary
  - Large orthopedic device company
  - Received 483 due to:
    - Insufficient procedural definition of Design Control program
    - Gaps identified within documentation of Design Inputs, Design Outputs, Design Verification and Validation, and Traceability within DHF
- Impacts
  - Required large project in order to remediate (>6mo)
  - Redeployment of resources from New Product Development to remediation
- Conclusion
  - Significant organizational impact
  - Significant cost in order to remediate Design Control program, DHF documentation, and close 483

FDA critical DHF assessment areas

QSIT Design Controls Narrative

Purpose/Importance

The purpose of the design control subsystem is to control the design process to assure that devices meet user needs, intended uses, and specified requirements. Attention to design and development planning, identifying design inputs, developing design outputs, verifying that design outputs meet design inputs, validating the design, controlling design changes, reviewing design results, transferring the design to production, and compiling a design history file help assure that resulting designs will meet user needs, intended uses and requirements.

QSR Preamble

The FDA provided an official interpretation of this requirement in the preamble when the QSR was published in 1996. That discussion of the requirement indicated that the DHF is intended to be a repository of the records required to demonstrate compliance with your design plan and your design control procedures.

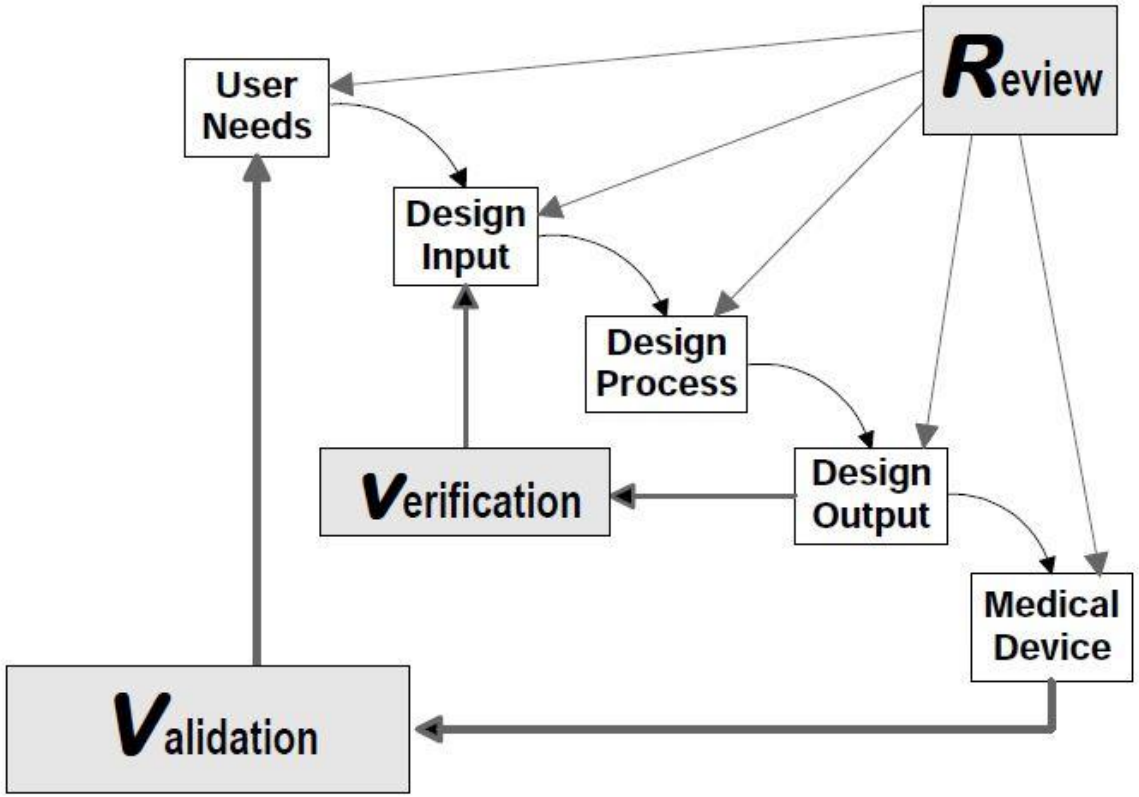
FDA critical DHF assessment areas

How

- Establish and maintain a design history file for each type of device
- Include in the DHF or reference records information necessary to demonstrate that the design was developed in accordance with the Design Plan and Quality System requirements.
- Per FDA Design Control Guidance: “diverse records need not be consolidated at a single location. The intent is simply that manufacturers have access to the information when it is needed.
  - There are no requirements on the location or organization of the design history file.
    - For simple designs, the designer may assemble and maintain the entire design history file.
    - For larger projects, a document control system will likely be established for design documents
- Assess impact of design changes to the DHF

FDA critical DHF assessment areas

FDA Design Control Guidance for Medical Device Manufacturers



- Requirements / Specifications
- Risk analysis
- Verification/Validation (dates)
- Trace Matrices
- Design Reviews
- Design Transfer

Virtually every section of the design control requirements specifies information which should be recorded

FDA critical DHF assessment areas

Common DHF deficiencies

Warning Letter Examples:

Alpine Oral Care (9/26/2008)

- Failure to establish and maintain a device design history file for each type of device to include or reference the records necessary to demonstrate that the design was developed in accordance with the approved design plan and the design control requirements of 21 C.F.R § 820, as required by 21 C.F.R § 820.30). Specifically, your firm has not maintained a design history file for the mouth guard devices to include documentation of design plans, design input requirements, design outputs, design reviews, design risk analysis, design changes, design verification or validation, and design transfer.

Common DHF deficiencies

Warning Letter Examples cont.

Boston Scientific (2/4/2016)

- Failure to establish and maintain procedures for validating the device design, as required by 21 CFR 820.30(g). For example, your firm's Design and Development procedure, Issue 3, dated August 5, 2014, does not include requirements for performing design validation under defined operating conditions on initial production units, lots, or batches, or their equivalents; testing production units under actual or simulated use conditions; and documenting the results of the design validation, including identification of the design, method(s), the date, and the individual(s) performing the validation in the Design History File (DHF). Additionally, **(b)(4)** Design Validation Testing, **(b)(4)**, do not have the date or signature of the individuals who conducted and approved the validation.

Common DHF deficiencies

Warning Letter Examples cont.

Nurse Assist Inc. (11/9/2007)

- Your firm promotes your "USP sterile solutions" for "wound care and irrigation," a modified intended use of the devices, on your firm's website at http://www.rnplus.com without conducting an adequate design risk analysis and design validation and documenting their results to ensure that the devices conform to defined user needs and intended uses. During the inspection, your firm's Vice President of Operations verbally stated that your firm had no design history file or design control records for the existing sterile water and sterile normal saline nor obtained their design control records from Welcon when your firm bought their 510(k)s, products, and manufacturing equipment in 2005.

Common DHF deficiencies

Warning Letter Examples cont.

A.R.C.O.S Sri (August 3, 2016)

- Failure to establish and maintain procedures to control the design of the device in order to ensure that specified design requirements are met, as required by 21 CFR 820.30(a). For example, your firm does not have written design control procedures, and has not conducted and documented design control activities for various models of compression socks, including TRAVELSOX, EUROS, CARESOX, and VITALSOX.

- We reviewed your firm's response and conclude that it is not adequate. Your firm indicated it will create design control procedures and design history files. However, there is no indication your firm plans to evaluate the potential impact of the lack of design controls on previously distributed devices.

Common DHF deficiencies

When / why is a DHF gap analysis warranted

When / why is a DHF gap analysis warranted

When:

- DHF audits at each phase gate of the product life cycle process (Independent review)
- Prior to Design Transfer
- Prior to audits or regulatory inspections
- If you suspect you may be out of compliance

Why:

- To ensure all the requirements for the Design History File have been established
- To preserve knowledge base which forms the basis for the product design
- Remediation costs significantly increase further into the products lifecycle
- Warning Letters negatively impact customer perception of the company and the quality of its product
- It's the right thing to do to assure safe and effective products

Question and answers

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