THE QUALITY SYSTEM REGULATIONS

SUBPART C – DESIGN CONTROLS

21 CFR 820.30
DESIGN CONTROLS

21 CFR 820.181
DEVICE MASTER RECORD

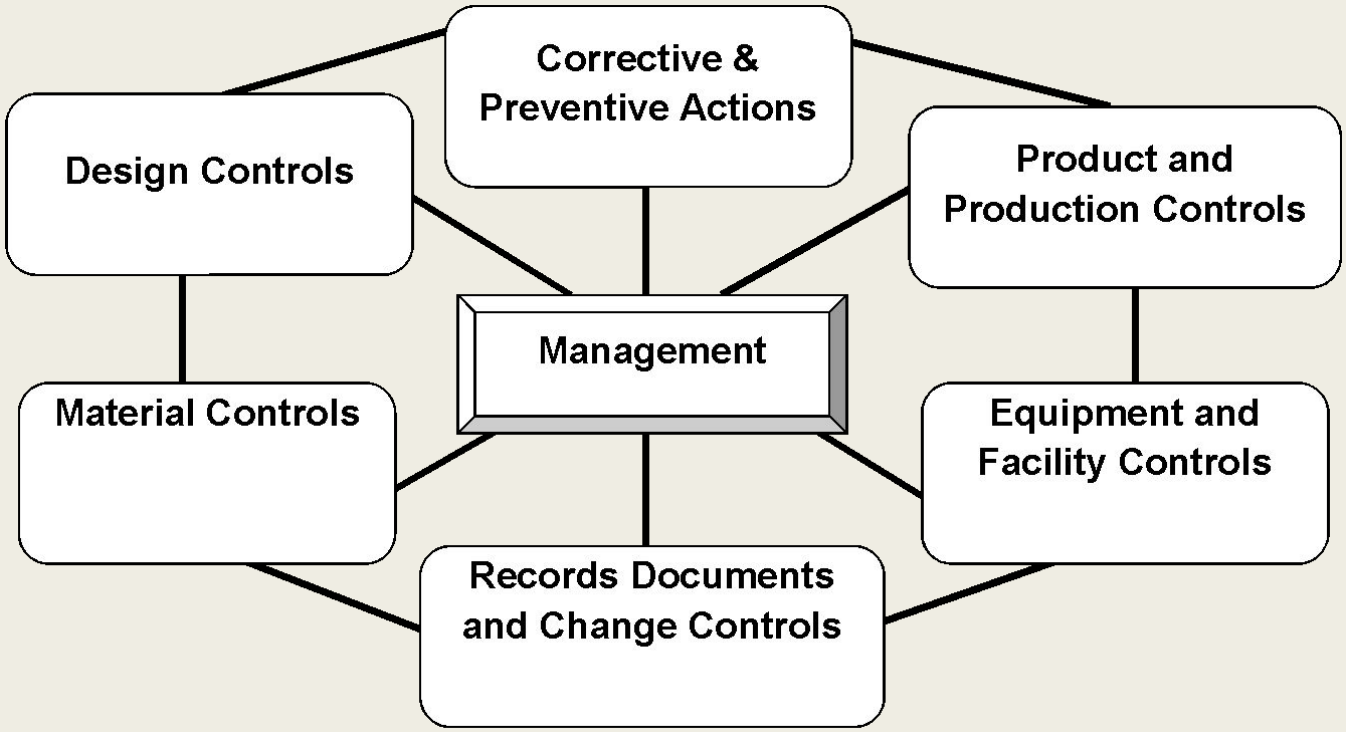
Why Design Controls?

- FDA noted that manufacturers were producing product that failed to meet design specifications
- Products were designed with inherent flaws
  - *Many times resulting in product failures and/or recalls*
- October 7, 1996 Design Controls became part of the FDA Medical Device Regulation and became effective June, 1 1997
- FDA requires the Medical Device industry to follow design controls

Elements of Design Controls

- *Design & Development Planning- 820.30(b)*
- *Design Input- 820.30(c)*
- *Design Output- 820.30(d)*
- *Design Review(s)- 820.30(e)*
- *Design Verification- 820.30(f)*
- *Design Validation- 820.30(g)*
- *Design Transfer- 820.30(h)*
- *Design Changes- 820.30(i)*
- *Design History File- 820.30(j)*

What parts of the QMS does Design Control impact?



21 CFR 820.30(a) Design Controls

(a) *General.*

- *(1) Each manufacturer of any Class III or Class II device, and the Class I devices listed in paragraph (a)(2) of this section, shall establish and maintain procedures to control the design of the device in order to ensure that specified design requirements are met.*

- *(2) The following class I devices are subject to design controls:*
  - *(i) Devices automated with computer software; and*
  - *(ii) The devices listed in the following chart*

Section	Device
868.6810	Catheter, Tracheobronchial Suction.
878.4460	Glove, Surgeon's.
880.6760	Restraint, Protective.
892.5650	System, Applicator, Radionuclide, Manual.
892.5740	Source, Radionuclide Teletherapy.

21 CFR 820.30(b) Design & Development Planning

(b)Design and development planning.

- *Each manufacturer shall establish and maintain plans that describe or reference the design and development activities and define responsibility for implementation.*
- *The plans shall identify and describe the interfaces with different groups or activities that provide, or result in, input to the design and development process.*
- *The plans shall be reviewed, updated, and approved as design and development evolves.*

- ISO 13485: 2016 section 7.3.2

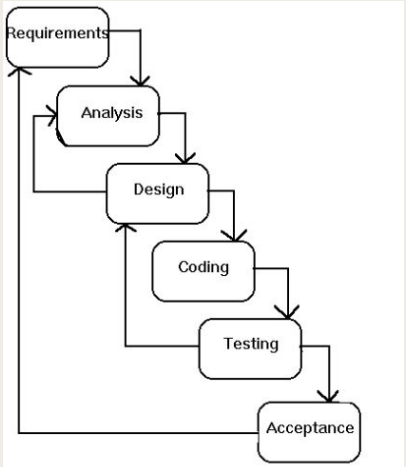
21 CFR 820.30(b)
When design control plans begin:

"To assist FDA in applying the regulation, manufacturers should document the flow of the design process so that it is clear to the FDA Investigator where research is ending and development of the design is beginning."

Reference the Preamble comment #63

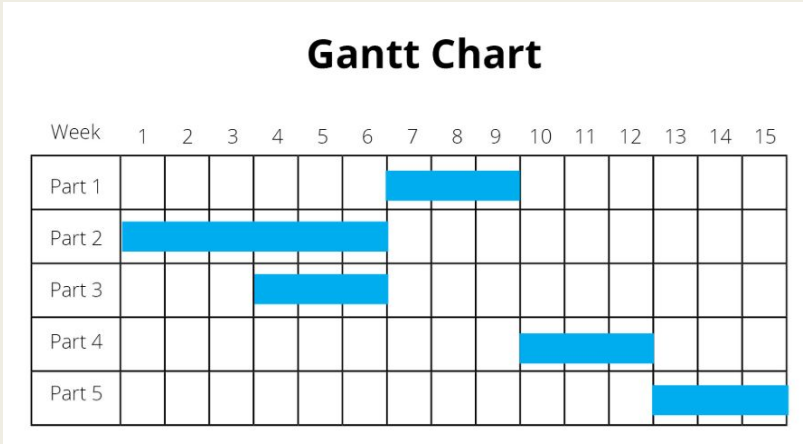
21 CFR 820.30(b) Design Planning Documentation

- The overall design activities can be defined in a flow chart or other graphic (may help with concept of design loop).
  - Flow Charts – for process.

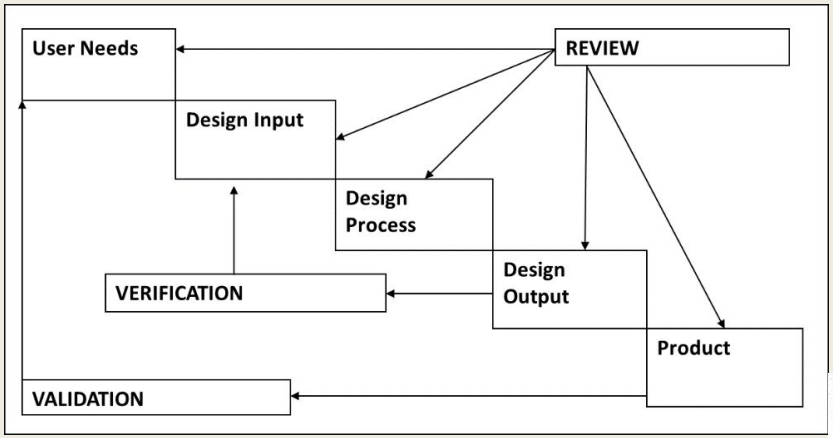


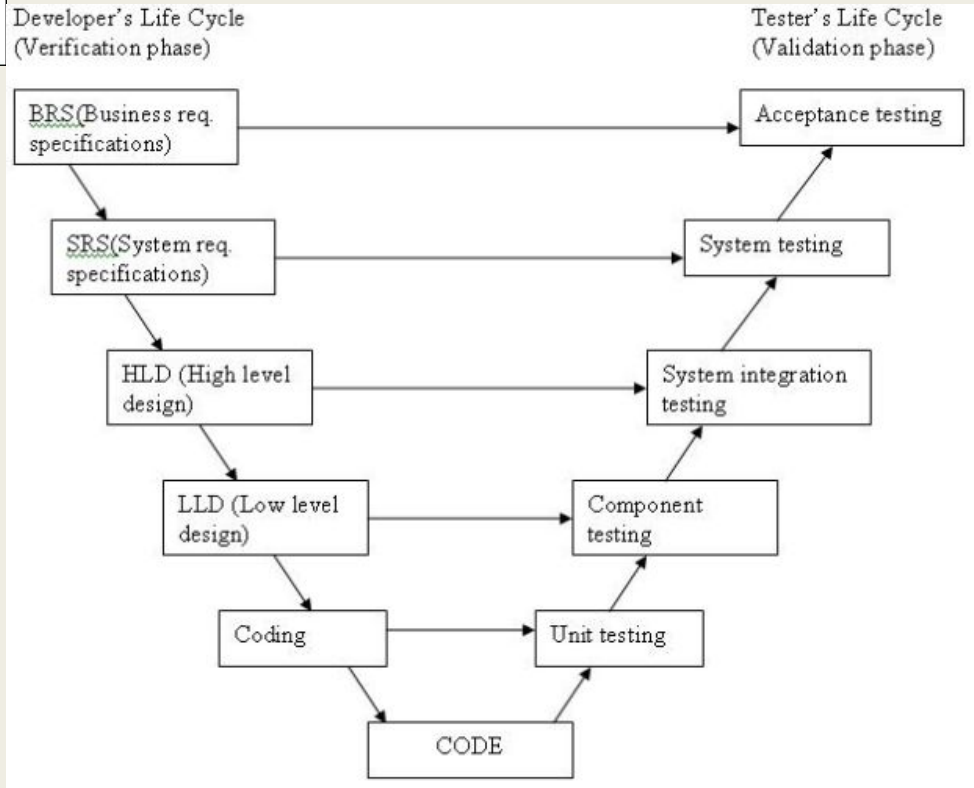
The waterfall model (Systems Development Life Cycle)

  - Gantt Charts – for the design plan.



The Design Process – Waterfall Diagram vs. V&V Model





*These charts are just two examples

Remember to take into account
820.50;
820.180, 820.120,
820.130-140-150-160-170, 820.200

21 CFR 820.30(c) Design Input

(c) Design Input.

- *Each manufacturer shall establish and maintain procedures to ensure that the design requirements relating to a device are appropriate and address the intended use of the device, including the needs of the user and patient.*
- *The procedures shall include a mechanism for addressing incomplete, ambiguous, or conflicting requirements.*
- *The design input requirements shall be documented and shall be reviewed and approved by a designated individual(s).*
- *The approval, including the date and signature of the individual(s) approving the requirements, shall be documented.*

- ISO 13485:2016 section 7.3.3

21 CFR 820.30(c) Design Input - Definition

- Design Input: means the physical and performance requirements of a device that are used as a basis for device design.

- Types of Design Inputs (for HW, FW, SW):
  - Functional – What the device does / qualitative
  - Performance – Performance specs / quantitative / environmental
  - User Interfaces – Safety, Interaction with senses

- NOTE: Design inputs must be complete, unambiguous, or conflicting. When conflicts occur – management with executive responsibility must make documented decisions.

21 CFR 820.30(c) Design Input

Considerations for Design Input:

- Intended Use
- Performance Characteristics (820.80; 820.86)
- Risk
- Biocompatibility
- Environmental compatibility (EMC /EMI)
- Regulatory Requirements
- Labeling (820.120; 820.60, 820.65)
- Human Factors (820.25)
- Voluntary standards
- Sterility

Not an all-inclusive list. Consider 820.50; 820.60; 820.65; 820.180; 820.120; 820.130-140-150-160-170; 820.200

21 CFR 820.30(d) Design Output

(d) Design Output.

- *Each manufacturer shall 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 shall contain or make reference to acceptance criteria and shall ensure that those design outputs that are essential for the proper functioning of the device are identified.*
- *Design output shall be documented, reviewed, and approved before release. The approval, including the date and signature of the individual(s) approving the output, shall be documented.*

- ISO 13485:2016 section 7.3.4

21 CFR 820.30(d) Expectation of Design Output

- The Design Inputs are translated into Design Outputs
- The total finished design output defines the elements of the Device Master Record (DMR- 820.181) and consists of the device (device specifications and production process specifications), its packaging, labeling, procedures, etc.
- Acceptance criteria are established
- Outputs that are considered to be “essential” to the proper functioning of the device are identified.
- Define the criteria for the determination of “essential” outputs in your Design Output procedures.

Consider 820.50; 820.80, 820.86; 820.180

21 CFR 820.30(d) Examples of Design Outputs:

- Design Outputs are the documented deliverables of the design phase and define the basis of the DMR (820.180)
- Diagrams
- Drawings
- Packaging & Labeling specifications (820.120; 820.130)
- Component specifications
- Production procedures (820.70; 820.72; 820.75)
- Installation and/or service procedures. (820.170; 820.200)

21 CFR 820.30(e) Design Review

(e) Design review.

- *Each manufacturer shall 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.*
- *The procedures shall ensure that participants at each design review include representatives of all functions concerned with the design stage being reviewed and an individual(s) who does not have direct responsibility for the design stage being reviewed, as well as any specialists needed.*
- *The results of a design review, including identification of the design, the date, and the individual(s) performing the review, shall be documented in the design history file (the DHF).*

- ISO 13485:2016 section 7.3.5

Consider 820.180; 820.40

21 CFR 820.30(e) Design Review

- Purpose of Design Review:
  - Ensure that the design satisfies design input requirements.
  - To detect and correct problems when they occur.
  - Discuss emerging issues.
  - Provide feedback to the design team (which should include quality).
  - Assess the project at defined intervals.
- Preamble Comment #78:
  - *…Design review includes […] whether the design outputs meet functional and operational requirements, the design is compatible with components and other accessories, the safety requirements are achieved, the reliability and maintenance requirements are met, the labeling and other regulatory requirements are met, and the manufacturing, installation, and servicing requirements are compatible with the design specifications.…*

21 CFR 820.30(f) DESIGN VERIFICATION

(f) Design verification.

- *Each manufacturer shall establish and maintain procedures for verifying the device design.*
- *Design verification shall confirm that the design output meets the design input requirements.*
- *The results of the design verification, including identification of the design, method(s), the date, and the individual(s) performing the verification, shall be documented in the DHF.*

- ISO 13485:2016 section 7.3.6

21 CFR 820.30(f)
Design Verification

- Design verification activities must be documented.
  - Procedure
  - Demonstrate that the device outputs reflect the design inputs.
  - Use of Protocols
  - Test Results
  - Verification activities are documented in the Design History File (DHF).

Design Verification vs. Design Validation

Design Verification	**Design Validation**
Confirmation of Specifications: *Did we design the device correctly?*	Confirmation of user needs and intended use(s): *Did we design the correct device?*

21 CFR 820.30(g) Design Validation

(g) Design validation.

- *Each manufacturer shall establish and maintain procedures for validating the device design.*
- *Design validation shall be performed under defined operating conditions on initial production units, lots, or batches, or their equivalents.*
- *Design validation shall ensure that devices conform to defined user needs and intended uses and shall include testing of production units under actual or simulated use conditions.*
- *Design validation shall include software validation and risk analysis, where appropriate.*
- *The results of the design validation, including identification of the design, method(s), the date, and the individual(s) performing the validation, shall be documented in the DHF.*

ISO 13485:2016 section 7.3.7

21 CFR 820.30(g)
Design Validation

As defined in 820.3:

- *(z)(1) Design validation: establishing by objective evidence that device specifications conform with user needs and intended use(s).*
- *(z) Validation: confirmation by examination and provision of objective evidence that the particular requirements for a specific intended use can be consistently fulfilled.*

21 CFR 820.30(g) Key Considerations for Design Validation

- Plan for design validation early in the design process (including software considerations).
  - Identify those performance characteristics that require validation (e.g. cannot be fully verified).
  - Address the needs of the patients and users.
  - Establish the validation methods and acceptance criteria to address labeling, packaging, human factors, etc.
  - Include the performance of clinical evaluations
  - include testing under simulated or actual use conditions.

21 CFR 820.30(g)
Key Considerations for Design Validation

- Confirm that the completed design validation did not leave any unresolved discrepancies. If the device contains software, confirm that the software was validated.
- Confirm that risk analysis was performed.
- It is the manufacturer's responsibility to demonstrate that equivalent devices are, in fact, equivalent.
- Confirm that design validation was accomplished using initial production devices or their equivalent.
- Design validation must be completed before commercial distribution of the device

21 CFR 820.30(h)
Design Transfer

(h) Design transfer

- *Each manufacturer shall establish and maintain procedures to ensure that the device design is correctly translated into production specifications.*

- ISO 13485:2016 section 7.3.8

21 CFR 820.30(h)
Design Transfer

- Design Transfer is the final phase – moving the design into production.
- The transfer process is a part of the design plan.
- Transfer of knowledge and information from design team to manufacturing team.

21 CFR 820.181
Device Master Record

820.181 Each manufacturer shall maintain device master records (DMR's). Each manufacturer shall ensure that each DMR is prepared and approved in accordance with 820.40 (Document Controls).

- *The DMR for each type of device shall include, or refer to the location of, the following information:*
  - *(a) Device specifications including appropriate drawings, composition, formulation, component specifications, and software specifications;*
  - *(b) Production process specifications including the appropriate equipment specifications, production methods, production procedures, and production environment specifications;*
  - *(c) Quality assurance procedures and specifications including acceptance criteria and the quality assurance equipment to be used;*
  - *(d) Packaging and labeling specifications, including methods and processes used; and*
  - *(e) Installation, maintenance, and servicing procedures and methods.*

- ISO 13485:2016 Section 7.1

21 CFR 820.30(i) Design Changes

(i) Design changes.

- *Each manufacturer shall establish and maintain procedures for the identification, documentation, validation or where appropriate verification, review, and approval of design changes before their implementation.*

- ISO 13485:2016 section 7.3.9

Consider 820.72; 820.75; 820.80; 820.86; 820.170; 820.180; 820.181; 820.184; 820.200

21 CFR 820.30(i)
Design Changes

- When changes are made to new or existing designs, design controls must be followed to ensure that changes are appropriate and the device will continue to perform as intended.
  - i.e. changes will not negatively impact a device's ability to meet user needs.

Consider 820.72; 820.75; 820.80; 820.86; 820.170; 820.180; 820.181; 820.184; 820.200

21 CFR 820.30(i) Design Changes

Examples:

- Changes made to approved inputs or outputs to correct design deficiencies identified in the V&V activities.
- Labeling changes which enhance the device's capabilities or are required to meet new requirements.
- Changes resulting from customer complaints (post-market feedback loop).
- Post production changes require the firm to link back into design control – though not necessarily to R&D.

21 CFR 820.30(i) Design Changes

- “Procedures must ensure that after the design requirements are established and approved, changes to the design, both pre-production and post-production are also reviewed, validated (or verified where appropriate), and approved.”

- “The records of these changes create a history of the evolution of the design, which can be invaluable for failure investigation and for facilitating the design of future similar products.”

Preamble response to comment 87

21 CFR 820.30(j)
Design History File

(j) Design history file.

- *Each manufacturer shall establish and maintain a DHF for each type of device.*
- *The DHF shall contain or reference the records necessary to demonstrate that the design was developed in accordance with the approved design plan and the requirements of this part (including post-market design changes).*

- ISO 13485:2016 section 7.3.10

21 CFR 820.30(j)
Design History File

- The Design history file is a compilation of records which describes the design history of a finished device.
- Purpose: “to ensure that the final design conforms to the design specification.”
- Not required to be a single file – but contains a reference to where all of the DHF documents are located.

21 CFR 820.30(j) Design History File

DHF must include clear evidence of meeting all design control requirements.

- Planning
- Inputs
- Outputs
- Reviews
- Verifications
- Validations
- Transfer
- Changes

Helpful tip: Use an index to navigate the DHF.

21 CFR 820.30
Design Controls

Warning Letter Examples

Design validation failed to ensure that devices conform to defined user needs and intended uses, as required by 21 CFR 820.30(g). For example:

a. At the time of clearance, the labeling of the Product XXX and Product XXX Systems allowed for the immediate analysis of whole blood samples after thoroughly mixing the blood/treatment reagent mixture and after storage of that mixture for up to 48 hours at room temperature or up to 7 days if stored refrigerated. The labeling of the Product XXXs System, at the time of clearance, allowed for the analysis of venous whole blood samples after storage of the blood/treatment reagent mixture for 24-48 hours at room temperature and up to 3 days if stored refrigerated. However, your firm did not provide any documents showing that your original validation studies tested under these actual use conditions and that these studies support the blood/treatment reagent mixture stability claims made in your labeling.

b. Your firm released the Product XXX System for commercial distribution in September 2013 after becoming aware of the potential for falsely low and falsely high test results for samples incubated less than 24 hours in the treatment reagent. For example, your firm's stability study for the treatment reagent provided during the inspection, entitled Blood in Treatment Reagent Stability Study Protocol-VP #XXX, Part 1, dated 09/05/2013, concluded that there was a "reproducible trend of increased [lead] signal with increased Sample/Treatment Reagent incubation time" as well as the possibility for "false lows or false highs"; and your firm's stability study for the treatment reagent, entitled Blood and Treatment Reagent Stability Study-VP #XXX, Part 2, dated 09/10/2013, stated that "Sample/Treatment Reagent Preparations **(b)(4)**."

21 CFR 820.30
Design Controls

- Warning Letter Examples:

Failure to ensure that design verification shall confirm that the design output meets the design input requirements, as required by 21 CFR 820.30(f).

For example: Your firm has a design input, ***(b)(4)***, of "the Remote Monitoring device shall only open network ports to authorized interfaces" which is documented in ***(b)(4)*** *Software System Requirements Specification, Document* ***(b)(4)***. This is implemented as a design output in your firm's *Merlin@home Software Requirements Specification Uploads* ***(b)(4)***.

This design output was not fully verified during your firm's design verification activities. According to your firm's testing procedures, ***(b)(4)***, *Final Configuration Test Procedures,* ***(b)(4)*** and *Final Configuration Test Procedures Document* ***(b)(4)***, the requirement was only partially verified by testing that the network ports opened with an authorized interface. Your testing procedures did not require full verification to ensure the network ports would not open with an unauthorized interface.

QUESTIONS?