FIND

DESIGN CONTROL

Olga Ordeig

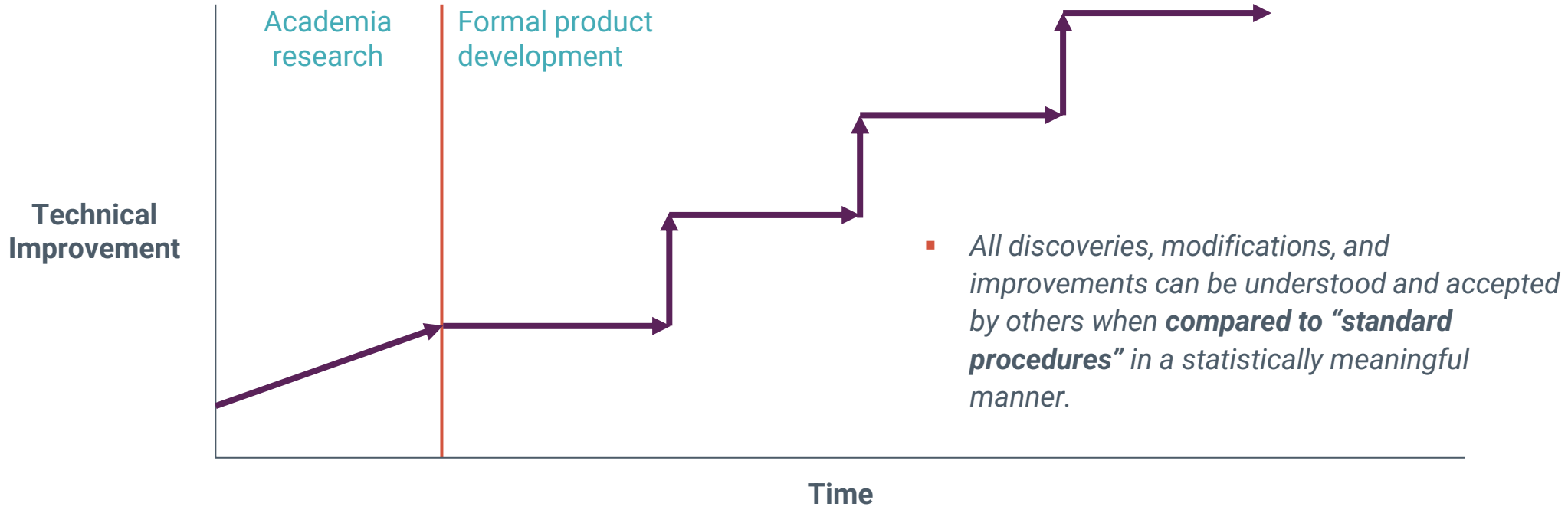
TOPICS

1. Product development: stepwise approach
2. Design Control: What? Why? When? How?
3. Design Control Process:
    1. Design Planning
    2. Desing Inputs
    3. Design Outputs
    4. Design Review
    5. Design Verification
    6. Design Validation
    7. Design Transfer
    8. Design Change
    9. Design History File

PRODUCT DEVELOPMENT

STEPWISE APPROACH

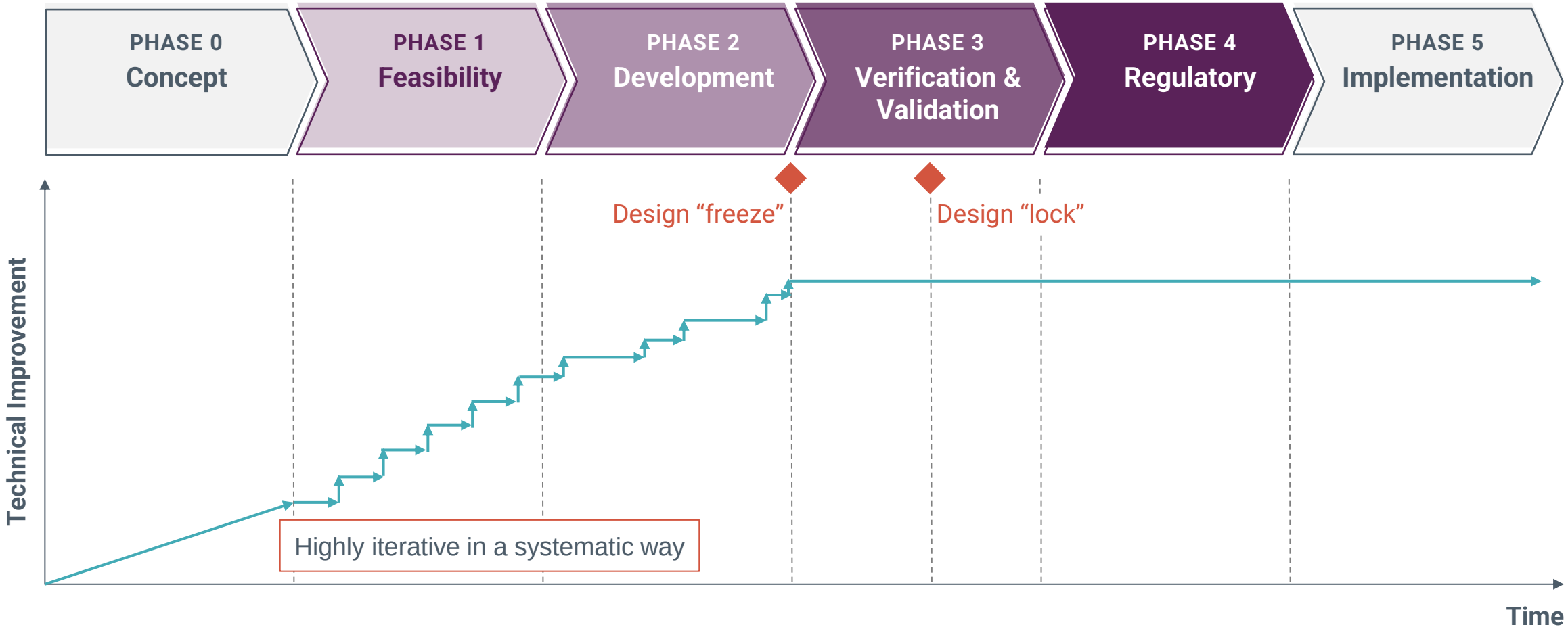
- **Product Development** needs to be a systematic approach to experimental design and test optimization. Everybody needs to run the test protocol in the same way and when a change is applied it is made systematically.



- *All discoveries, modifications, and improvements can be understood and accepted by others when **compared to "standard procedures"** in a statistically meaningful manner.*

FIND PHASE GATE SYSTEM

PRODUCT DEVELOPMENT PROCESS



DESIGN CONTROL

WHAT?

Design Controls are an interrelated set of quality practices and procedures that are incorporated into the Design and Development process of a medical device.

DESIGN CONTROL

WHY?

Design controls are a **regulatory requirement** in certain regions and countries.

FDA

FDA 21 CFR Quality System Regulation
§ 820.30 Design Controls

§ 820.30 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**.

Santé Canada Health Canada

Medical Device Regulation
SOR98/282

MDSAP
MEDICAL DEVICE SINGLE AUDIT PROGRAM

World Health Organization

IMDRF GRRP WG/N47
FINAL:2018
Essential Principles of Safety and Performance of Medical Devices and IVD Medical Devices

IVD Regulation (EU) 2017/746

European Commission

DESIGN CONTROL

WHY?

Design controls are intended to demonstrate that a device:

- has been design to address the needs of users and patients.
- has been design to meet inputs and requirements.
- has been proven to meet applicable standards.
- meets the performance acceptance criteria.

The **cost to correct design errors is lower when errors are detected early** in the design and development process.
Good design control reduce risks, but **do not** substitute risk management.

RESOURCES

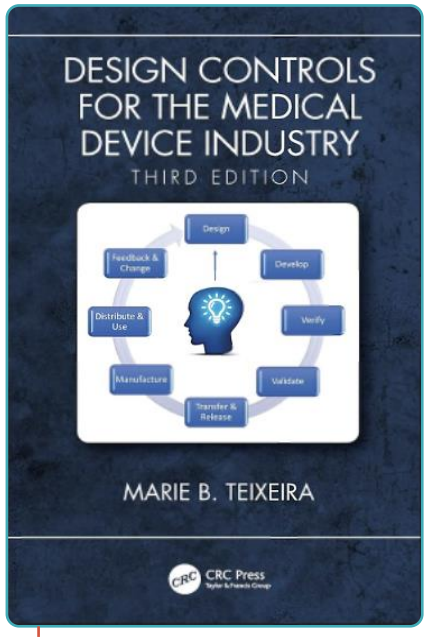
- The literature contains an abundance of information on tools and techniques for Design Control:

- FDA Quality System (QS) Regulation/Medical Device Good Manufacturing Practices; Subpart C - Design Controls

  https://www.fda.gov/regulatory-information/search-fda-guidance-documents/design-control-guidance-medical-device-manufacturers

- ISO 13485:2016 Medical devices - Quality management systems - Requirements for regulatory purposes; Section 7.3 Design and Development

  https://www.iso.org/obp/ui/#iso:std:iso:13485:ed-3:v1:en

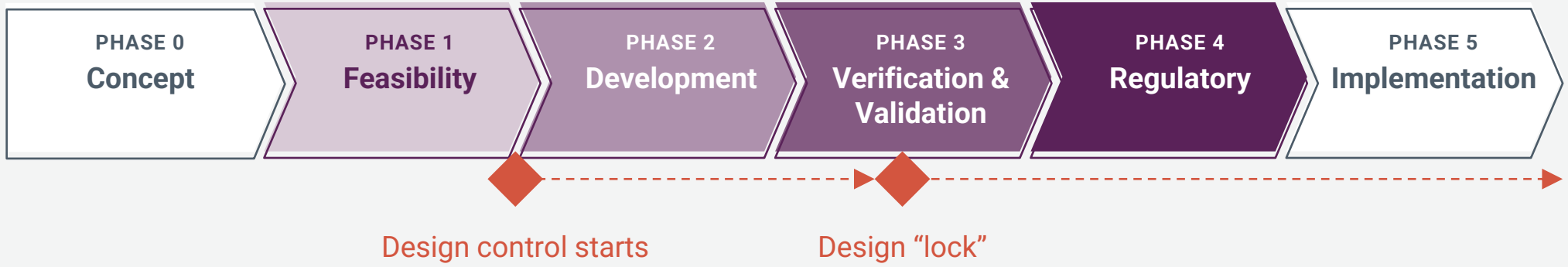


- Design Controls for the Medical Device Industry, 3rd edition (2019). Teixeira, Marie B.

DESIGN CONTROL

WHEN?

Design control begins somewhere between **Feasibility** and **Development**, and it will cover the entire product life-cycle.



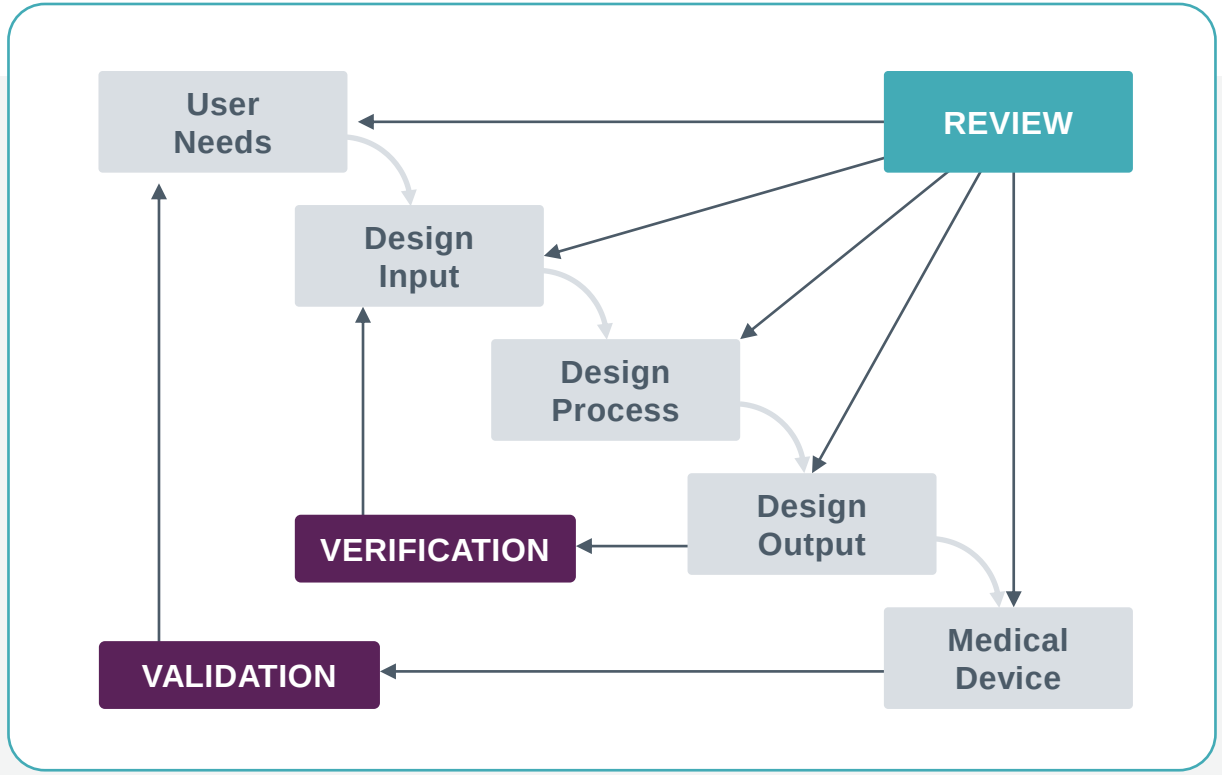
DESIGN CONTROL

HOW?

In the **FDA waterfall model**, the design process proceeds in a sequential manner with multiple review points.

Design reviews are an important part of the design process and are shown between each phase in this schematic model.

Requirements are developed, the device is designed to meet those requirements, the design is evaluated, transferred to production and manufactured.



FDA Quality System (QS) Regulation/Medical Device Good Manufacturing Practices

DESIGN CONTROL PROCESS

1. **Design Planning**
2. Design Inputs
3. Design Outputs
4. Design Review
5. Design Verification
6. Design Validation
7. Design Transfer
8. Design Change
9. Design History File

DESIGN CONTROL PROCESS

DESIGN PLANNING

WHAT TO PLAN?

*"The organization shall **plan and control the design and development** of a product. As appropriate, design and development planning **documents** shall be maintained and updated as the design and development progress."*

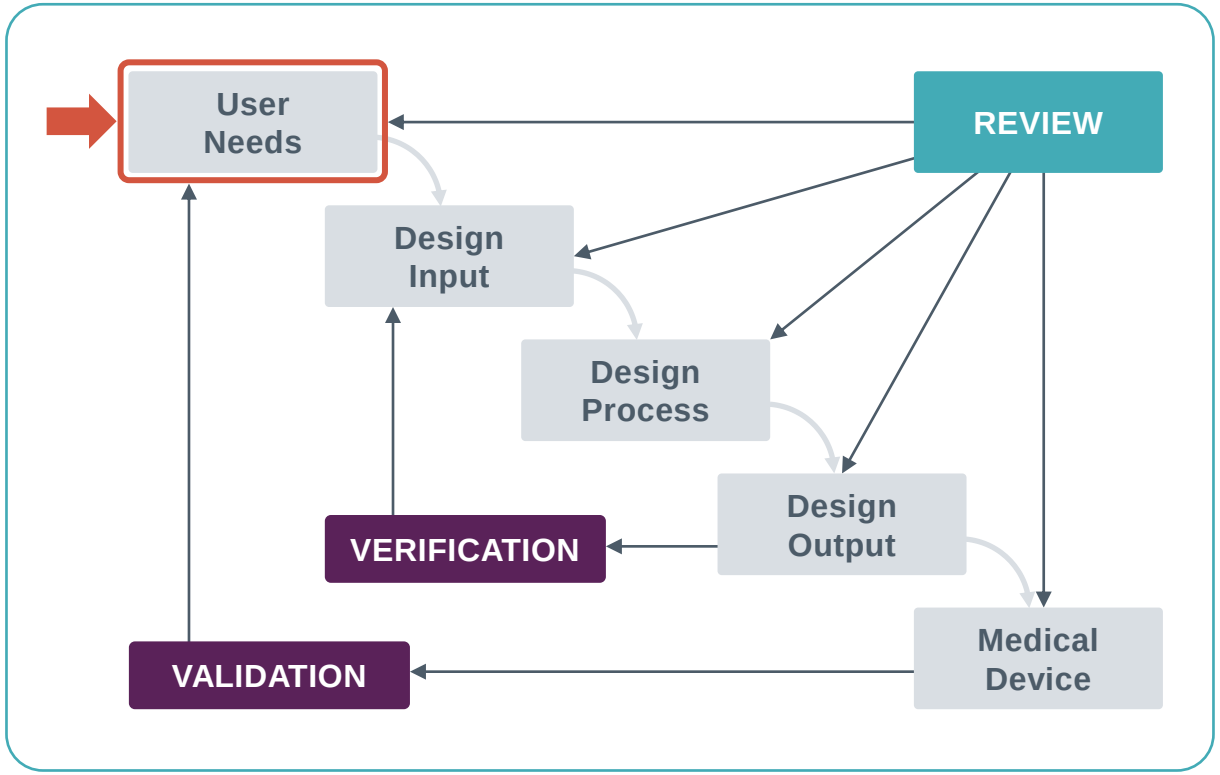
- Stages
- **REVIEW** needed at each phase
- Verification, validation and design transfer activities
- Responsibilities and authorities
- **TRACEABILITY** of design outputs to design inputs
- Resources needed, including necessary **COMPETENCE** of personnel

DESIGN PLANNING

Market Requirements Document (MRD) / User Needs:

Ensures that design requirements relating to a device are appropriate and address the intended use of the device, including the needs of the user and patient.

- **End user requirements:** specimen(s), work volume, protocols, assay format, specimen ID, performance, data/results handling, shelf-life, packaging.
- **Market Requirements:** competitive landscape, product positioning, impact on clinical pathway, geographical distribution, pricing, cost of goods target, reimbursement, forecast.



FDA Quality System (QS) Regulation/Medical Device Good Manufacturing Practices; Subpart C - Design Controls

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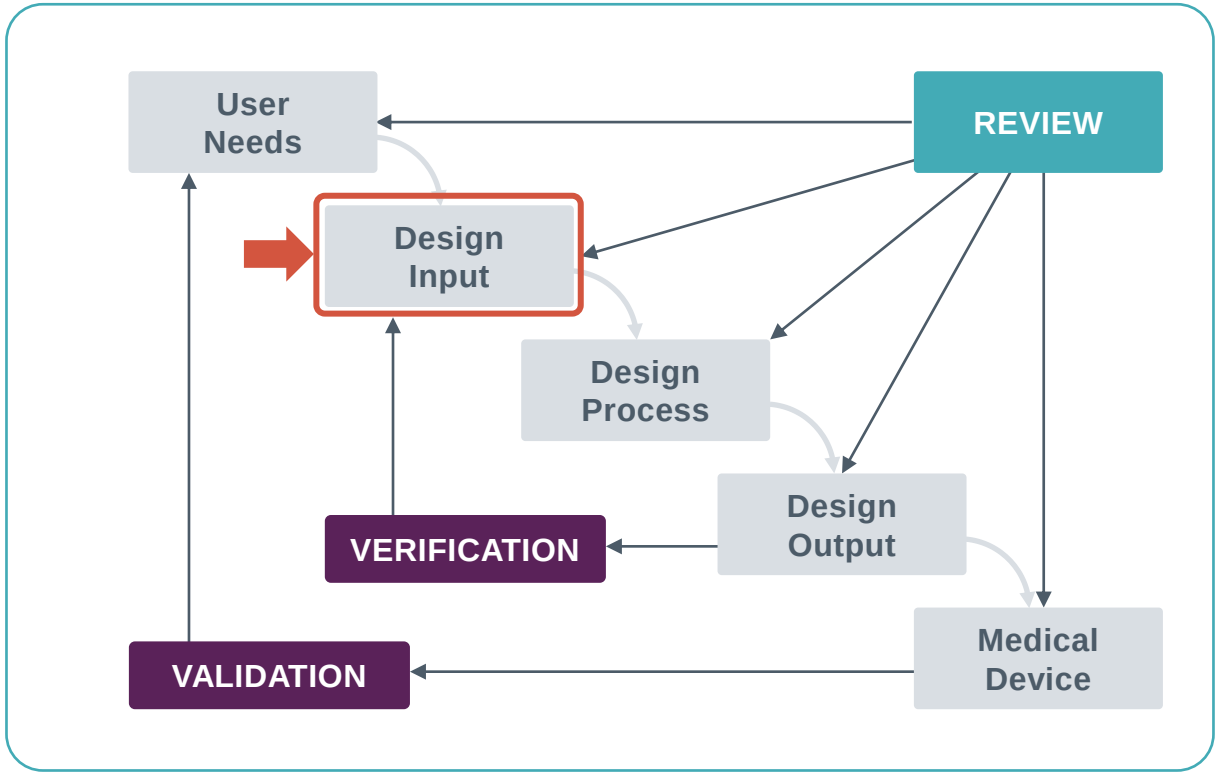
DESIGN INPUTS

Market Requirements and Regulatory requirements fit to the **Product Requirements Document (PRD)**, which is a high-level overview of what the product should do and why

Product Requirements are expanded and transformed into a complete set of **Design Inputs** which are written to an engineering level of detail in a quantitative and measurable manner.

Design input must be prepared, reviewed and approved by a multidisciplinary team.



FDA Quality System (QS) Regulation/Medical Device Good Manufacturing Practices; Subpart C - Design Controls

NOTICE:
One requirement may be associated with multiple design inputs

DESIGN INPUTS

Each requirement should be able to be verified by an objective method of analysis, inspection, or testing.

When creating the **Design Inputs**, it is important to make sure they are:

- Clear and conscience.
- Self-consistent – should not conflict with one another or a reference standard.
- Can be tested to Pass/Fail.

Characteristic	Minimal	Optimal	Source	Output
Analytical sensitivity (Limit of detection)	Equivalent to an on-market assay	Superior to an on-market assay	MRD; Regulatory requirement	

AMBIGUOUS

Characteristic	Minimal	Optimal	Source	Output
Analytical sensitivity (Limit of detection)	200 CFU/mL	≤ 100 CFU/mL	MRD; Regulatory requirements	

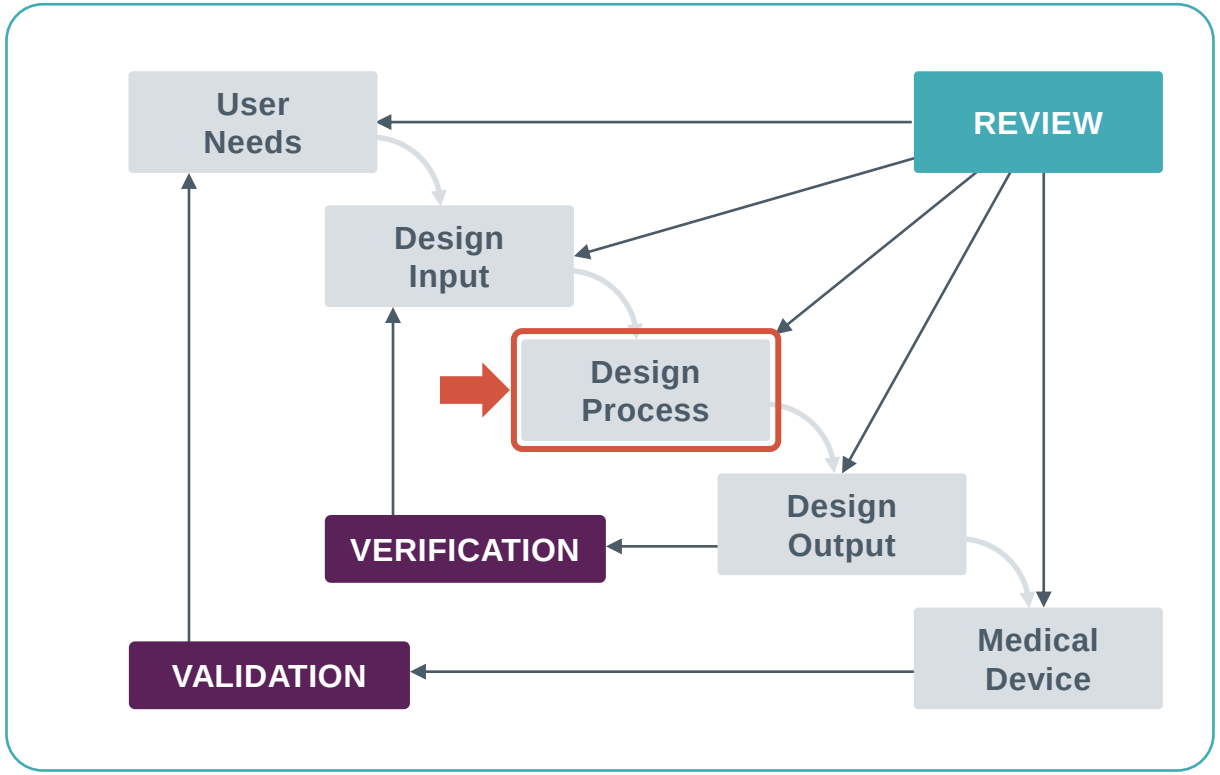
UNAMBIGUOUS

REMEMBER: Revise your risk assessment and make sure **each risk has a design input** to be mitigated.

DESIGN PROGRESS

Once **Design Inputs** are defined, **Design Process** starts.

Since all the Design Input Requirements are listed out with quantifiable objectives, design engineers can now start designing a prototype that aims to meet these objectives.



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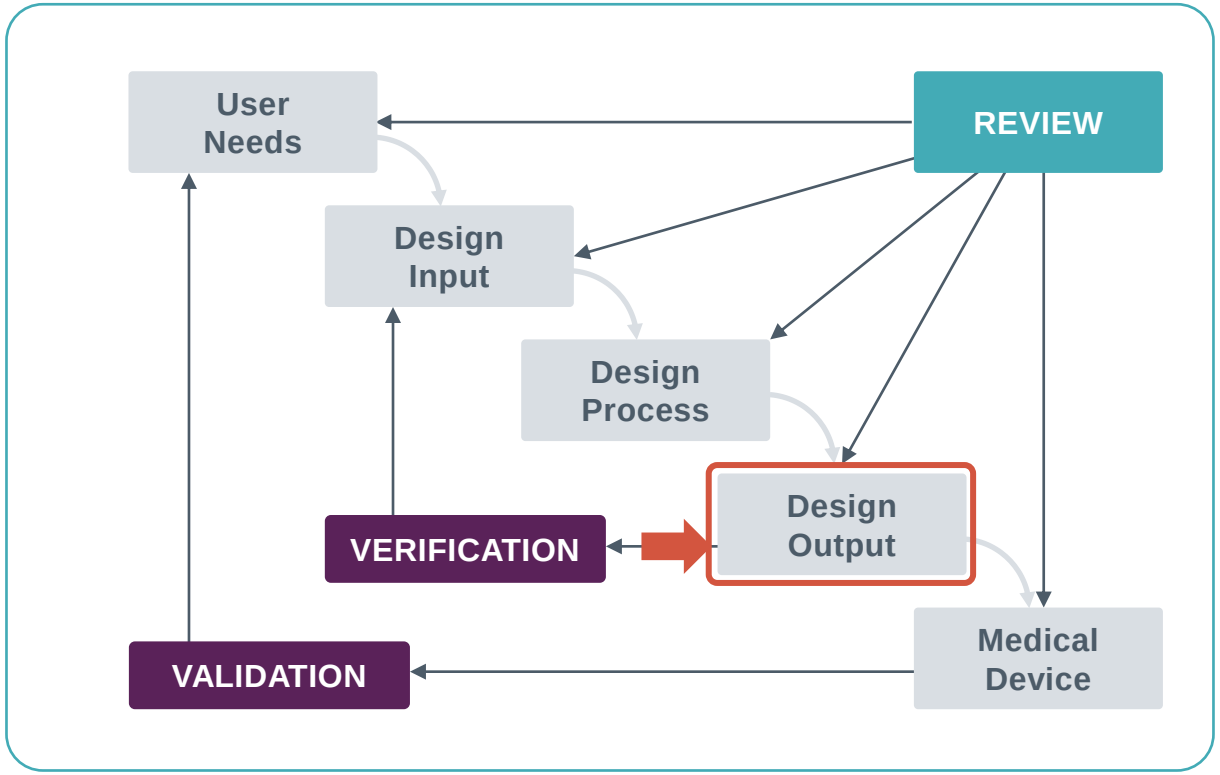
DESIGN OUTPUTS

A **Design Output** is anything that can be generated to prove or support the argument that a Design Input is met.

A Design Output can include things like :

- material specifications.
- test methods.
- engineering drawings.
- test reports and data analyses.
- components, parts, and pieces that go into the IVD.

Design Outputs must contain and/or make reference to pre-defined “acceptance criteria”.



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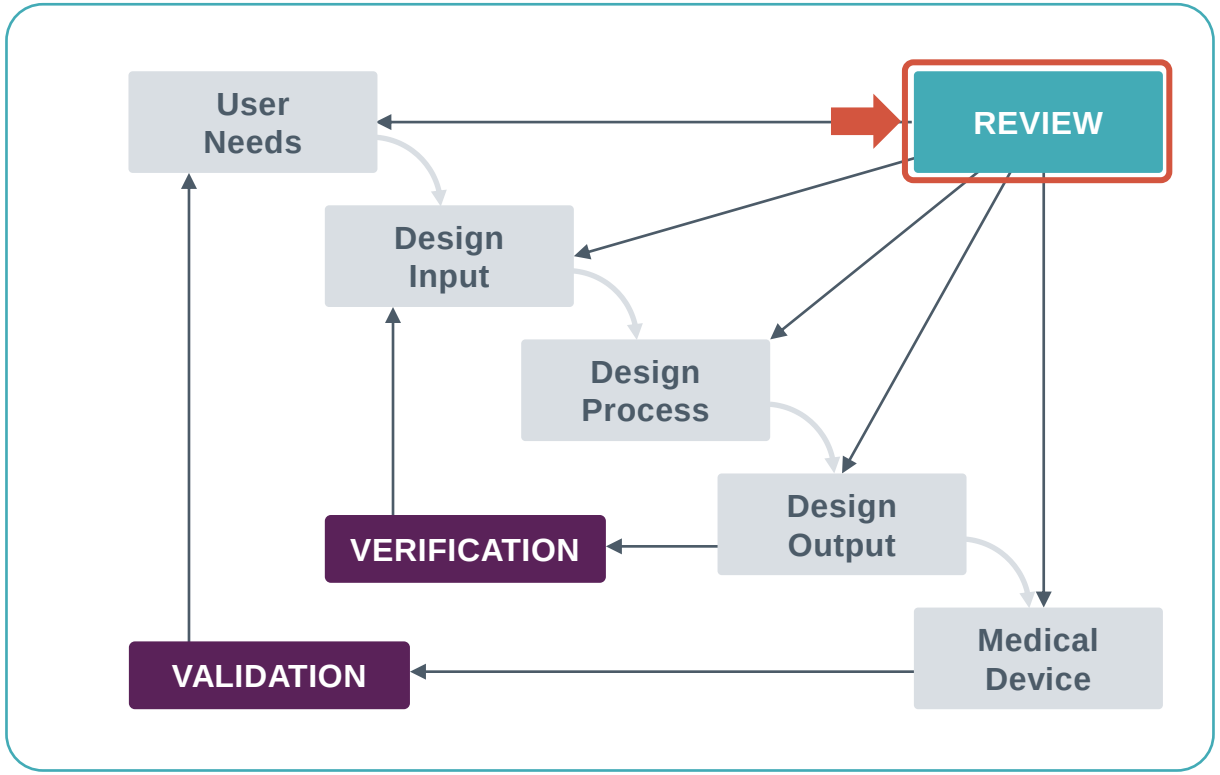
DESIGN REVIEW

Design Reviews are moments to evaluate the availability of the results to meet the requirements and to identify and propose necessary actions.

- No specific requirement with regards the number and frequency that reviews need to be conducted.
- All appropriate functions with a variety of expertise are part of the **Design Review Team**; and include clinical/medical experts. Sometimes independent reviewers can be engaged.
- Design reviews need to be documented.



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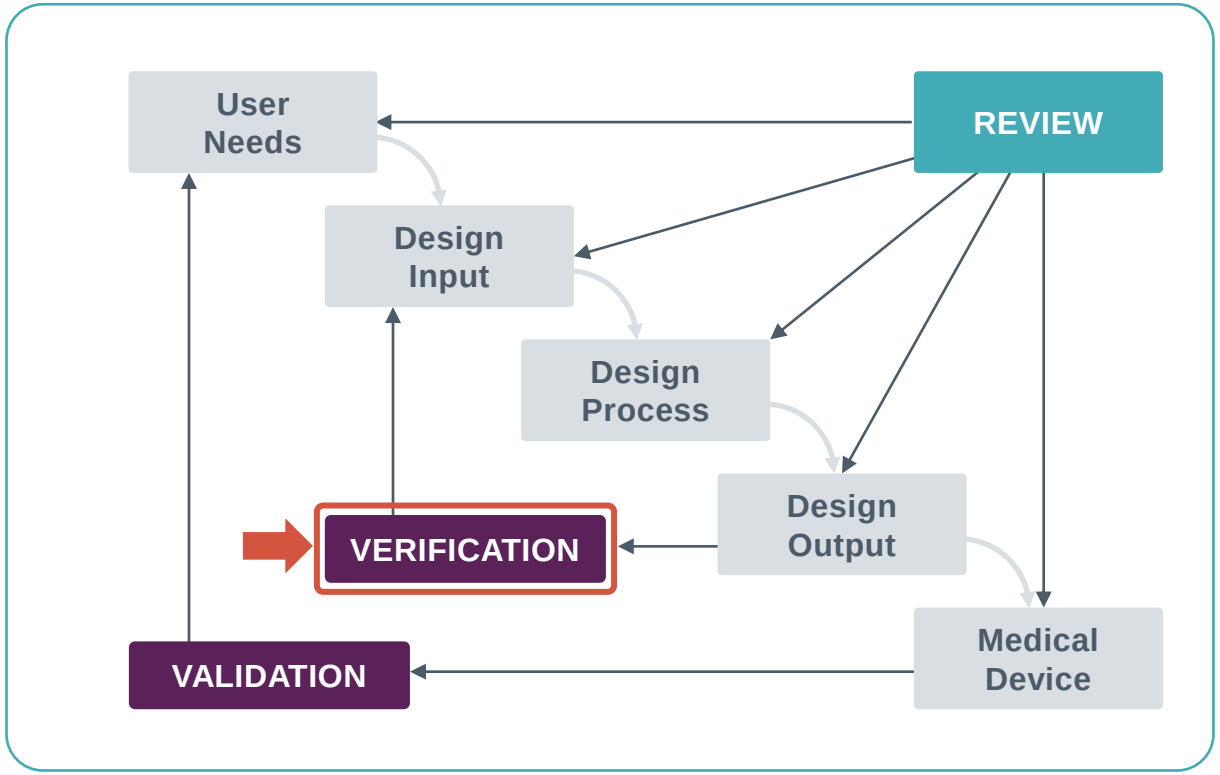
DESIGN VERIFICATION

Design Verification confirms that the Design Outputs meet Design Inputs.

Confirmation is done by objective laboratory procedures.

Examples:

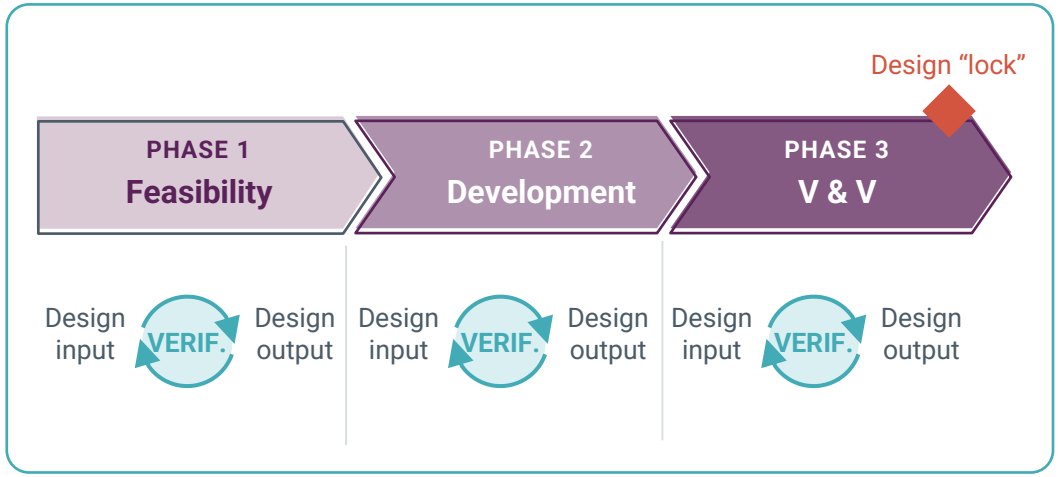
- Limit of Detection
- Analytical Sensitivity
- Analytical Specificity
- Reproducibility
- Hook effect
- Assay range
- Cross-reactivity
- Interfering substances
- Carry-over contamination
- Assay stability
- Sample stability

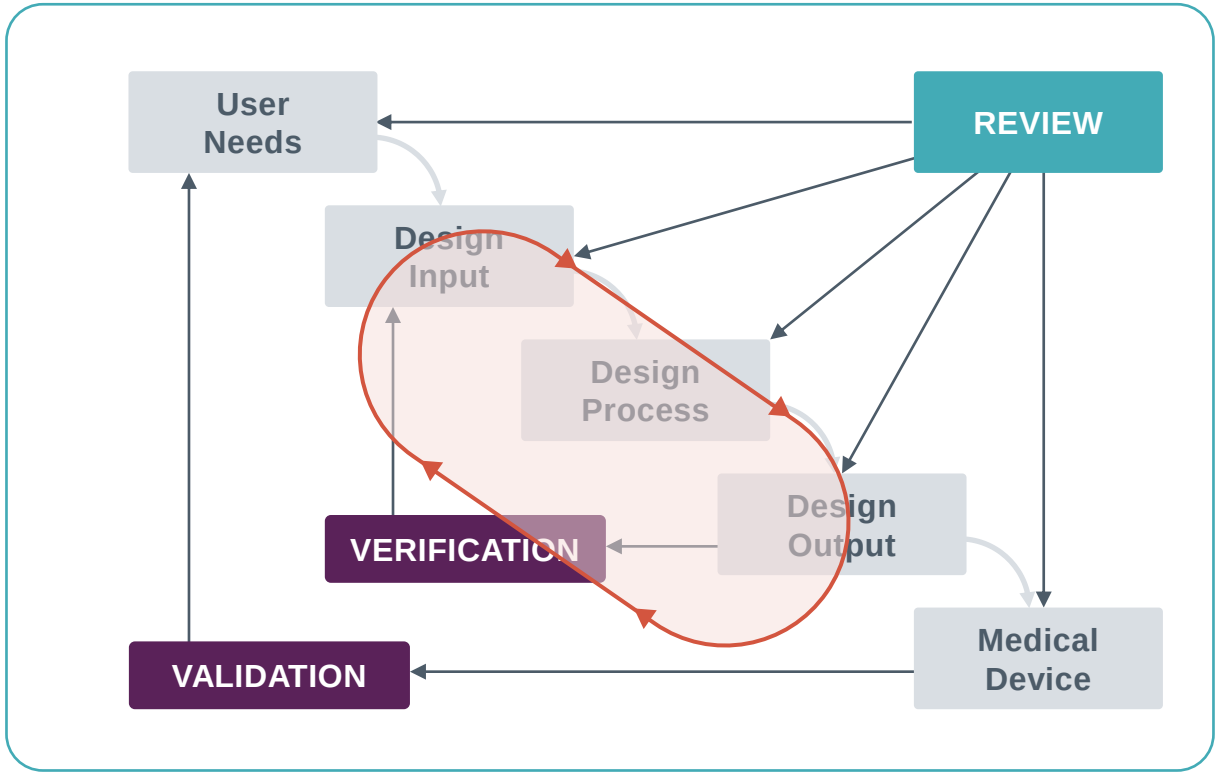


FDA Quality System (QS) Regulation/Medical Device Good Manufacturing Practices; Subpart C - Design Controls

DESIGN CONTROL PROCESS

In reality, Design Input, Design Process, Design Output and Verification is an iterative process along all product Development Phases that finalizes with “design lock”.





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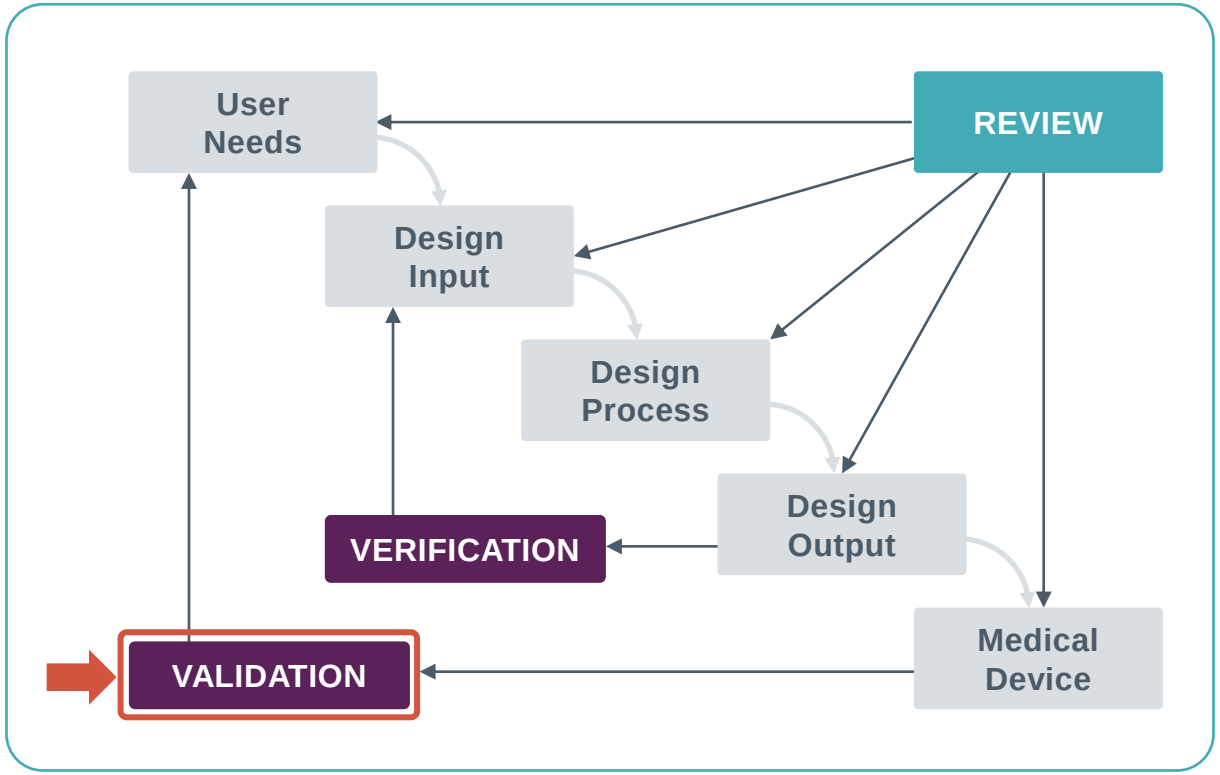
DESIGN VALIDATION

Design Validation is the process to ensure that the final product can consistently meet all the User Needs determined in the first stage.

All devices require clinical evaluation. This means that the end-user(s) should be involved, and the device should be tested in the actual use environment as part of the validation.

REMEMBER:
Validation must address all IVD components including the label, the instructions for use, the packaging, and everything inside the packaging.

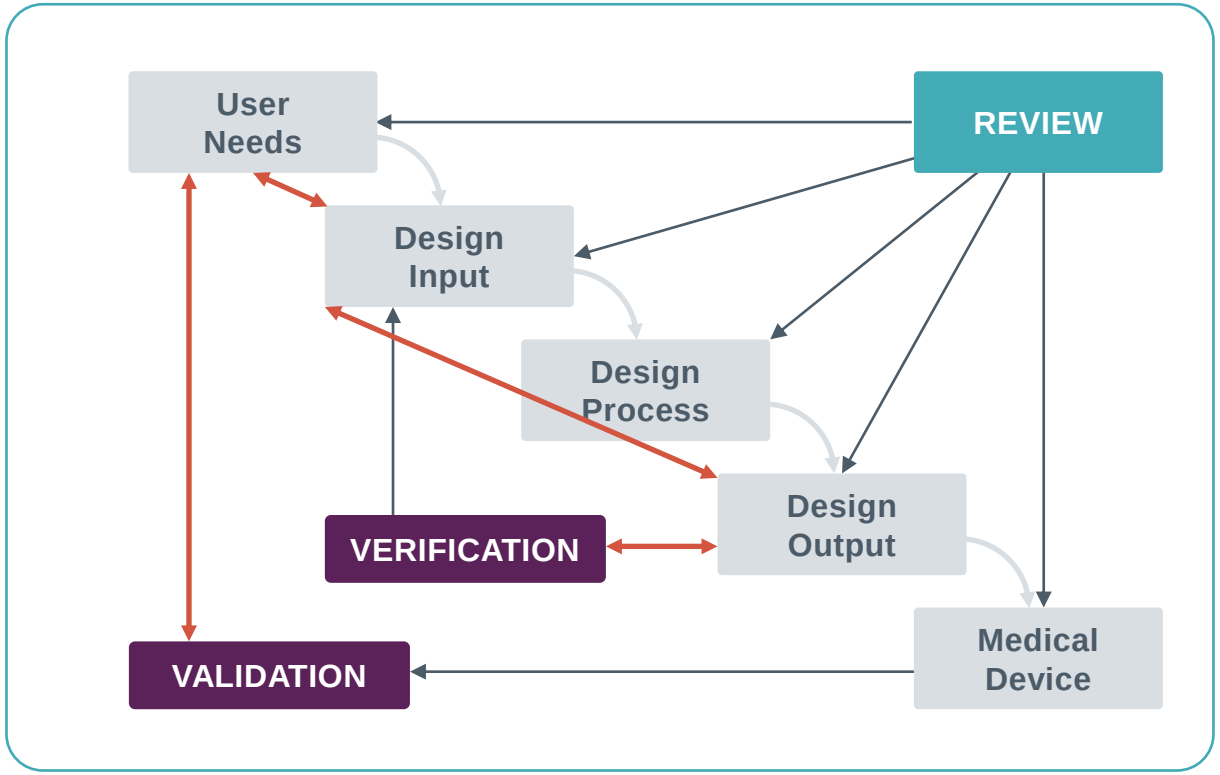


FDA Quality System (QS) Regulation/Medical Device Good Manufacturing Practices; Subpart C - Design Controls

DESIGN TRACEABILITY MATRIX

Design Traceability Matrix is a visual way to summarize the design and development activities:

- Easy to see the link between Product Requirements and Design Inputs.
- Shows the link between Design Outputs and Design Inputs.
- It shows which verification activities were used to demonstrate that the outputs match the inputs
- and which validation activities were used to demonstrate that the user needs were met.



FDA Quality System (QS) Regulation/Medical Device Good Manufacturing Practices; Subpart C - Design Controls

DESIGN CONTROL PROCESS

DESIGN TRACEABILITY MATRIX

EXAMPLE

Spec#	Design Requirement	Source	Design Input	Critical (Y/N)	Test Proposal	Reference	Design Output
1. Shelf Life and Stability							
1.1	Shelf Life	Internal					
1.1.1	Refrigerated (2-8ºC)	Internal, FDA, HC, EU	Min: 13 months from date of manufacture Opt: 25 months from date of manufacture	Y	Stability Panel – NEG, LOW POS, MOD POS tested on three lots of materials, n=3 each. Day 0 and minimum 5 timepoints.	CLSI EP25	STA-23-001-FR
1.1.2	Room temperature (18-25ºC)	Customer Feedback	Min: 13 months from date of manufacture Opt: 25 months from date of manufacture	Y	Stability Panel – NEG, LOW POS, MOD POS tested on three lots of materials, n=3 each. Day 0 and minimum 5 timepoints.	CLSI EP25	STA-23-002 - FR
1.2	Kit Transport Simulation: Freeze/Thaw	Internal, FDA, HC, EU	Performance post-stress as expected using defined stability test panel to end of product shelf life as defined in 1.1.1 and 1.1.2.	N	One lot of materials, same panel as 1.1.1. Freeze for a minimum of 8h, thaw for 1 hr at 18-25ºC for up to 5 F/T cycles	CLSI EP25, ASTM D4169-14	STA-23-003-FR
			Defined limitation on shelf-life post-exposure	Y			

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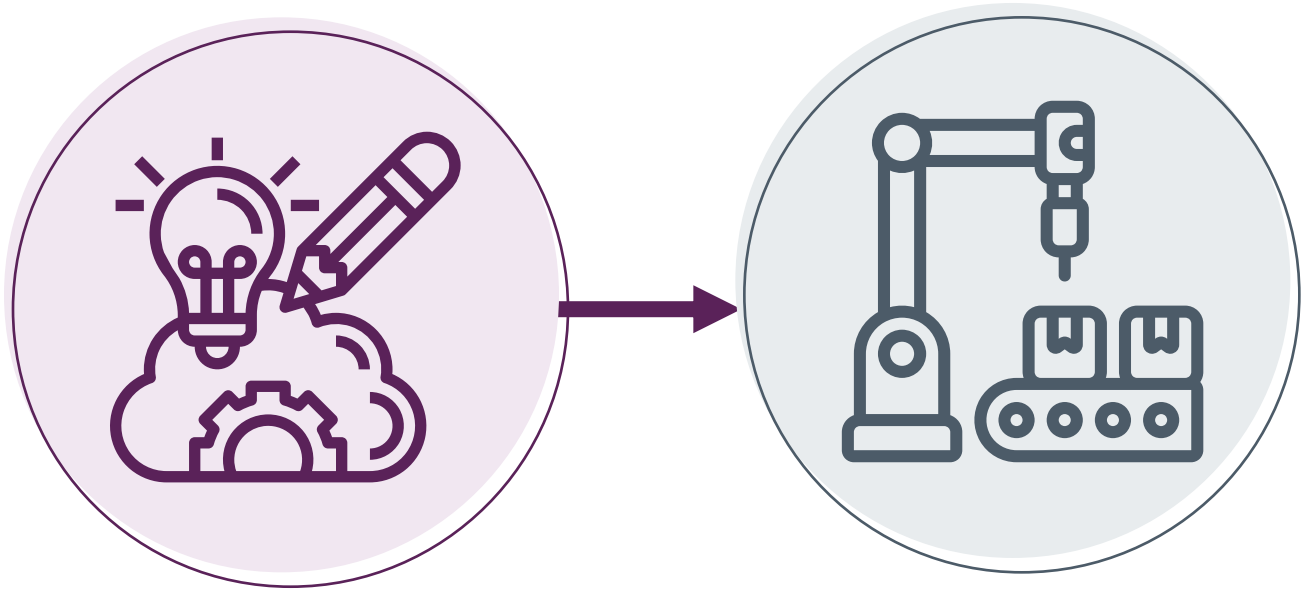
DESIGN TRANSFER

- **Design Transfer** is the process by which a device's design is transferred to production.

Examples of Documentation: training materials, manufacturing processes, test and inspection/ analytical methods.



TOP TIPS:

- Don't wait until the end to begin. Involve manufacturing from the start.
- Make sure your suppliers can meet your timelines and compliance requirements.
- Build design transfer into your design controls.

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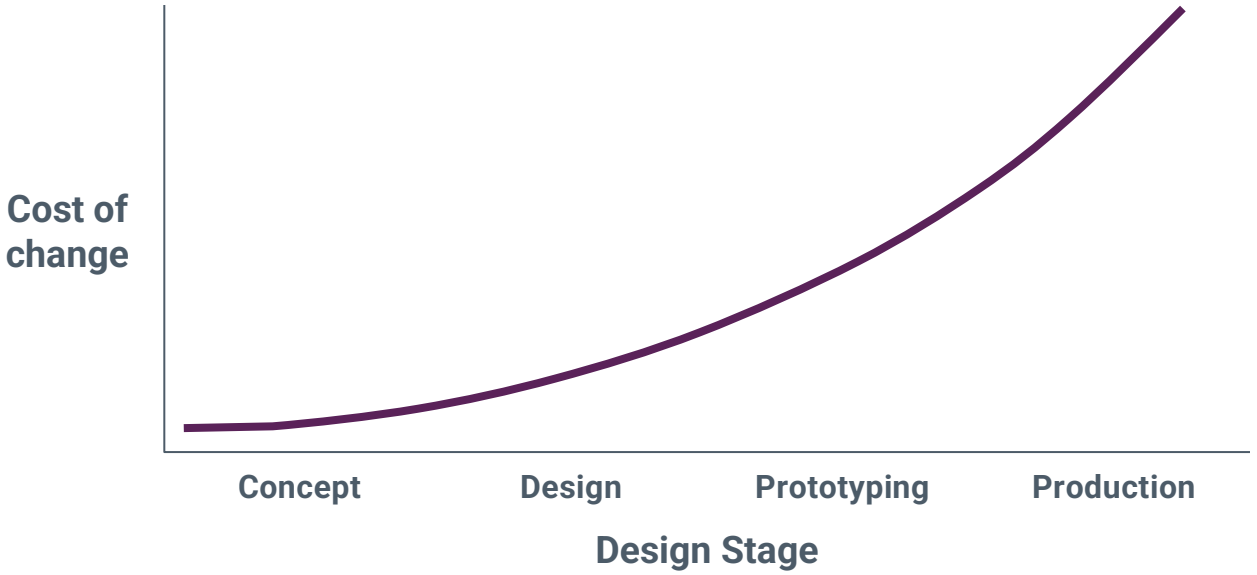
DESIGN CHANGE

Design changes:

- are often made to improve the functionality, usability, or appearance of a product.
- can happen at any stage in the product development process or after release.
- are less expensive when happen early compared to those that take place after it is introduced into full-scale production.



Design changes must be documented using change controls: enumeration of deficiencies, corrective actions arising from design verification & review.

If a post-market design change is approved, you'll need to verify whether or not the changes requires approval from the corresponding regulatory agency.

A **Reportable Change** is one that is demonstrated, through risk analysis, to have a potential impact on the function, performance, usability, or safety of an authorized IVD.

DESIGN CHANGE: POST-MARKET

Examples of reportable changes:

- of the intended use, indication, contraindication
- of performance characteristics
- of a supplier(!)
- due to risks which have not yet been considered
- warnings
- as a result of considerations arising from market surveillance, including incidents, recalls, or complaints
- affecting production
- that affect the safety and performance of the product

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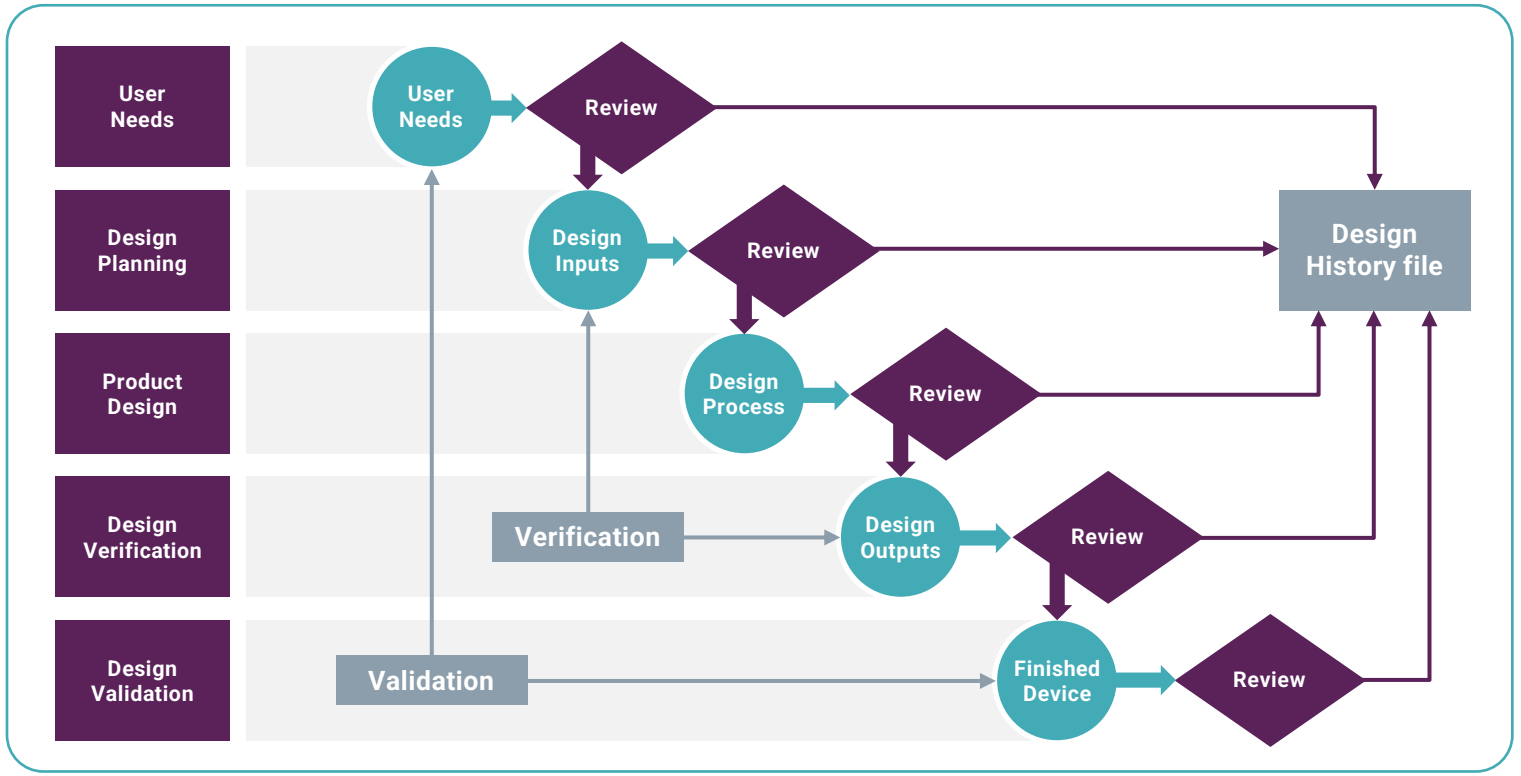
DESIGN HISTORY FILE (DHF)

Design History File is:

- the collection of documents of all the product design and development processes pertaining to a finished device.
- used to provide evidence that all the design control procedures were appropriately applied and documented.
- one of the first documents that a regulatory body inspects for accrediting purposes.



Your Design History File should contain **all the documentation created during the product development phase**, even if you were not the developer of the test.

DESIGN CONTROL PROCESS

DESIGN HISTORY FILE – COMMON PITFALLS

- **Not having a DHF when designing:**

  The DHF should contain all documents created during product development. It is crucial to generate those documents during the design of the product, not after.

- **No traceability to outputs:**

  If outputs of the design control elements are not well documented, you do not have a proper Design Control Traceability Matrix.

- **A disorganized DHF:**

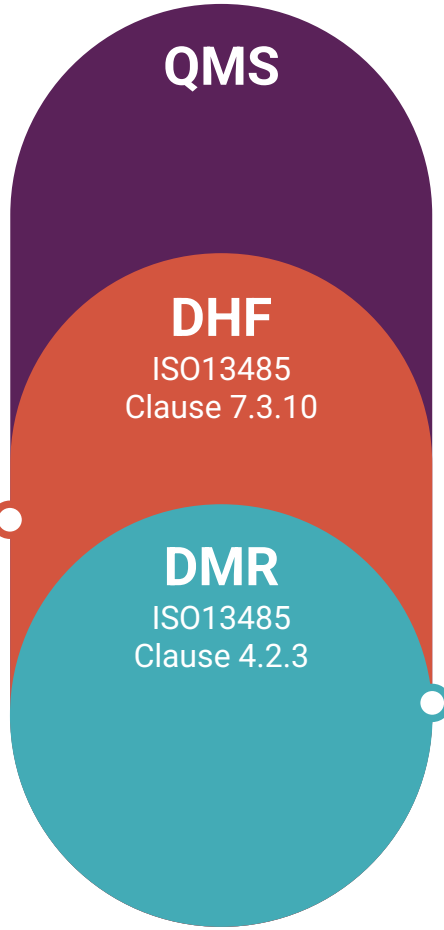
  If the outputs are not well organized, it is very easy to lose track of it. This happens more often to organizations that still maintain a paper-based quality management system.

DESIGN CONTROL PROCESS

DESIGN HISTORY FILE VS DEVICE MASTER RECORD

DESIGN HISTORY FILE

- **Purpose:** Documents the entire design and development process of an IVD
- **Contents:** Includes records of design inputs, outputs, verification, validation, risk analysis, design reviews, and design changes
- **Focus:** Demonstrates that the device was developed in accordance with the approved design plan and regulatory requirements
- **Audience:** Primarily used by regulatory bodies to ensure the design controls and development process were followed.



DEVICE MASTER RECORD

- **Purpose:** Serves as the comprehensive "recipe" for manufacturing an IVD
- **Contents:** Includes manufacturing processes, equipment specifications, materials, quality assurance procedures, and packaging and labeling instructions
- **Focus:** Ensures consistent production and quality of the device by detailing how it is made and controlled
- **Audience:** Used by the manufacturing team to produce the device and may be reviewed by regulatory bodies during inspections or audits

DESIGN CONTROL

KEY TAKEAWAYS

1

Design Controls help organizations accomplish five critical objectives:

- Deliver quality products
- Ensure user needs are met
- Maintain regulatory compliance
- Keep costs down
- Accelerate time to market

2

Design Control include the following elements: Desing Planning, Design Inputs, Design Outputs, Design Review, Design Verification, Design Validation, Design Change, Design Transfer, and Design History File.

3

Design History File collects all documents that describe the design and development of a device. Its purpose is to demonstrate that the device was developed using the design control process.

FIND

QUESTIONS & FEEDBACK