Design Change – Understanding What is Missing

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FDANEWS

Outline

- Creating the Design
- Design Changes
- Production and Process Changes
- A New Version or Model under UDI
- A New 510(k) Decision
- The Risk Management File
- Summary

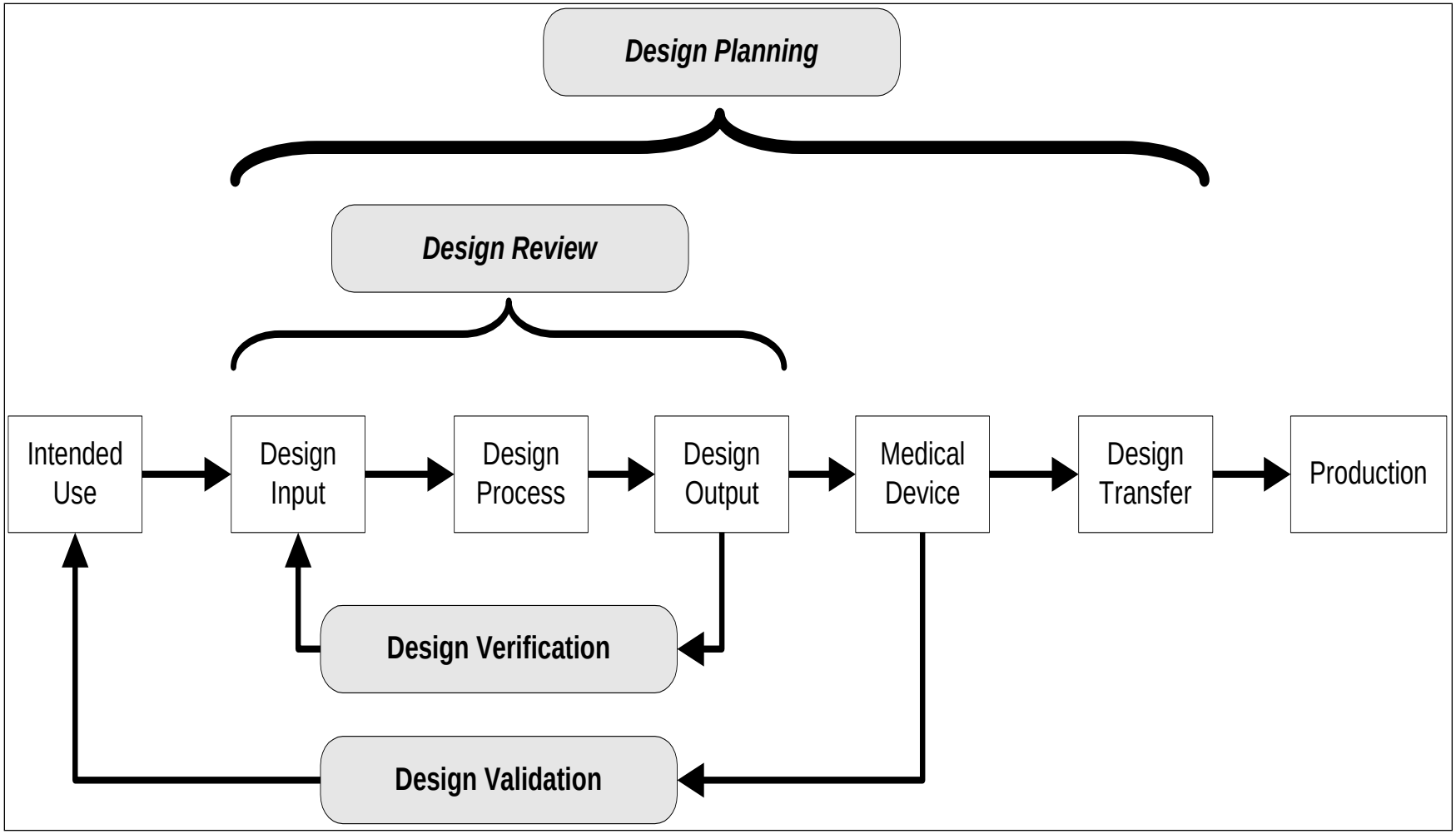
Creating the Design

Design Control

- Design Control produces a design that has some important characteristics:
  - The device is safe
  - The device is effective
  - The device is manufacturable
  - The device satisfies regulatory requirements

- The next slide provides a standard view of design control

QSR Design Control Overview

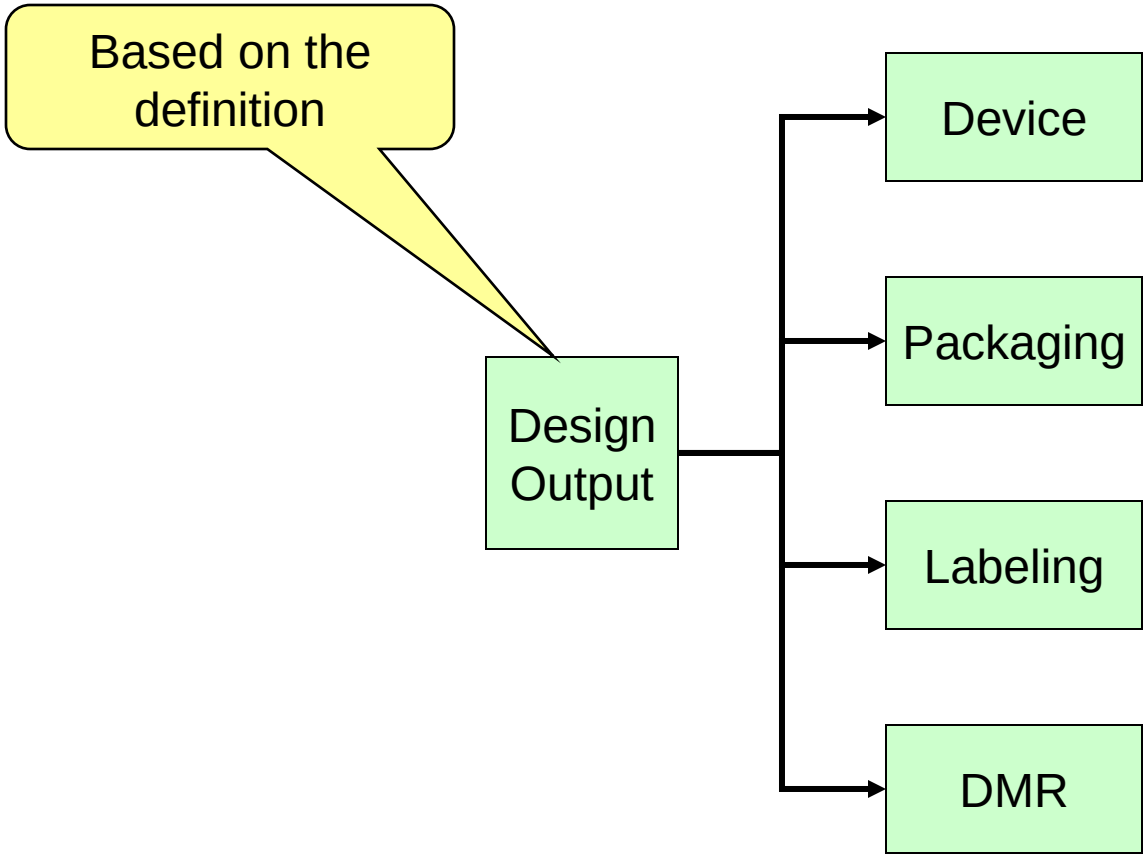


Definitions

- 820.3(g) Design output means the results of a design effort at each design phase and at the end of the total design effort. The finished design output is the basis for the device master record. The total finished design output consists of the device, its packaging and labeling, and the device master record.

- 820.3(j) Device master record (DMR) means a compilation of records containing the procedures and specifications for a finished device.

Overview


Based on the definition
Design Output
Device
Packaging
Labeling
DMR

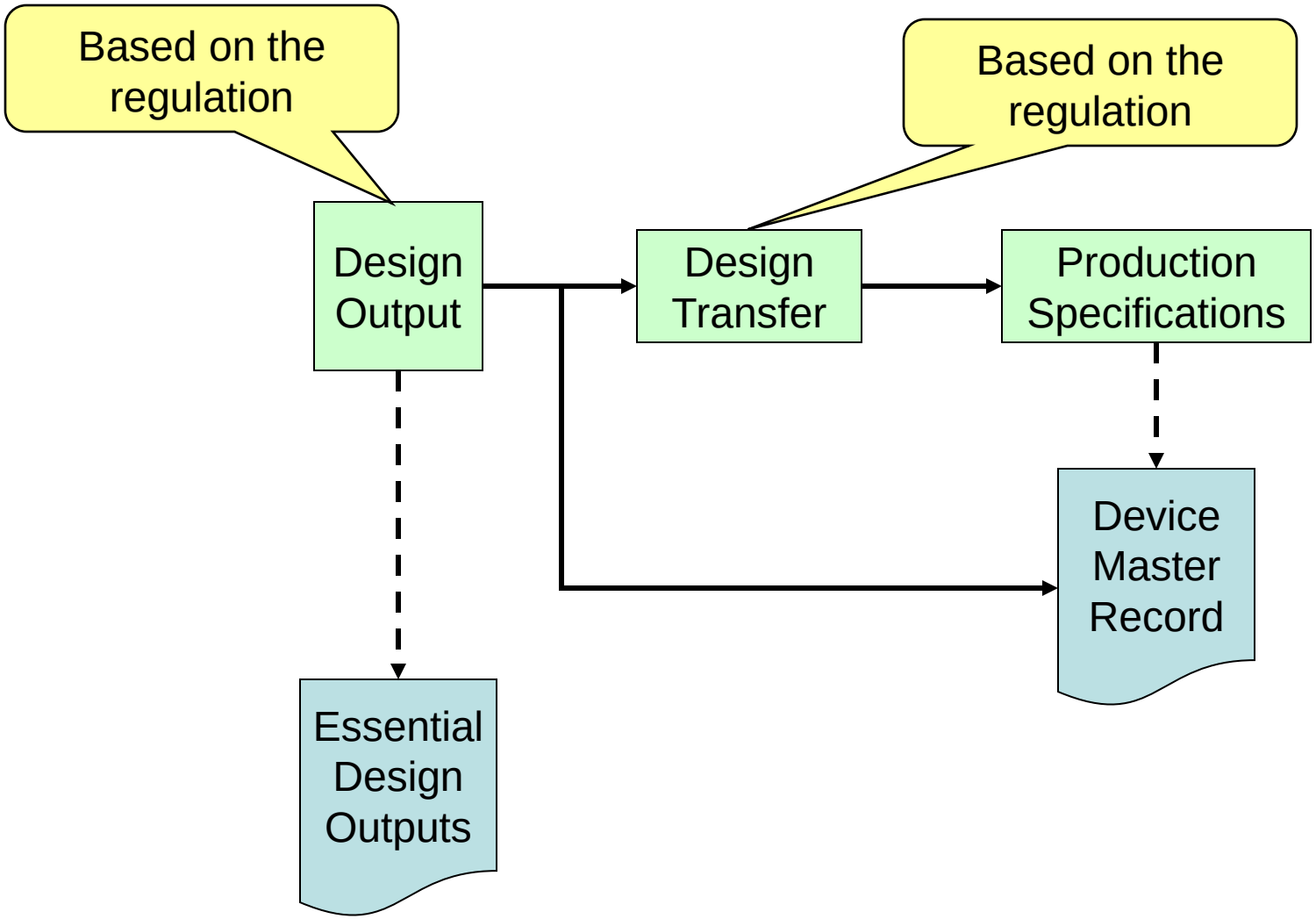
Design Output

- 820.30(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.

Design Transfer

- 820.30(h) Design transfer
- Each manufacturer shall establish and maintain procedures to ensure that the device design is correctly translated into production specifications

Overview


Based on the regulation
Based on the regulation
Design Output
Design Transfer
Production Specifications
Device Master Record
Essential Design Outputs

The Result

- The design output provides the specifications for:
  - Components and finished devices acquired through the Purchasing Controls, 820.50
  - Components and finished devices produced through the Production and Process Controls, 820.70
  - Acceptance activities implemented through 820.80
- In addition, Design Output becomes Production Specifications through Design Transfer, 820.30(h)

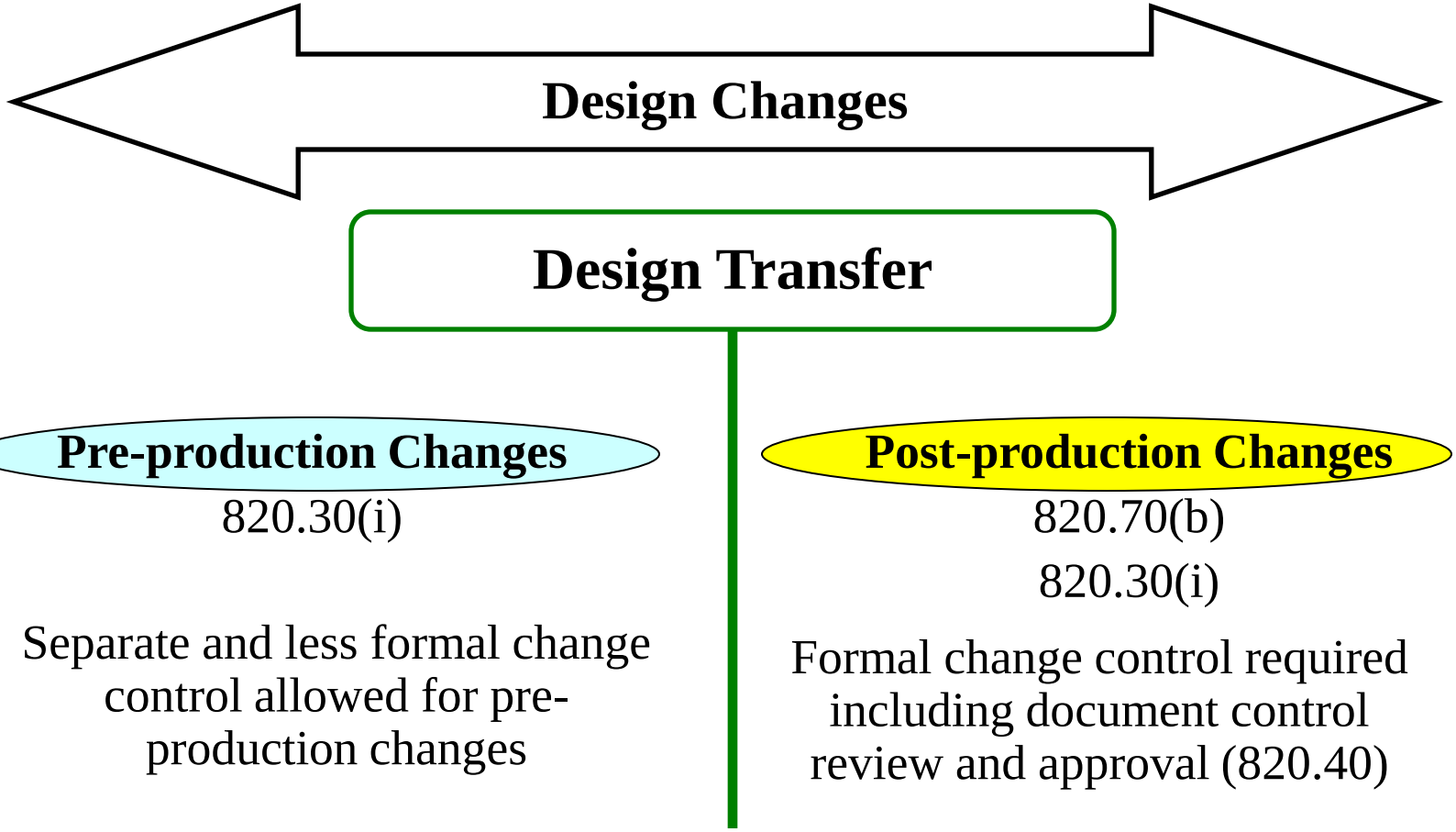
Design Changes in 820.30(i)

Design Changes

- 820.30(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.

- This presentation focuses on identification of design changes in the post-production phase.

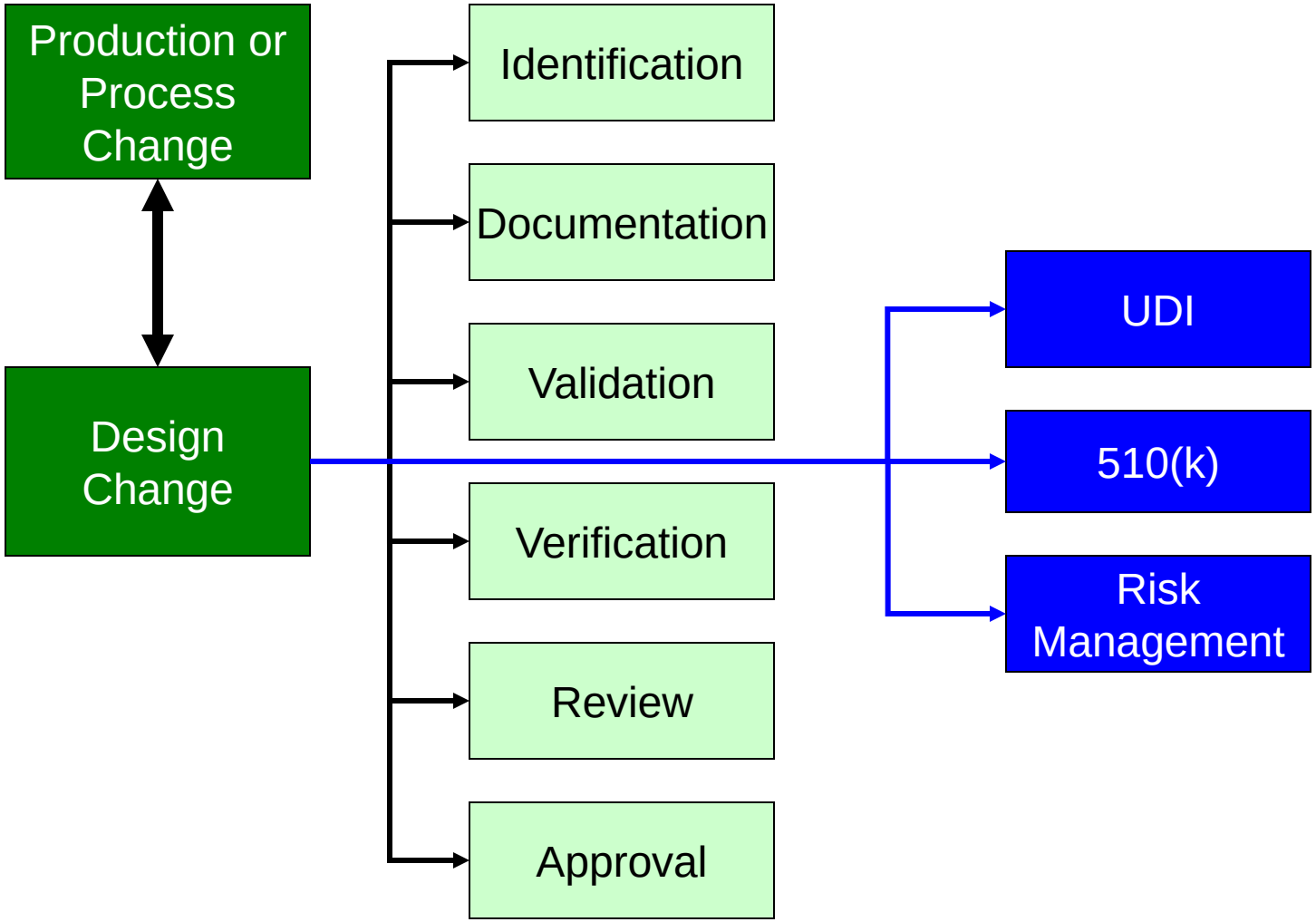
Design Changes



Preamble #87

- 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. Otherwise, a device may be rendered unable to properly perform, and unsafe and ineffective.

Overview


Production or Process Change
Design Change
Identification
Documentation
Validation
Verification
Review
Approval
UDI
510(k)
Risk Management

Production and Process Change

Production & Process Change

- 820.70(b) Production and process changes

- Each manufacturer shall establish and maintain procedures for changes to a specification, method, process, or procedure. Such changes shall be verified or where appropriate validated according to 820.75, before implementation and these activities shall be documented. Changes shall be approved in accordance with 820.40.

QSIT

- Design Controls Inspectional Objective #13 – Confirm that changes were controlled including validation or where appropriate verification.

- The design change control section [820.30(i)] is linked to and **is redundant with** Section 820.70(b) Production and process changes of the regulation.

QSIT

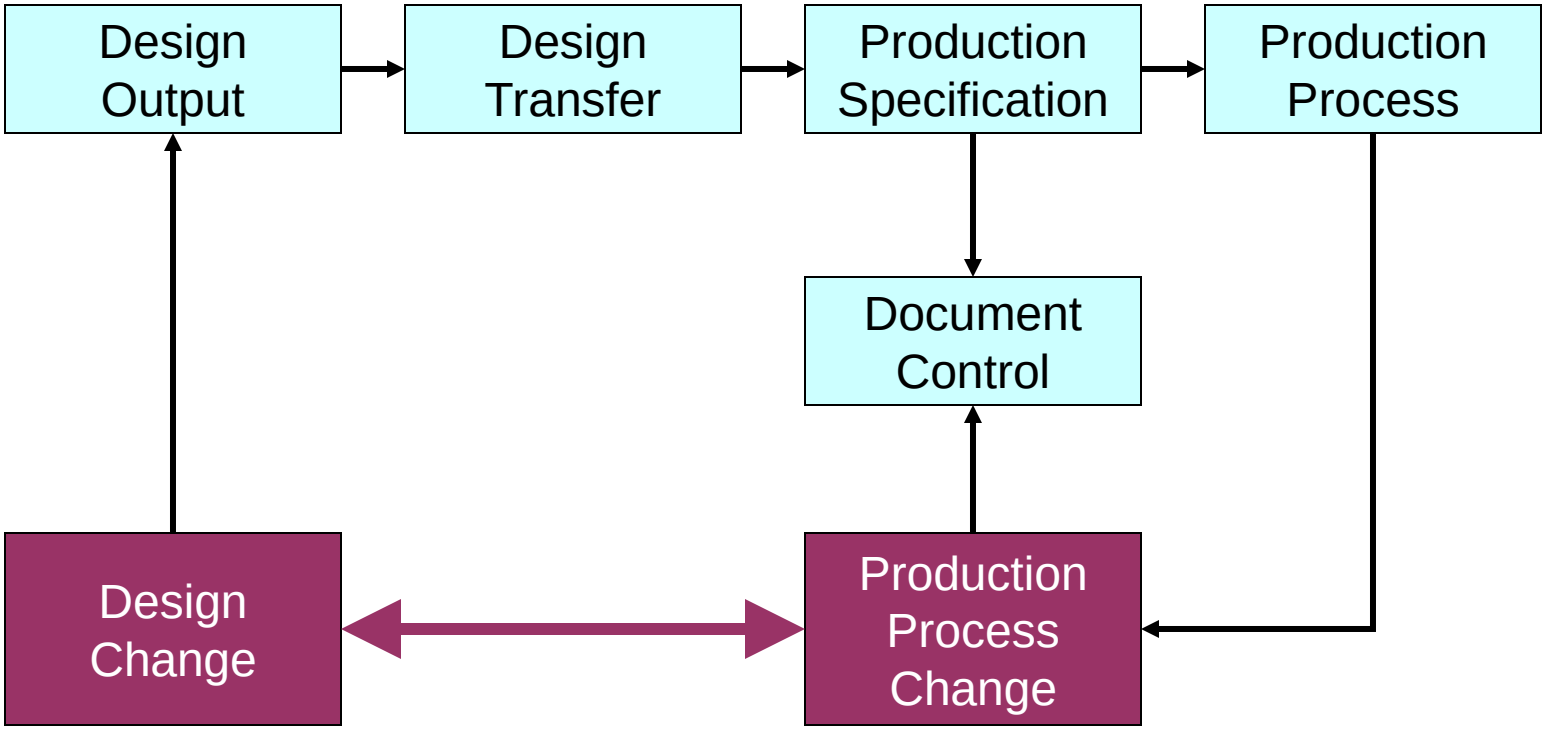
- Design Controls Inspectional Objective #13 – Confirm that changes were controlled including validation or where appropriate verification.

- Post-production design changes require the firm to loop back into the design controls of Section 820.30 of the regulation. This does not mean that post-production changes have to go back to the R&D Department for processing. This track is dependent on what the firm specifies in their change procedure. It is acceptable for the manufacturing department to process the entire design change and to implement the controls of Section 820.30.

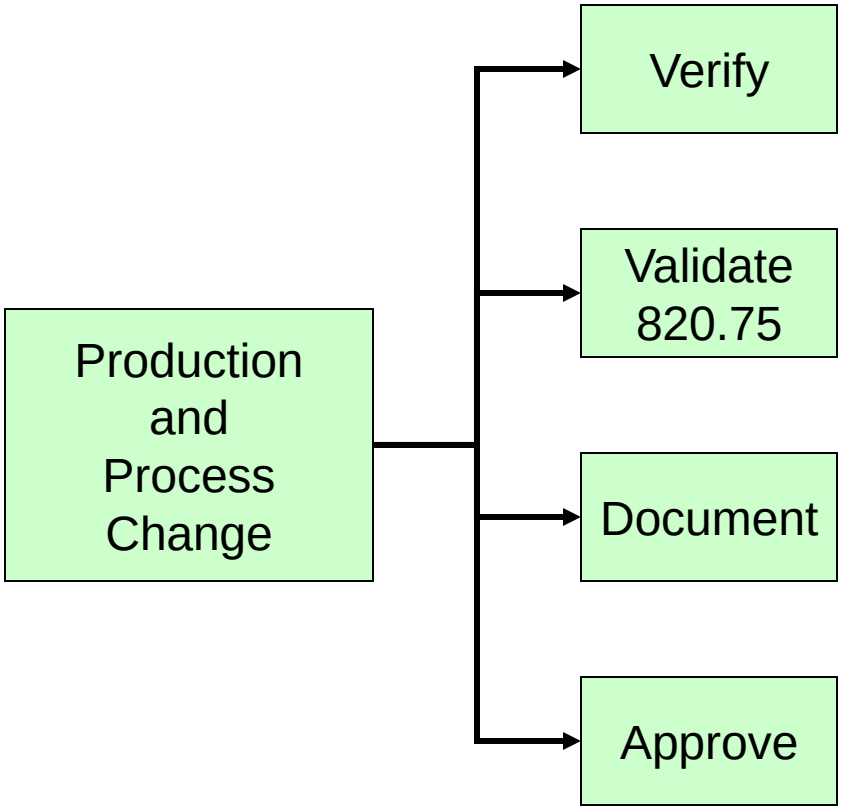
Preamble #96

- FDA has moved the requirement for validating production and process changes to Sec. 820.70(b), “Production and process changes”, and notes that changes to the design specifications, at any time during the lifetime of the design of the device, must conform to the requirements in Sec. 820.30(i), “Design changes”.

The Model


Design Output
Design Transfer
Production Specification
Production Process
Document Control
Design Change
Production Process Change

Overview

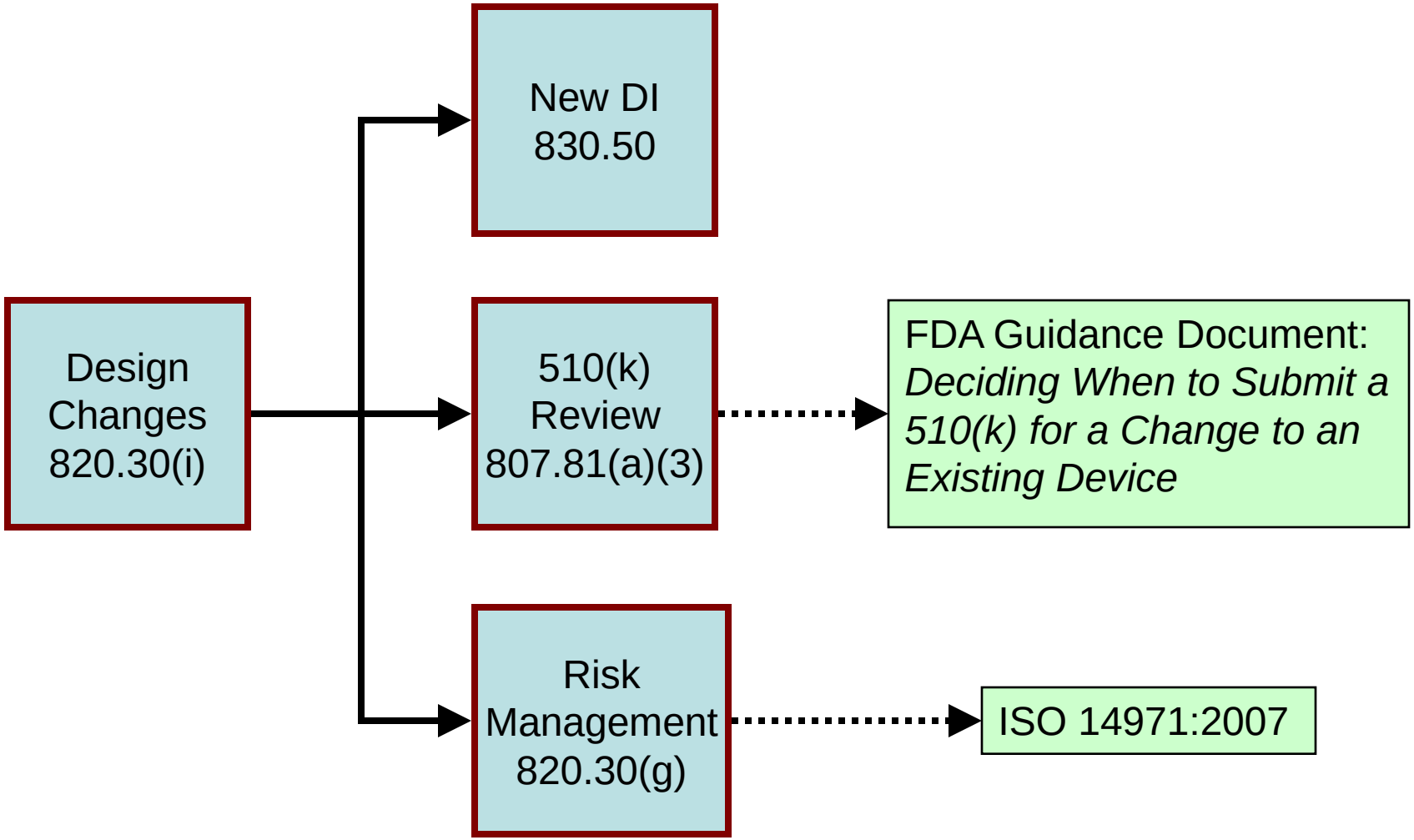

Production and Process Change
Verify
Validate 820.75
Document
Approve

Implementation

- QSIT links “design changes” and “production and process changes”
- Preamble #96 notes that design specification changes at any time in the life-cycle are “design changes”
- Recommendation:
  - Identify any changes to a specification, method, process, or procedure
  - If it **did** come from a design output, including design transfer, follow design change in 820.30(i)
  - If it **didn’t** come from design, follow document control in 820.40

Relationships

Design Change Interrelationships

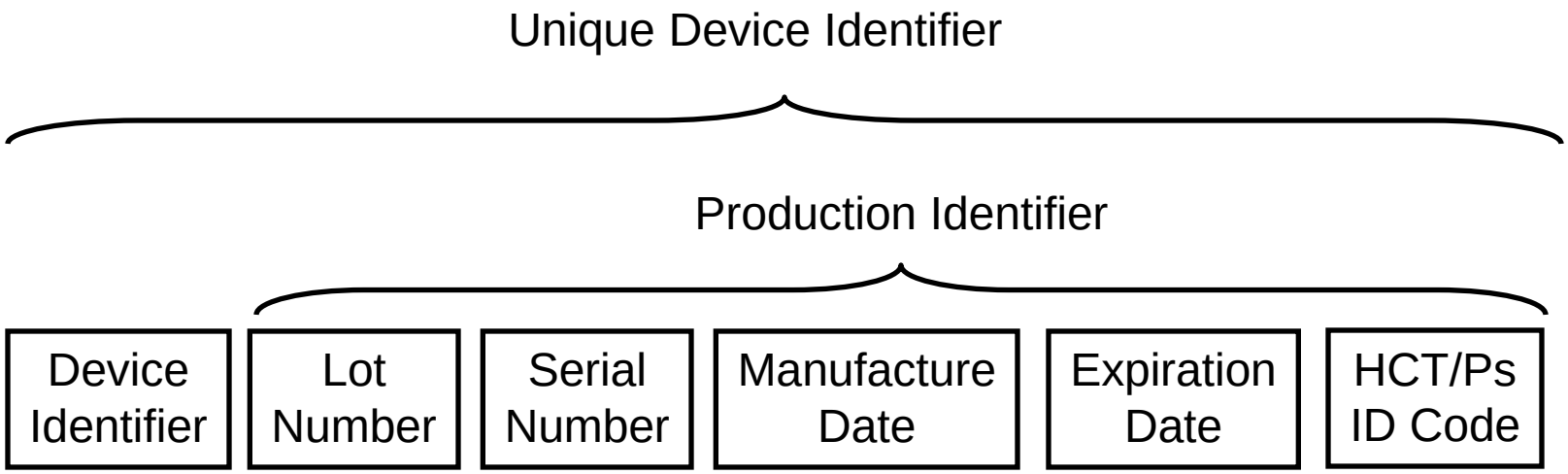


A New Version or Model Under UDI

The Basic Concept

- The label of a medical device uniquely identifies the version or model of a device by the device identifier (DI)
- The DI allows user access to a database (GUDID) that contains specific information and attributes about the device
- The manufacturer (labeler) populates the information in the GUDID

Overview – UDI Elements



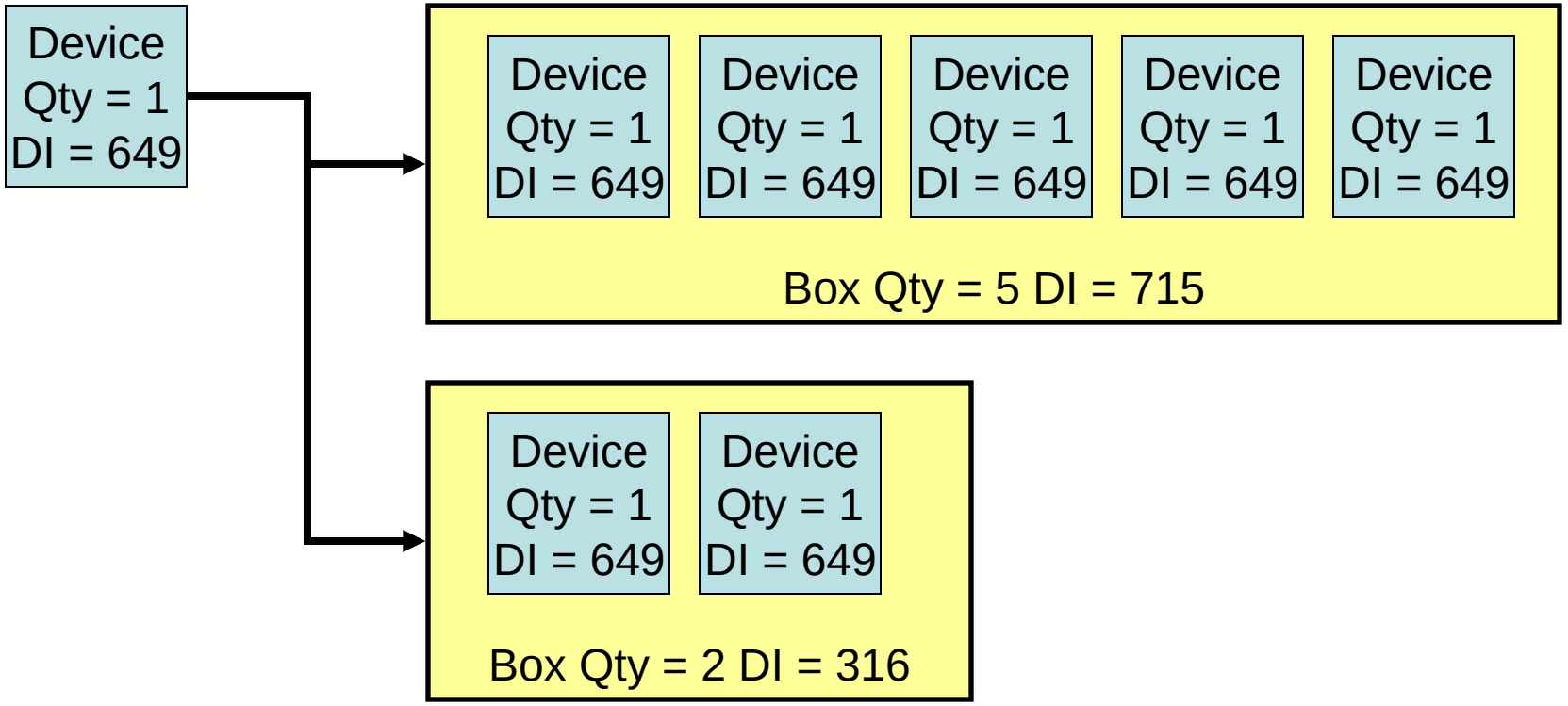
The elements of the Production Identifier are optional. If they are on the label, they must be part of the UDI.

The elements of the UDI must be shown in both human readable form and machine readable form.

Stand-alone software has a different format.

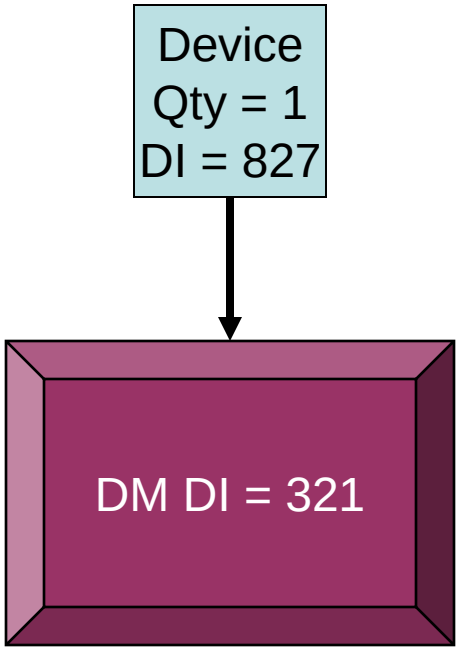
Overview – Package Level

- The concept extends upward from the device label to the packaging configuration



Overview – Device Level

- The concept may extend downward from the device label to the device using a direct marking device identifier (DM DI)



New Version or Model

- *Version or model* means all devices that have specifications, performance, size, and composition, within limits set by the labeler. [§830.3 Definitions]
- The implicit assumption is that the labeler defined the attributes and, therefore can recognize when a change goes outside the limits.
- 830.50(a) requires a new device identifier when a change results in a new version or model.
- The determination should be part of the design change procedures that implement 820.30(i).

Version or Model Checklist

- Compile a list of all devices the manufacturer currently markets
- For each device, define and document the following characteristics and their limits:
  - Specifications
  - Performance
  - Size
  - Composition
- For the Design Change procedure, include evaluation and documentation of the proposed change
- For the Design History File (DHF) include a documented decision of whether the change creates an new version or model.

The GUDID Guidance

- FDA-CDRH issued a guidance document *Global Unique Device Identification Database (GUDID)*
- In addition, they issued a document that defines the GUDID attributes (UCM396592)
- One question is when a change to an attribute triggers a new DI

New DI Trigger

- The draft guidance on GUDID identifies changes to the following data elements as requiring a new DI
  - Issuing Agency
  - Primary DI Number
  - Device Count (Number of devices in the base package)
  - Brand Name
  - Version or Model
  - Kit (The device is a convenience, combination, IVD, or medical procedure kit)
  - Combination product
  - For Single Use
  - Labeled as containing natural rubber latex or dry natural rubber
  - Change in MRI safety information on the label
  - Device packaged as sterile

- Cover all of these changes in at least one change control procedure

New DI Trigger Checklist

- Compile a list of all devices the manufacturer currently markets
- For each device, document the GUDID elements that trigger a new DI
- Determine the organizational element with responsibility for the value of the GUDID element
- If a change in the value would not involve a design change, determine the appropriate control measure
  - A “device packaged as sterile” would probably be a Design Change
  - A “brand name” would probably not be a Design Change

Records

- Develop a checklist of device characteristics (Specifications, Performance, Size, and Composition) and their limits
- Develop a checklist of GUDID data elements that trigger a new DI
- As part of the design change, complete the checklists, discuss them at a design review, and file the checklists in the DHF

A New 510(k) Decision

Preamble #87

- 820.30(i) Design changes
- Note that when a change is made to a specification, method, or procedure, each manufacturer should evaluate the change in accordance with an established procedure to determine if the submission of a premarket notification (510(k)) under 21 CFR §807.81(a)(3) … is required. Records of this evaluation and its results should be maintained.

21 CFR §807.81(a)(3)

(a) Except as provided in paragraph (b) of this section, each person who is required to register his establishment pursuant to 807.20 must submit a premarket notification submission to the Food and Drug Administration at least 90 days before he proposes to begin the introduction or delivery for introduction into interstate commerce for commercial distribution of a device intended for human use which meets any of the following criteria:

(3) The device is one that the person currently has in commercial distribution or is reintroducing into commercial distribution, but that **is about to be significantly changed or modified in design, components, method of manufacture, or intended use**. The following constitute significant changes or modifications that require a premarket notification:

(i) A change or modification in the device that could significantly affect the safety or effectiveness of the device, *e.g.,* a significant change or modification in design, material, chemical composition, energy source, or manufacturing process.

(ii) A major change or modification in the intended use of the device.

The 1997 Guidance

Chronology

- FDA issued the 510(k) guidance on January 10, 1997.
- The FDA QSR has an effective date of June 1, 1997, with the design control implementation delayed until June 1, 1998
- The guidance recognizes QSR, but the citations are to the 1978 GMP requirements

Changes

- The guidance requires that each change must be assessed individually and collective with other changes made since the last 510(k) clearance
- The new 510(k) should include the change that triggered the submission as well as all other changes
- The new cleared 510(k) becomes the basis for comparison for change evaluation

The Guidance

- The guidance uses five flowcharts to help evaluate the change
  - Main types of changes (Main Flowchart)
  - Labeling changes (Flowchart A)
  - Technology or performance specifications changes (Flowchart B)
  - Materials changes (Flowchart C), and
  - Materials changes for *in vitro* devices (IVDs) (Flowchart D).

Questions

- The flowcharts use a series of decision boxes
- Each decision box is numbered and has an associated question that helps explain the information desired
- Each flowchart terminates with a “new 510(k)” or “documentation”
  - New 510(k) means “strongly consider filing a new 510(k)”
  - Documentation means “document your analysis and file it for future reference”

Definitions

- The guidance has a set of definitions to use with the flowcharts
- When possible, the definitions come from the law, regulations, or other FDA documents
- In other cases, the definitions are dictionary definitions

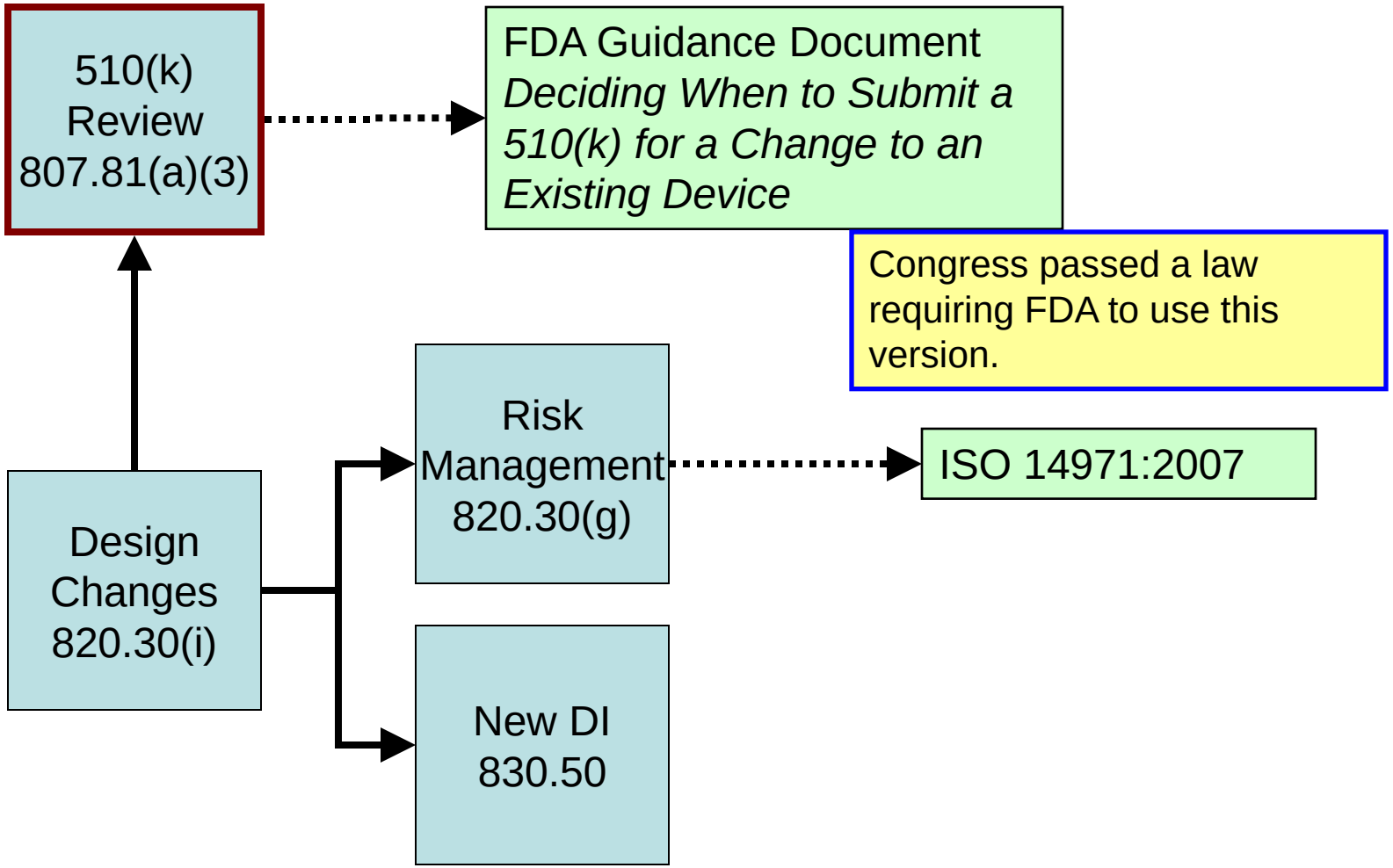
Change

- The definition of change is very important

- Change: As used in the model, this means a proposed change and not the impact of a proposed change. Important impacts of a proposed change are identified on the flow chart.

- For example, a manufacturer may propose a change in method of sterilization. This change could impact on performance specifications because of potential chemical or physical damage to the device. The proposed change (in method of sterilization) is the change that should be used in the model.

510(k) Change Analysis Interrelationships



510(k) Guidance

- In July 2012, the President signed the Food and Drug Administration Safety and Innovation Act (FDASIA) into law

- The law requires FDA to withdraw the draft guidance entitled “Guidance for Industry and FDA Staff—510(k) Device Modifications: Deciding When to Submit a 510(k) for a Change to an Existing Device”, dated July 27, 2011

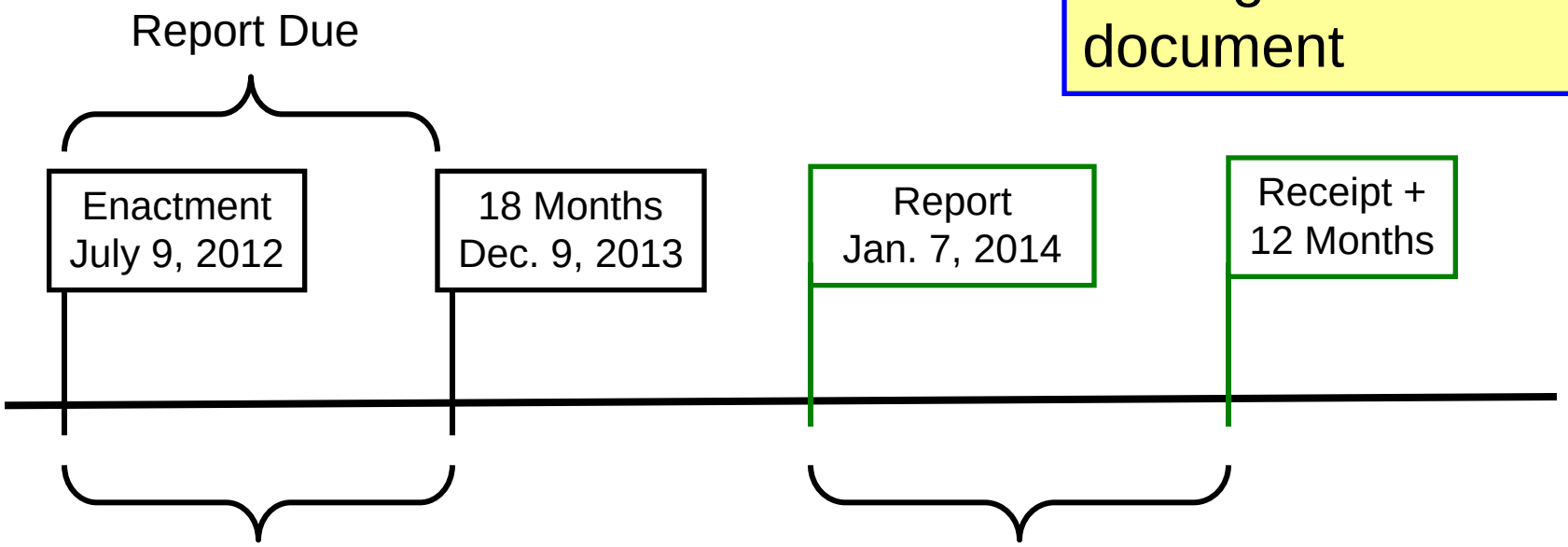
- Instead, FDA must follow the guidance entitled “Deciding When to Submit a 510(k) for a Change to an Existing Device”, dated January 10, 1997 until FDA meets certain conditions.

Certain Conditions

- FDA must issue a report within 18 months of the law's enactment date (July 9, 2012) about premarket notification
- FDA must withdraw "Guidance for Industry and FDA Staff—510(k) Device Modifications: Deciding When to Submit a 510(k) for a Change to an Existing Device"
- FDA may not issue draft guidance or proposed regulations before receipt of the report.
- FDA may not issue any final guidance or regulation for one year after receipt of the report.
- The FDA guidance entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device", dated January 10, 1997 is in effect.

510(k) Change Analysis

FDASIA instructs FDA to revert to the 1997 guidance document



FDA Actions

- On June 13, 2013 FDA held a public meeting to discuss the issue.
  - The meeting videos are on the FDA website http://www.fda.gov/MedicalDevices/NewsEvents/WorkshopsConferences/ucm347888.htm
- FDA opened a docket for comments
  - FDA-2013-N-0430
- Commissioner Hamburg signed the report on January 7, 2014

Proposed Actions

- Clarify key terms from 807.81(a)(3)
- Manufacturer determines if the design modification could impact safety and effectiveness and uses design verification and design validation to conform or refute the assessment
- Include practical considerations regarding change in materials
- Update the guidance to include advanced technology such as software and wireless devices
- Clarify the text and flowcharts to ensure they are congruent
- Add an appendix that includes examples of changes that would and would not likely require a new 510(k)
- Add an appendix on how to document the decision process

Excerpt From the Meeting

- Michael Ryan is explaining some results and why FDA-CDRH does not consider the documentation adequate.

- https://collaboration.fda.gov/p14218a094l/?launcher=false&fcsContent=true&pbMode=normal
- Time: 13:20 to 16:40

510(k) Analysis Records

- Use the guidance document as the basis for a record.
- Start with Flowchart A and identify the path from each decision point.
- At each decision point record the question, your decision, and write an explanation of why you made that decision.
- As part of the design change, complete the documentation, discuss it at a design review, and file the checklists in the DHF.

510(k) Analysis Records

- Keep records that document your decision to submit or not submit a 510(k) revision for the change

- Minimum documentation should include:
  - Written analysis of the questions in the FDA Guidance Document *Deciding When to Submit a 510(k) for a Change to an Existing Device*

  - Written documentation in the ISO 14971:2007 Risk Management File that shows the changes do not exceed the criteria for risk acceptability defined in the Risk Management Plan

Risk Management

820.30(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 14971:2007

- This is the international standard for Medical Device Risk Management
- FDA-CDRH recognizes it as a consensus standard
- It is the *de facto* standard for device risk management
  - The emphasis is shifting to the more restrictive EN ISO 14971:2012

Initial Design

- Risk Analysis, during the initial design, identified hazards (normal & fault conditions) and estimated risk
- Risk Evaluation determined if the estimated risk is acceptable
- Risk Reduction reduced the estimated risk to an acceptable level when required
- The results are in the Risk Management File

Design Change

- A design change will change the design output and may change the identified design outputs that are essential for the proper functioning of the device

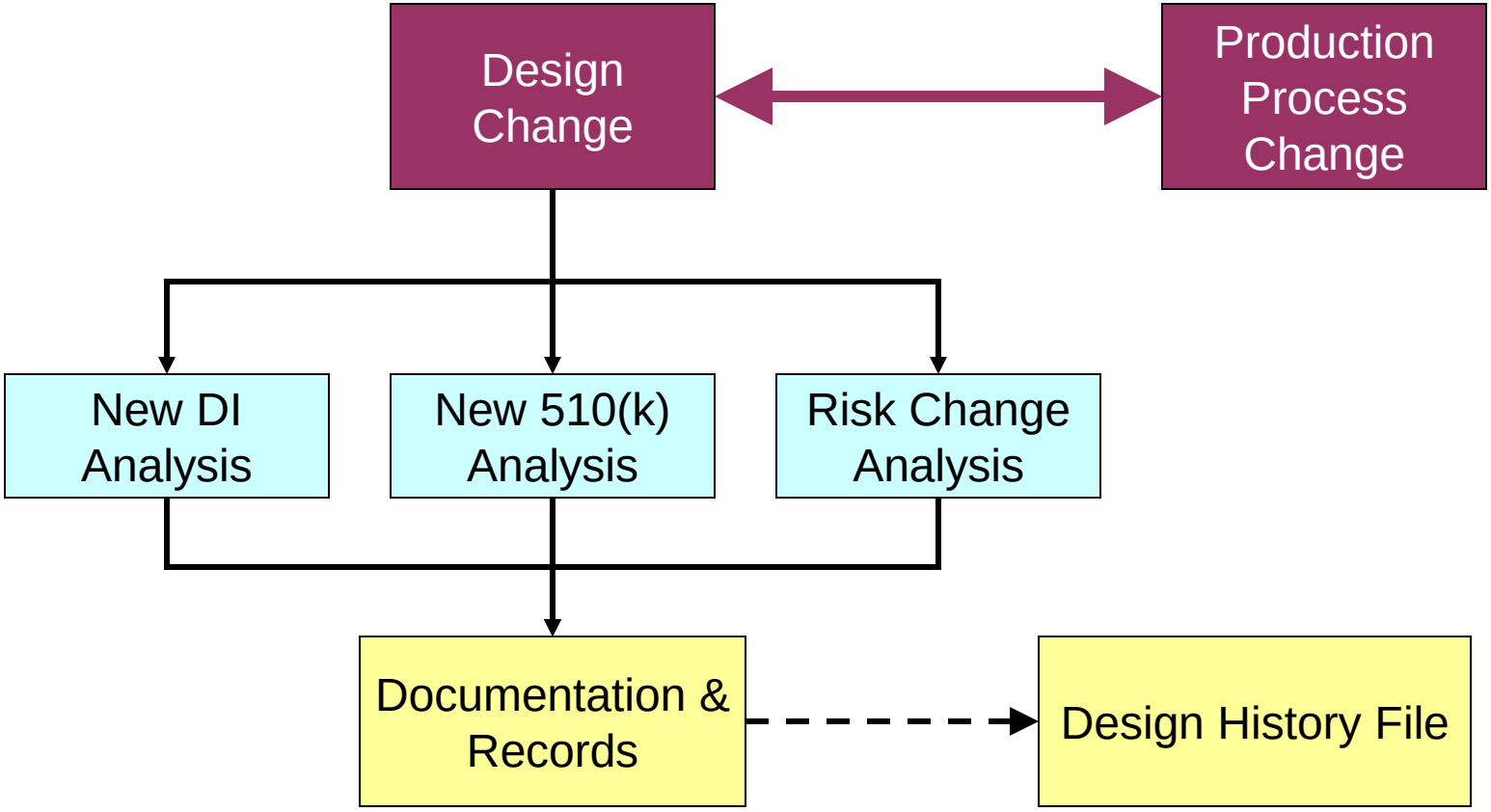
- Review the Risk Management File to determine any implications:
  - Determine any impact on the essential design output
  - Look for cases where the change will affect a risk reduction measure taken
  - Determine if the change introduces any new hazards
  - Determine if the change affects any current sequence of events
  - Determine if the change introduces any new hazardous situations

Records

- Create a checklist of items in your Risk Management File that could affected by the design change
- Use the checklist to identify any areas that need review
- Review and update the identified areas
- Record the changes and identify any new hazards, any new hazardous situations, any changes to risk reduction, and any cases where the estimated risk is not acceptable
- As part of the design change, complete the checklist, update affected areas, discuss it at a design review, and file the documentation in the DHF

The Results

The Model


Design Change
Production Process Change
New DI Analysis
New 510(k) Analysis
Risk Change Analysis
Documentation & Records
Design History File

FDA Inspections

Inspectional Implications

- Prepare for the next FDA Inspection
- The FDA Investigator will have access to (at least) three sets of data:
  - All devices you list
  - All devices you have cleared by the 510(k) process
  - All Device Identifiers in the GUDID
- For each design change, it would be “fair game” for the FDA Investigator to ask for:
  - The analysis to determine if the change is a new version or model and requires a new DI
  - The analysis to determine if the change is significant and requires a new 510(k)
  - The analysis of the change, through design validation, to determine its impact on risk

Summary

Summary (1)

- There are two ways to handle design changes
  - 820.30(i) Design changes
  - 820.70(b) Production and process changes
- The changes can be managed by any part of the organization
  - Design changes do not have to go to R&D or the design group
- The important issue is to establish correct procedures and follow them

Summary (2)

- The changes need to determine three important points:
  - Does the change require a new Device Identifier (DI)?
  - Does the change require a new 510(k)?
  - Does the change require an updated Risk Management File
- Answer these questions by developing checklists for each area
- The areas are independent, so each could have a different Yes/No answer
- Document your analysis and include it in the Design History File (DHF)

QUESTIONS