GLISLAND® TRAINING SERIES:

DESIGN CONTROL:
REQUIREMENTS AND IMPLEMENTATION

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Part I

Regulatory Requirements

The Law and Regulations

1. Federal Food Drug & Cosmetic (*FD&C*) Act
2. Code of Federal Regulations (*CFR*)
3. Title 21 *CFR* Parts 800-1299

How FDA Regulates Medical Devices

Three Levels of Controls

1. General Controls
2. Special Controls
3. Premarket Approval

Device Classification

- Class I
- Class II
- Class III

Risk Based Controls

Class I: General Controls
Class II: General Controls, Special Controls
Class III: General Controls, Special Controls, PMA

FDA Quality System Regulation

1. 1976 Medical Device Amendments - *cGMP* for medical devices: 520(f) of FD&C Act (21 U.S.C. 360j(f))
2. Codified in 21 CFR Part 820, effective December 1978 (focusing on production process in 1978 GMP)
3. **Added design control provision in 1990 amended by *SMDA*** (*Safe Medical Device Acts*)
   a) Added section 803 (21 *U.S.C* 383)
   b) Revised 1978 *cGMP* and harmonized with EU standard
   c) Rename *cGMP* for medical device to *QSR*
   d) **Design Control effective June 1, 1998**
4. **The new *QSR* applies to the entire life cycle of a device**

GMP & cGMP vs. QSR

1. GMP – Good Manufacturing Practice
2. cGMP – Current Good Manufacturing Practice
3. QSR – Quality System Regulation (21 CFR 820):

   "Current good manufacturing practice (CGMP) requirements are set forth in this quality system regulation. "

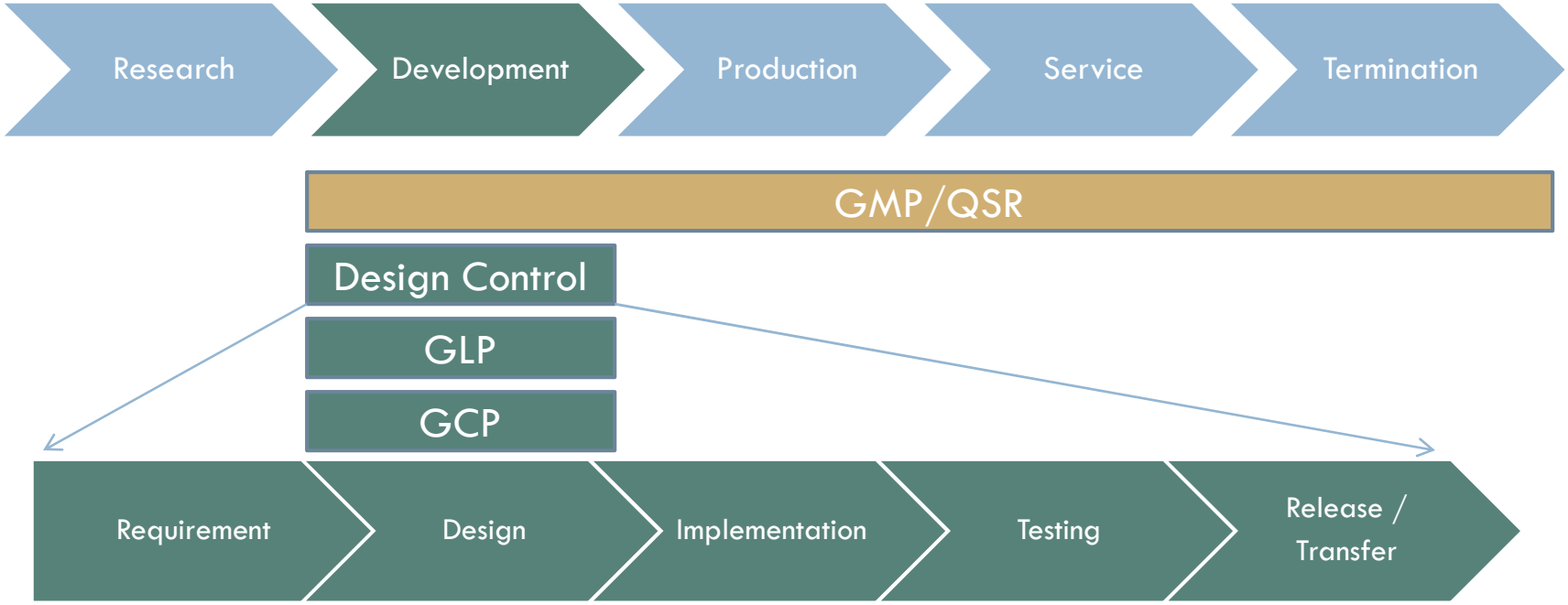
   "The failure to comply with any applicable provision in this part renders a device adulterated under section 501(h) of the act. Such a device, as well as any person responsible for the failure to comply, is subject to regulatory action."

Design Control in QSR

- Subpart A - General Provisions
- Subpart B - Quality System Requirements
- **Subpart C - Design Controls**
- Subpart D - Document Controls
- Subpart E - Purchasing Controls
- Subpart F - Identification and Traceability
- Subpart G - Production and Process Controls
- Subpart H - Acceptance Activities
- Subpart I - Nonconforming Product
- Subpart J - Corrective and Preventive Action
- Subpart K - Labeling and Packaging Control
- Subpart L - Handling, Storage, Distribution, and Installation
- Subpart M - Records
- Subpart N - Servicing
- Subpart O - Statistical Techniques

Development Stage Regulatory Compliance

Typical Product Lifecycle



Typical Development Process

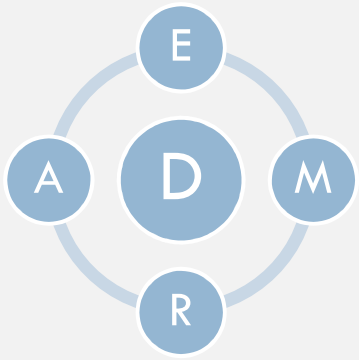
21 CFR 820 Subpart C - Design Controls

Elements

a) Required: Any class III, class II, and some class I (820.(a)(2))
b) Design and development planning
c) Design input
d) Design output
e) Design review
f) Design verification
g) Design validation
h) Design transfer
i) Design changes
j) Design history file

Action Keywords

- Establish
- Maintain
- Review
- Approve
- Document



What's Wrong with this Glass?

A plastic glass

A closer look

Intended use: cold beverage glass; Target market: children in the US

21 CFR 829 Subpart D – Document Controls

Establish and maintain procedures to control **all documents** that are required by this part:

a) Document approval and distribution
   - Review and approval prior to issuance
   - Available at all locations necessary
   - Remove obsolete documents promptly

b) Document changes
   - Original review and approval
   - Timely communication of changes
   - Change records

Electronic Records and Electronic Signatures

1. *21 CFR* Part 11 and Final Guidance
2. Enforced rules and requirements:
   a. System access controls
   b. Enforce Sequence Steps
   c. Application Access Controls
   d. Device checks
   e. Competence of People
   f. Accountability
   g. System document control
   h. Controls for open systems
3. e-signature requirements

FDA Enforcement Actions

- Establishment registration and product listing
- Marketing clearance/approval
- Reports
- Inspections
- Notice of Violations (FDA-483, Warning Letters…)
- Recalls
- Civil money penalties
- Seizure
- Injunction
- Prosecution

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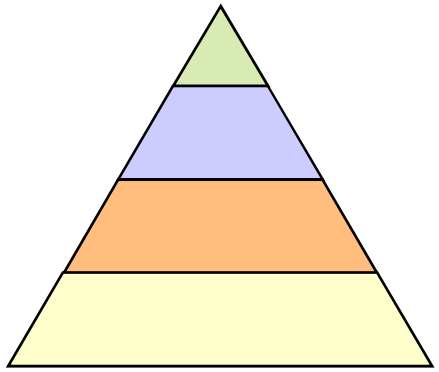
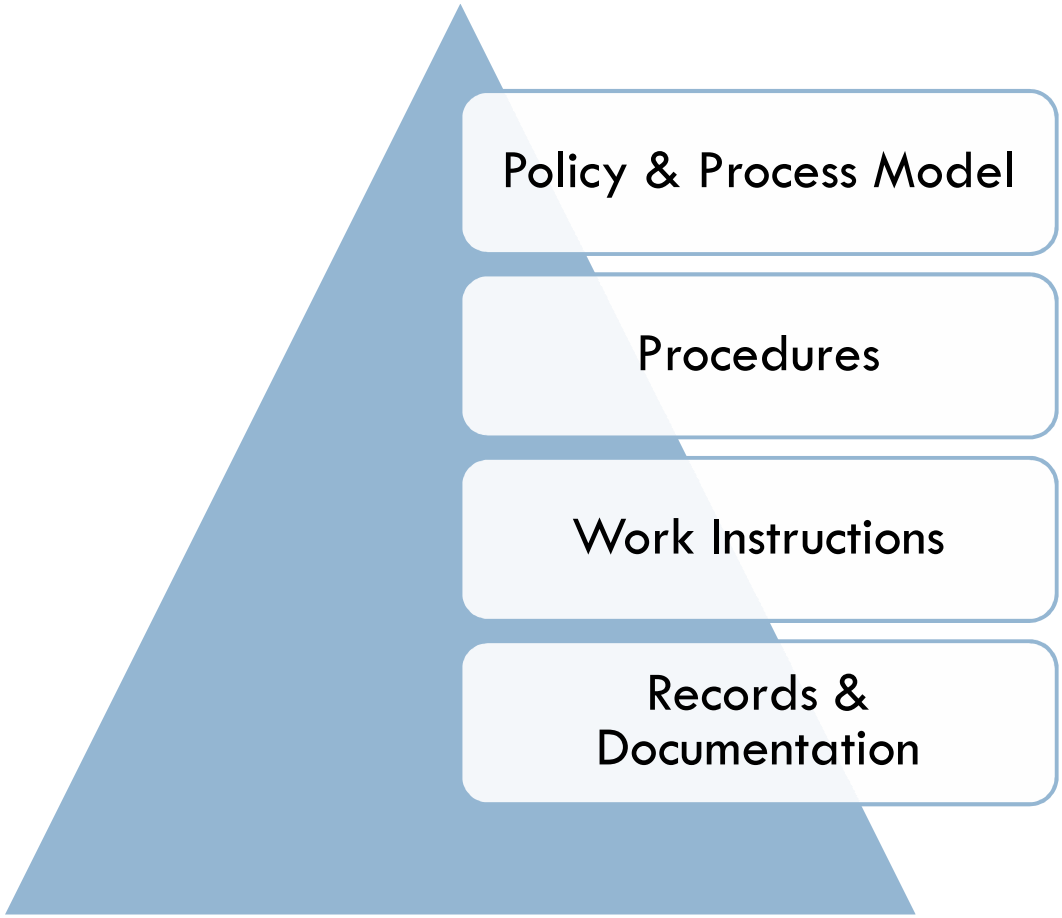
Part II

Implementation

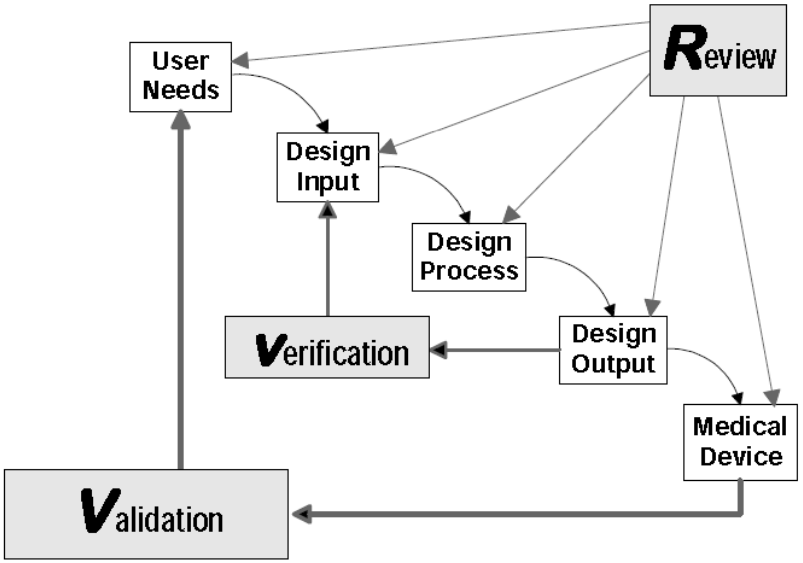


Design Control Pyramid



Application of Design Controls

FDA Example



What Process Model to Apply?

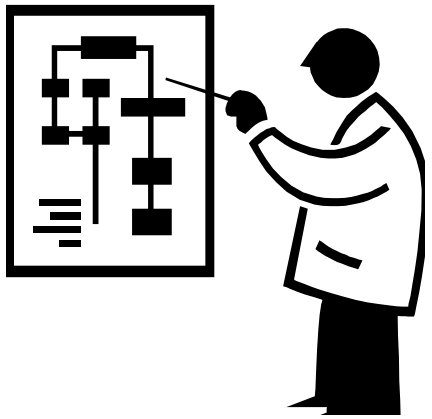
- Waterfall Process
- Concurrent Engineering
- Iterative Process

Deciding on Process Model

- Waterfall Process
- Concurrent Engineering
- Iterative Process

FDA GUIDANCE:

"appropriate tools and techniques used by competent personnel"



Design Planning

- Goals and objectives of the design and development
- Organizational responsibilities and interface with contractors
- Tasks, deliverables, resources, schedule
- Major reviews and decision points
- Policy, process, and standards
- Document and Change controls

Design Input

- Physical and performance requirements
- A set of principles to be followed
- Written to an engineering level of detail
- Rapid prototyping for design input development
- Full participation including production and service personnel, key suppliers
- Review and approval
- Change controls

Design Output

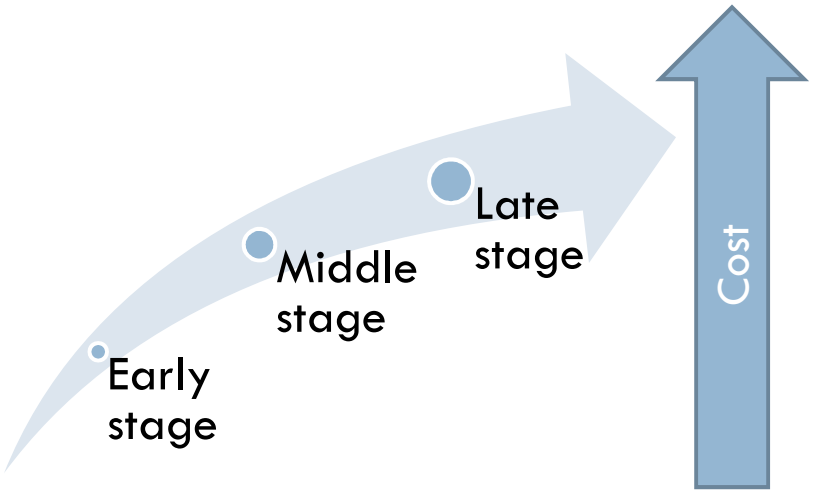
- Phase design output
- Finished design output
  - The device
  - Packaging
  - Labeling
  - Device master record
    - Specification
    - block diagrams
    - flow charts
    - software high-level code
    - Procedures
    - Work instructions
- Risk management file
- Production specification
- Acceptance criteria

Design Review

How to review

- Evaluate the adequacy of the design requirements
- Evaluate the capability of the design to meet these requirements
- Identify problems
- Independent and objective reviews
- Design review meeting
- Resolution of concerns

Cost of change



Design Verification

- Establish design phase conformance: design output vs. design input
- Methods
  - Tests
  - Inspections
  - Analyses
- Documentation

Design Validation

- Validation Planning
- Validation Methods
  - Clinical evaluation or clinical trials
  - Testing production unit in the actual or simulated use environment
  - Analysis and inspection
  - Scientific literature
  - Historical evidence
- Validation Review
- Documentation

Design Transfer

- Production Specification
  - assembly drawings
  - component procurement specifications
  - workmanship standards
  - manufacturing instructions,
  - inspection and test specifications.
- Procedures
  - assessment of the completeness and adequacy of the production specifications (transfer protocols)
  - Review and approval

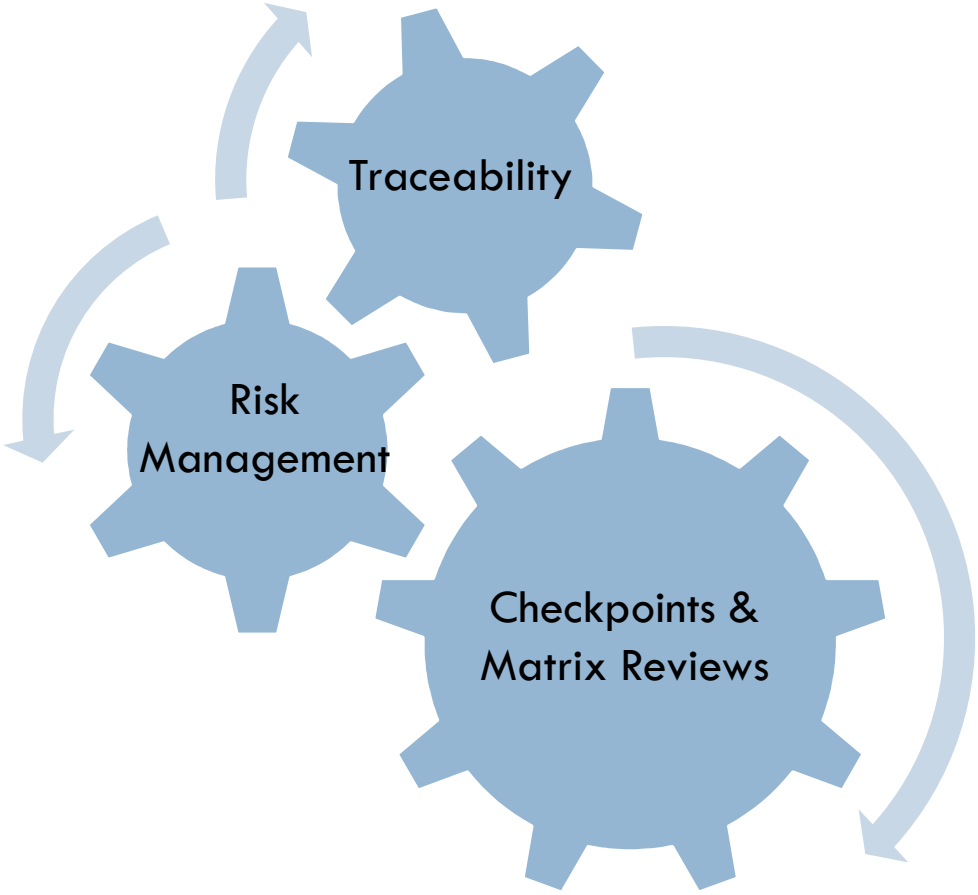
Design Changes

- Document control
  - Enumeration of design documents
  - Status
  - Revision history
- Change control
  - Enumeration of deficiencies and corrective actions
  - Tracking of resolution

Design History File (DHF)

- Detailed design and development plan specifying design tasks and deliverables.
- Copies of approved design input documents and design output documents
- Design review documentation
- Validation documentation.
- When applicable, copies of controlled design documents and change control records

Secret Weapons



References

- *Fundamentals of US Regulatory Affairs*, 5th Edition, RAPS, 2007
- *Milestones in U.S. Food and Drug Law History*, http://www.fda.gov/opacom/backgrounders/miles.html
- Significant Amendments to the FD&C Act, http://www.fda.gov/opacom/laws/
- 21 CFR Part 820, http://www.gpoaccess.gov/nara/index.html
- *FDA Regulatory Procedure Manual 2007*, http://www.fda.gov/ora/compliance_ref/rpm/
- FDA Guidance Documents: http://www.fda.gov/cder/guidance/index.htm

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Glisland Design Control Services

- Process Development (including SOP & WI writing)
- Design Planning
- Project Management
- Risk Analysis
- Design Review
- Verification & Validation
- Compliance Audit
- Training

