



HORIZONS

Think. Challenge. Excel.

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Defining Where Research Ends and Design Controls Begin

Denise D. Dion, EduQuest, Inc.

Lourdes Valentin-Aponte, Schering-Plough



- Design Objectives and Tools

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Objective of Design Controls

- To provide an organized, disciplined approach for product and process design (development), verification, validation, and change maintenance

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Design Controls Purpose

- Purpose
 - To assure that products and processes meet
 - Users' needs and intended uses
 - Requirements, Specifications, Process Parameters
 - Regulatory requirements
 - Are Safe and Effective
 - Can be reproducibly and reliably manufactured

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Design Control Tools

- Tools for achieving purpose
 - Establish design control procedures
 - Develop plans for design projects (Include interfaces between R&D and other units)
 - Control changes during design development and to existing products and processes

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Design Control Tools

- Tools for achieving purpose
 - Identify design inputs - requirements and high level specifications for the product and/or process
 - Develop design outputs (final specifications/parameters)
 - Verify through measurement, test or inspection that outputs fulfill input requirements

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Design Control Tools

- Tools for achieving purpose
 - Transfer outputs to production
 - Validate that product/process meets user needs and intended uses and is safe and effective
 - Conduct design reviews throughout process
 - Document design activities in design (development) history file

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- Research versus Design

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There is no R in Design

- Design (Development) is a process that must be controlled
- Research was never meant to be subject to design controls
- Concept and feasibility are research steps – they need to stay there when practical

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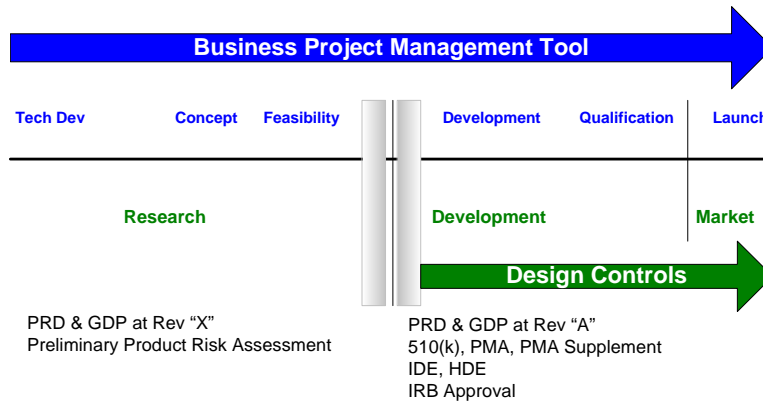
There is no R in Design

- Manage the business process of R&D separate from the regulatory process of design
 - Business process asks “Should we continue?”
 - Regulatory or Quality process asks “Can we continue?”

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Product Lifecycle



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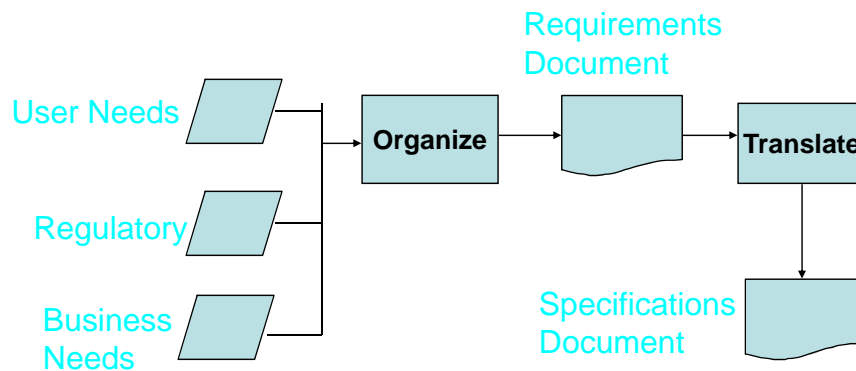
Concept and Feasibility

- This is the time to determine the requirements of the device
- Design starts once your initial requirements are approvable
- Preliminary risk analysis (top-down) should be done concurrent with determining your requirements

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Design Input Model



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- **Critical Elements for Process Design**

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Guiding Principles

Quality should be built into the product,
and testing alone cannot be relied on to
ensure product quality.”

Quality Systems Approach to Pharmaceutical Current Good Manufacturing
Practice Regulations, September, 2004.

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FDA’s “Desired State”

- FDA’s desired state of manufacturing and regulation
 - Product quality and performance are ensured through the design of effective and efficient manufacturing processes

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FDA's "Desired State"

- Product and process specifications are based on a mechanistic understanding of how formulation and process factors affect product performance
- Continuous real-time quality assurance
- Relevant regulatory policies and procedures are tailored to accommodate the most current level of scientific knowledge

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Fundamental Concept

- Manufacturers shall
 - Conform to GxPs/Quality System Regs.
 - Have written procedures
 - Have personnel trained in the use of those procedures
 - Follow the procedures as documented and trained
 - Support activities with documentation

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Quality Built-In Through Knowledge

- The design of manufacturing processes using principles of engineering, material science, and quality to ensure acceptable and reproducible product quality and performance throughout a product's expected shelf life.

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Design and Optimization

- Design and optimization of drug formulations or product specifications and manufacturing steps can include the following –
 - Identify and measure critical material (components) and process attributes relating to product quality
 - Design process controls that provide adjustments to ensure control of all critical attributes

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Design and Optimization

- Develop mathematical relationships between product quality attributes and measurements of critical material (components) and process attributes
- Design a process measurement system to allow real-time or near real-time (e.g., on-line, in-line, or at-line) monitoring of all critical attributes

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• Design Compliance Techniques

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Using Trace as a Verification Tool

- Trace requirements through specifications to tests and test results (IOVV)
- Tracing provides assurance that all requirements have been specified and verified/validated
- Allow no widows, no orphans
- Keep as a living document

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Using Trace as a Verification Tool

- Use trace matrices
 - To help identify affected parts of design when changes are made
 - To Identify tests to be repeated on changed design
- Use automated trace tools for complex devices
 - examples: ReqPro, Doors

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Design Verification/Validation

- Written and approved protocols
- Written and defined acceptance criteria
- Sample size justification
- Calibrated test equipment
- Validation – actual or simulated use conditions
- Validation – production or production equivalents

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The DHF – Your Design Story

- Keep by product or process family
- Link changes over time to DHF
- Combine living documents with historical
 - Risk Management Files
 - Requirements and Specifications
 - Trace Matrix

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Marketing/Customer Surveys

- If done to determine customer satisfaction with design during design activities
 - A design validation activity
- Needs to be done per approved protocol, with documented acceptance criteria and with statistically valid sample size and calibrated equipment

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Design/Technology Transfer

- Design and Manufacturing share responsibility
- Not a throw-it-over-the-wall activity
- Begin the design transfer during the feasibility stage
- Manufacturability is integral to design

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Design/Technology Transfer

- Need design risk assessment in order to do process risk assessment
- Need defined process, approved product master record, and process risk assessment to adequately validate process
- Suppliers need to be qualified

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Design/Technology Transfer

- Transfer Must Include Qualification of
 - Equipment
 - Tools
 - Test Fixtures (SW and HW)
 - Process
 - Personnel
- Include evaluation of manufacturing environment for suitability to device design

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Design/Technology Transfer

- Processes Must Be Validated for Their Intended Use
 - Repeatability
 - Reproducibility
 - Protocols, Plans
 - Objective Evidence

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Design/Technology Transfer Review

- Include a determination that:
 - Manufacturing and control processes are validated
 - Final process risk and trace matrix have been updated
 - Manufacturing and control process validation reports are accurate and complete
 - The product master record is updated, reviewed and approved
 - Training is complete and documented

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Design/Technology Transfer Review

- Don't forget to prove products used for design validation are equivalent to production units
 - Were the units from the process validation runs or after?
 - If no, what changed in the process or product design from units used to do design validation and those from the process validation runs?

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- The Yin/Yang of Design/CAPA

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The Yin/Yang of Design/CAPA

- Design is the beginning
- Risk Analysis – (product and process) begins with Design
- Production and Post-Production Planning feeds the CAPA system

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Cradle-to-Grave Concept of Product Design and Process Development



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The Yin/Yang of Design/CAPA

- Production and Post-Production data is used to
 - Assure our original risk assessments were correct
 - Assist us in proper evaluation and investigation of nonconformances (product, process, system)
 - Identify needed actions to improve our product design, processes and systems

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The Yin/Yang of Design/CAPA

- In deciding on requirements for design changes or new designs
 - Marketing data
 - Voice of the Customer
 - Human Factors
 - Regulatory/Standards
 - Production/Post-production data from similar designs

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Key Phases of Investigations

- Three key phases (some companies break these out into more than three)
 - Investigation - to assess whether the observed result is valid
 - Expanded investigation - to assess cause
 - Corrective (or preventive) action - to identify action(s) to correct the cause of the problem (or the potential problem) and ensure the nonconformity cannot recur (or occur)

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Purposes of Investigation Reports

- To create a clear record (synopsis) of what was done
- To convince any potential reader that you properly responded to the findings and reached appropriate and fully supported conclusions

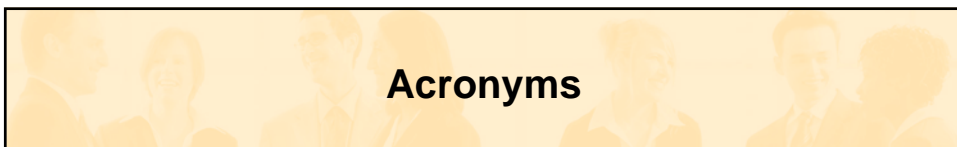
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• Questions?

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Acronyms

- R&D – Research and Development
- CAPA – Corrective and Preventive Action
- DHF – Design or Development History File
- IOVV – Input Output Verification Validation

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