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Implementing a Periodic Validation Review Program A Case Study

Implementing a Program at a Manufacturing Site

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Problem Statement

- Regulatory Agencies require us to have a Periodic Validation Review Program
- What does "periodic" mean?
- How to develop a *defendable* rationale behind the actual program
- How do we get started and maintain it without draining our resources?

Objectives

- Develop an understanding of how:
  - To align with Regulatory expectations
  - To align with the new FDA Process Validation requirements
  - To align with current owner validation programs
  - Leverage existing programs

Regulatory Requirements FDA

Maintenance of the facility, utilities, and equipment is another important aspect of ensuring that a process remains in control. Once established, qualification status must be maintained through routine monitoring, maintenance, and calibration procedures and schedules (21 CFR part 211, subparts C and D). **The equipment and facility qualification data should be assessed periodically to determine whether re-qualification should be performed and the extent of that re-qualification. Maintenance and calibration frequency should be adjusted based on feedback from these activities.**

FDA Guidelines for Industry; Process Validation: General Principles and Practices

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Facilities, systems, equipment and processes, including cleaning, should be periodically evaluated to confirm that they remain valid. Where no significant changes have been made to the validated status, a review with evidence that facilities, systems, equipment and processes meet the prescribed requirements fulfills the need for revalidation.

Annex 15 *to the EU Guide to Good Manufacturing Practice:* ***Title: Qualification and validation***

Getting Started

- What do we want this program (embodied in a guide) to do?
  - provide guidance and instruction
  - provide a structured/documented approach.
  - provide a sound rationale/basis for review periods
  - provide additional assurance of maintenance of the qualified and validated state.
  - define requirements and scheduling for recertification/requalification.

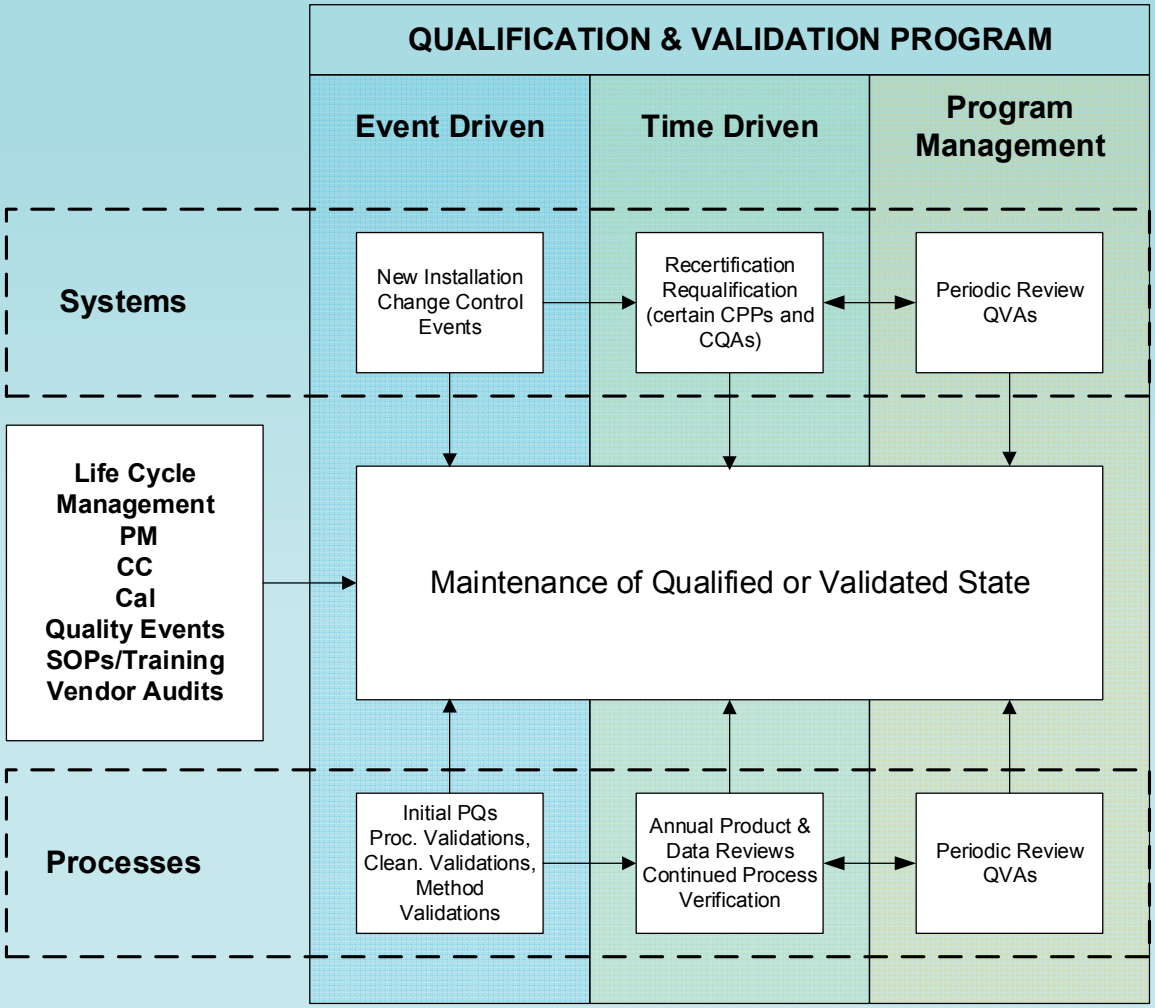
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Getting Started

- What does it cover?
  - Qualified Direct Impact Systems
    Qualified Laboratory Equipment
  - Qualified Controlled Environments
  - Qualified Computerized Information Systems
  - Validated Analytical Methods
  - Validated Processes (including Cleaning)

The Concept in Focus

QUALIFICATION & VALIDATION ASSESSMENT
OVERVIEW AND REALATIONSHIP TO RELATED PROGRAMS



Agreement on the Key Concepts

- The Event Driven activities
- Rationales supporting the Time Drive Requalifications and Recertifications
- The Program Management activities

Agreement on the Key Concepts

- Time Driven
- Time Driven activities = "Re-Qualification"?
- Group systems by type and impact

Agreement on the Key Concepts Time Driven Examples

- Controlled Temperature Storage Units and Areas (Direct Impact, used for drug product storage). Refer to SOP XXXXXX, *Controlled Temperature Chamber Requalification Program*.
  - The frequency and requirements for each of these type systems are based on the following rationales. For each type of system listed, the frequency and supporting rationales were listed:
    - The systems are monitored and alarmed
    - They are managed under Change Control
    - They are subject to Preventive Maintenance (PM) and Calibration activities
  - Refrigerators and Freezers – For Drug Product
  - Refrigerators and Freezers – for non Drug Product Storage (e.g., components, ingredients, media, WIP, etc.)
  - Stability Chambers
  - Incubators (used for Sterility Testing)
  - Controlled Temperature Storage Facilities (e.g., controlled condition warehouse or storage rooms)

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Agreement on the Key Concepts
Time Driven Examples

- Controlled Environments (used for manufacturing, processing, holding drug substance, drug product components and drug product as applicable). The systems involved in controlling these environments may be a combination of Direct and Indirect Impact Systems or single Direct Impact Systems.
  - Classified, Controlled Clean Rooms
    - HEPA Filters:
      - Frequency and Requirements:
      - Rationale:
    - Room/Space Classification
      - Frequency and Requirements:
      - Rationale:
  - Laminar Flow Booths, BioSafety Cabinets, ISO 5 enclosures and Isolators (enclosures)
    - Frequency and Requirements:
    - Rationale:

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Agreement on the Key Concepts
Time Driven Examples

- **Sterilizers, Dry Heat Ovens and Vaporous Hydrogen Peroxide (VHP) (Direct Impact)**
  - The frequency and requirements for each of these type systems are based on the following rationale:
    - The systems are monitored and alarmed
    - They are managed under Change Control
    - They are subject to Preventive Maintenance (PM) and Calibration activities
  - **Sterilizers (component prep)**
    - Frequency and Requirements: Chamber mapping, load mapping, load verifications, cycle verifications every (1) year.
  - **Depyrogenation Ovens (Dry Heat)**
    - Frequency and Requirements: Chamber mapping, load mapping, load verifications, cycle verifications every (1) year.
  - **VHP Decontamination Units**
    - Frequency and Requirements: The VHP decontamination cycle is requalified annually per SOP XXXXXX, *Use, Operation and Environmental Monitoring of the Sterility Test Isolator.*

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Agreement on the Key Concepts Time Driven Examples

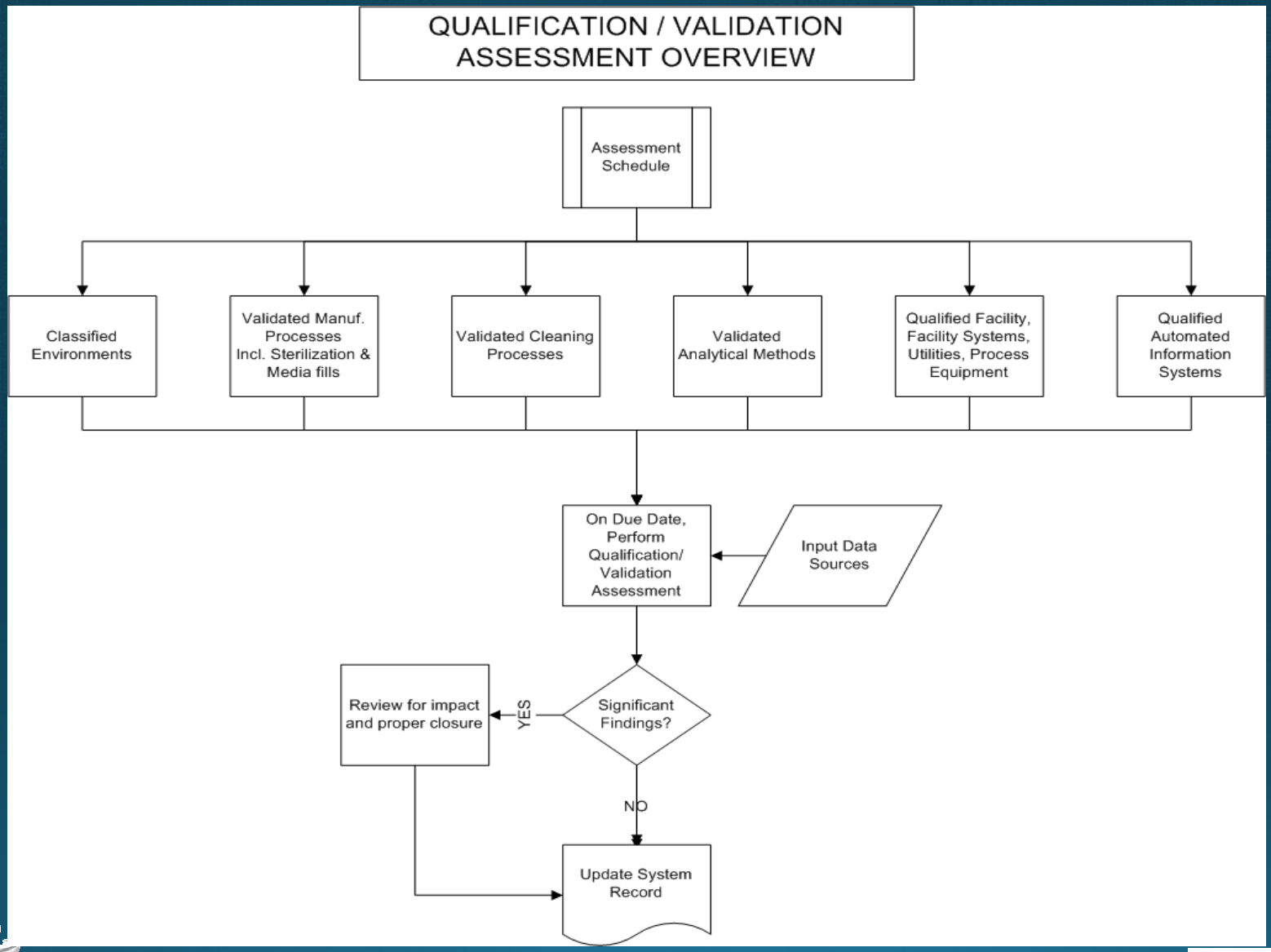
- Outcomes of this alignment of Rationales
  - Inconsistencies across similar systems
  - Supporting data or basis not clear or known

Application of the Key Concepts Now on to the Program Itself

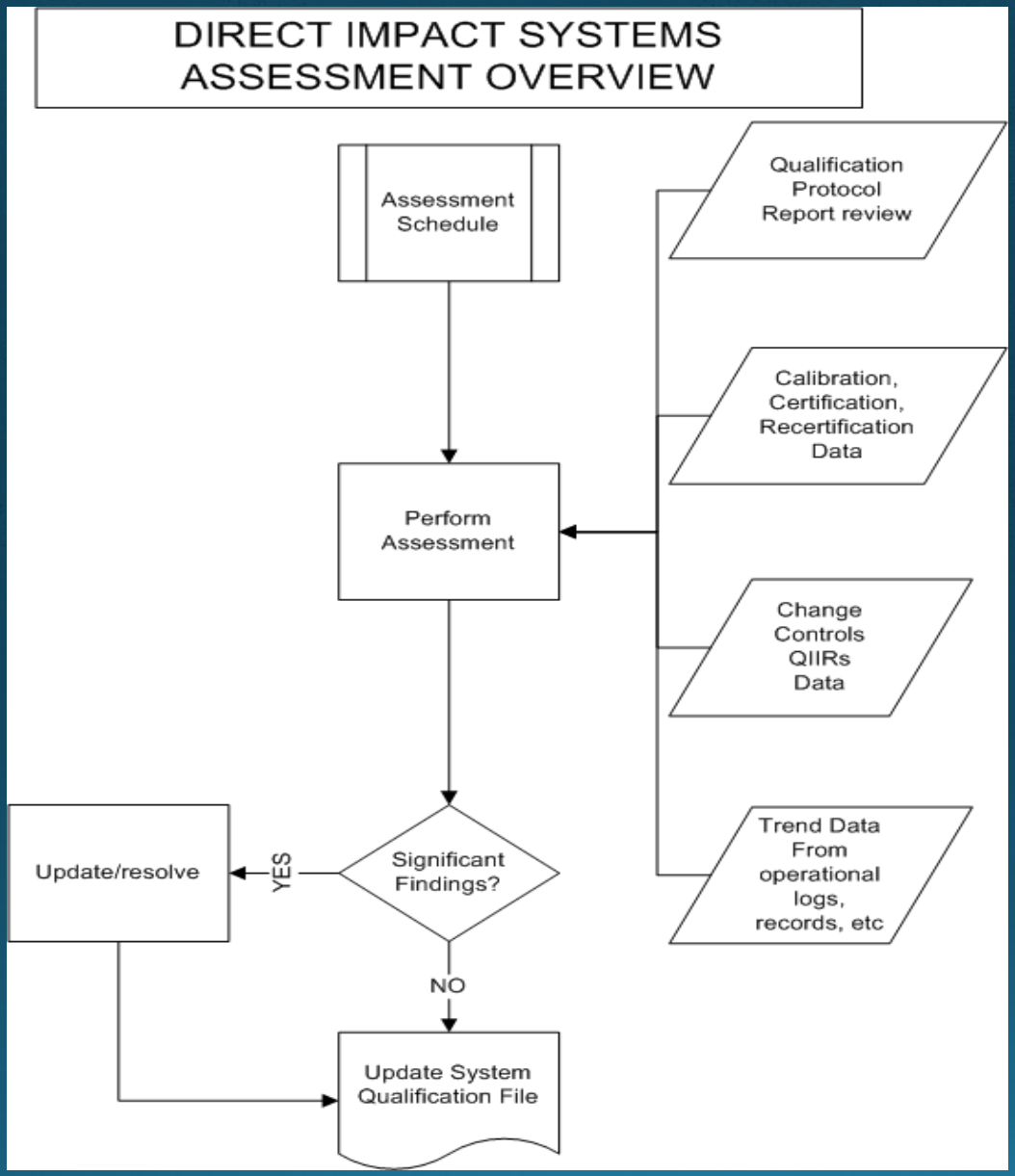
- Map the activities
- Flow chart the overall processes by category
  - Qualified Direct Impact Systems (equipment, support systems, facility systems, utilities)
  - Qualified Laboratory Equipment
  - Qualified Controlled Environments
  - Qualified Computerized Information Systems (examples follow)
  - Validated Analytical Methods
  - Validated Processes (including Cleaning)

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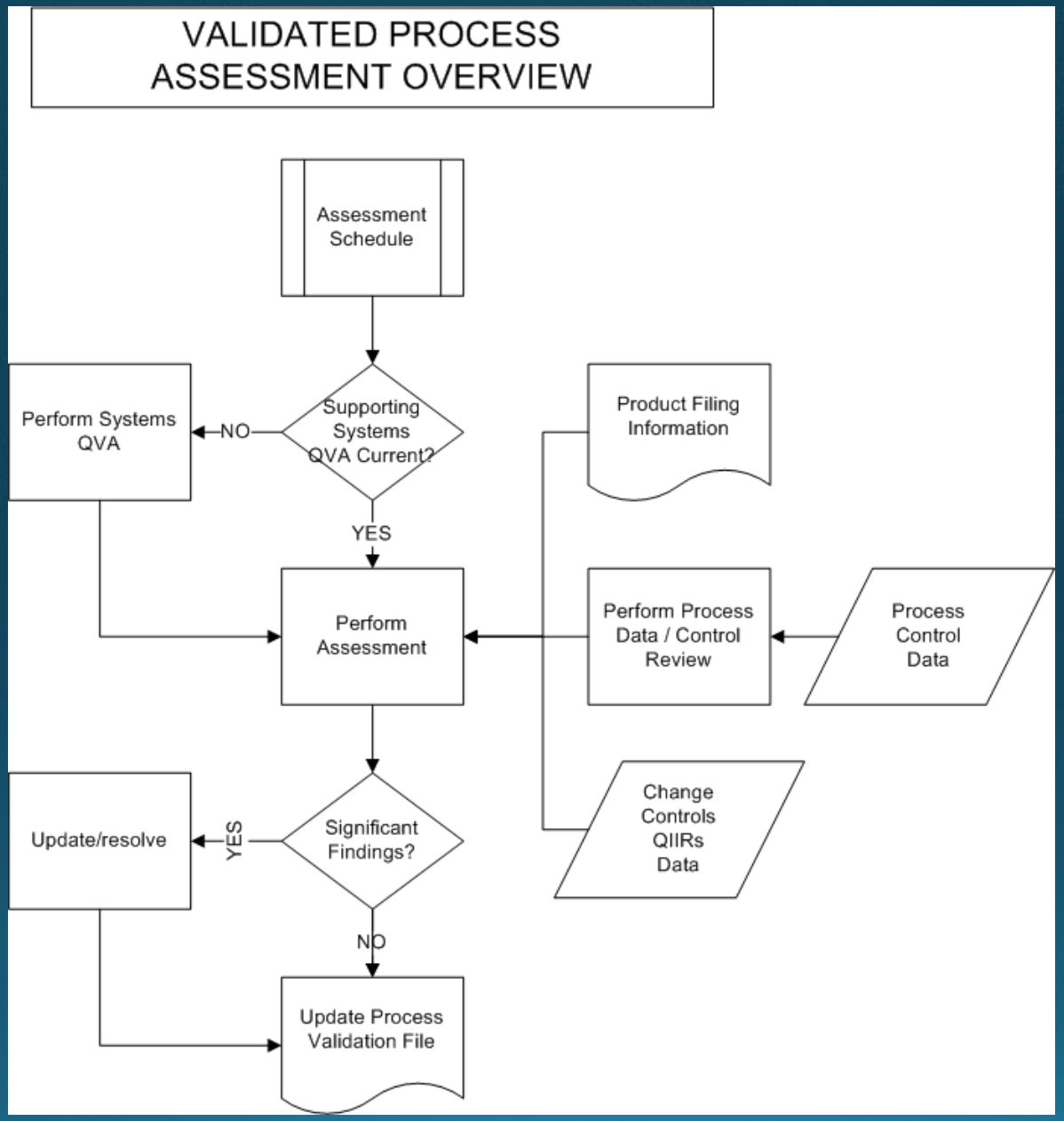
Application of the Key Concepts



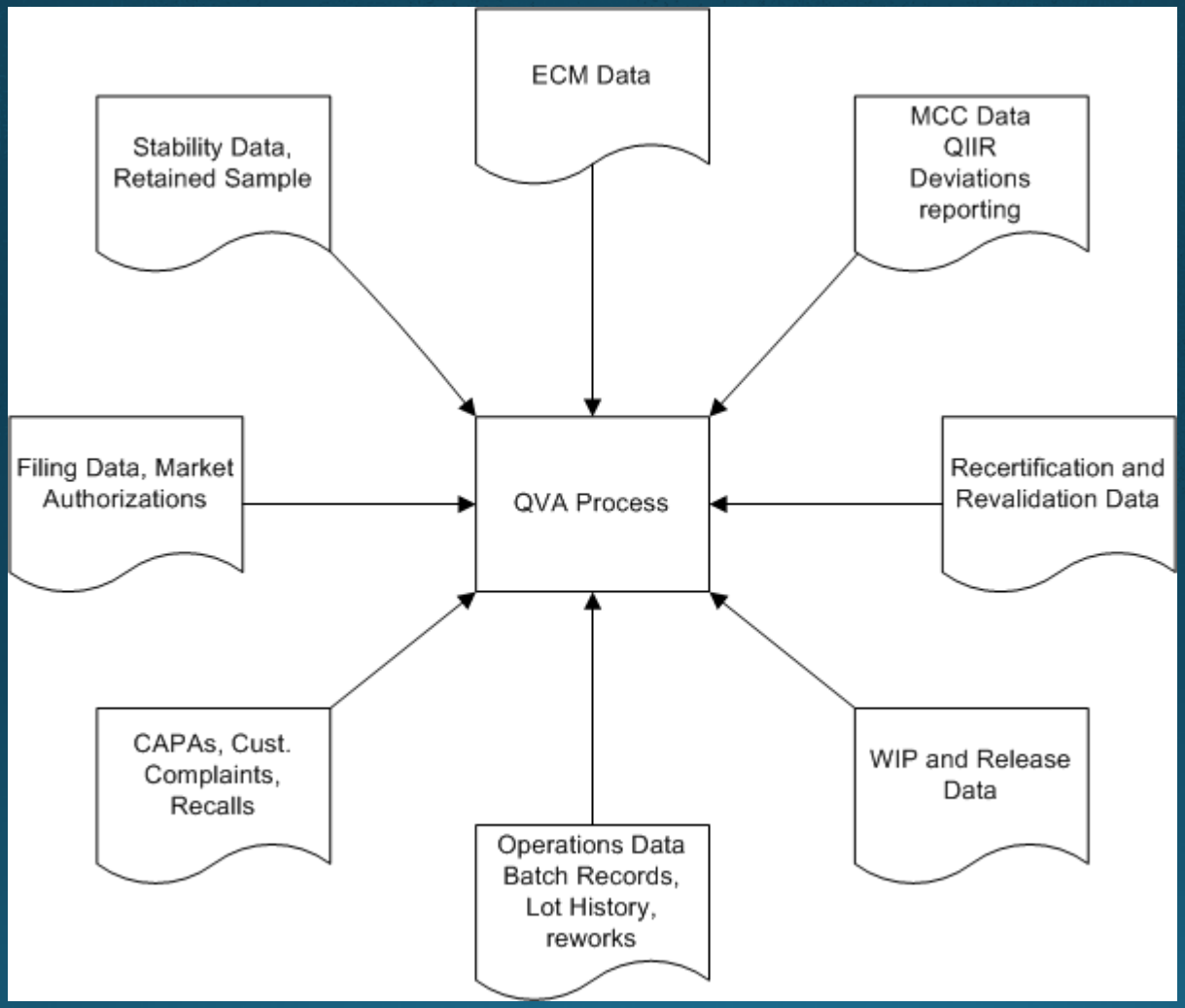
Application of the Key Concepts



Application of the Key Concepts



Application of the Key Concepts



Application of the Key Concepts

- What did we learn by this approach?
  - Opportunities for efficiency
  - Opportunities for alignment
  - Opportunities for improved compliance

Application of the Key Concepts

- What should we select as the program intervals for the key categories?
  - Processes and related Analytical Methods
  - Equipment, Instruments
  - Cold Boxes became a “special issue”

Application of the Key Concepts OUTCOMES

- By mapping out the program, we:
  - Reduced waste
  - Found opportunities for improving compliance and reducing cost (waste)
  - Enhanced the recently implemented Impact Assessment model being driven into all asset based life cycle activities (especially maintenance and calibration)

QUESTIONS?

Thank You !

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