Impact Assessment in a Science & Risk Based Environment

R. Legland

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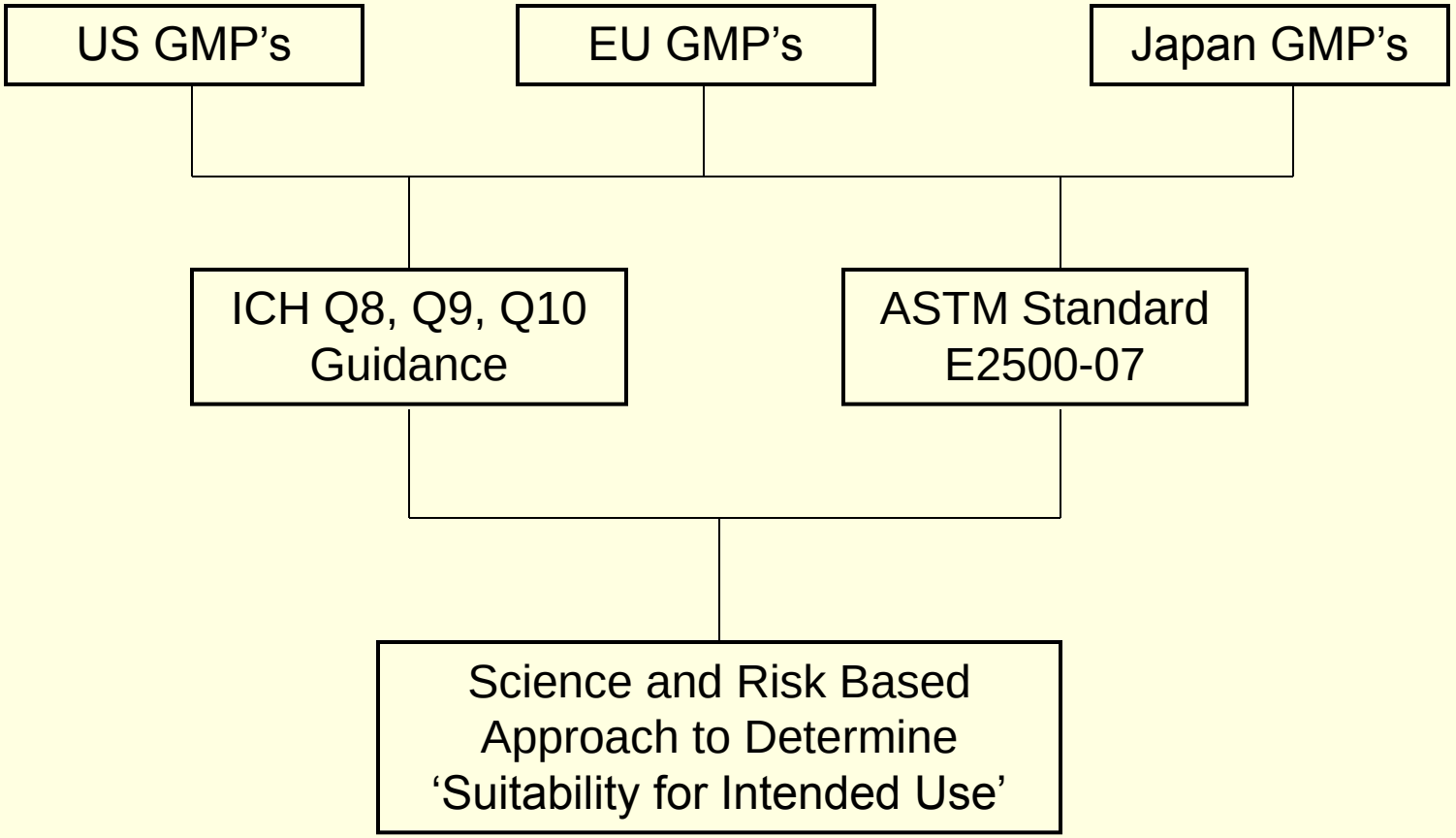
Background


US GMP's
EU GMP's
Japan GMP's
ICH Q8, Q9, Q10 Guidance
ASTM Standard E2500-07
Science and Risk Based Approach to Determine 'Suitability for Intended Use'

Regulatory Drivers

- GMP's
  - US Code of Federal Regulations Title 21 Part 211
  - EU EudraLex (The Rules Governing Medicinal Products in the European Union), Volume 4 EU Guidelines to Good Manufacturing Practice Medicinal Products for Human and Veterinary Use

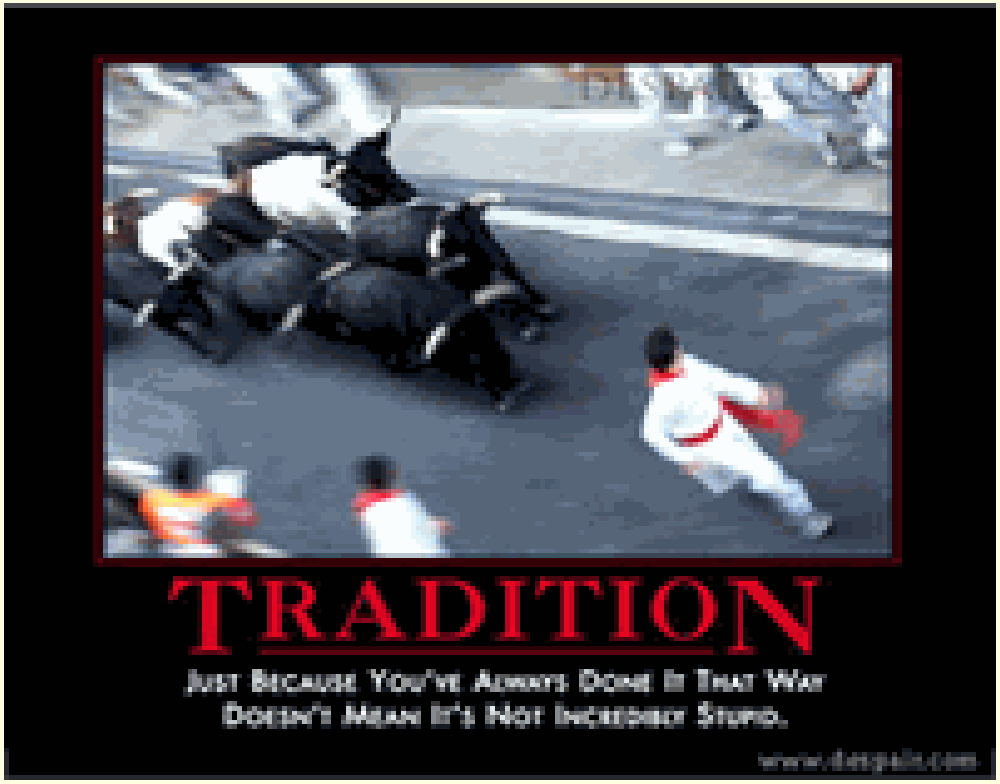
- ICH: International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use
  - Q8 Pharmaceutical Development
  - Q9 Quality Risk Management
  - Q10 Pharmaceutical Quality System

- ASTM Standard E2500-2007: Guide for Specification, Design and Verification of Pharmaceutical and Biopharmaceutical Manufacturing Systems and Equipment

Concepts

- Suitability for Intended Use
  - Manufacture of safe and effective products
- Science Based Approach
  - Product and Process Understanding
    - Definition of Critical Quality Attributes (CQA's) and Critical Process Parameters (CPP's) usually compiled in a User Requirements document and serves as the basis of the process control strategy to assure suitability
  - Subject Matter Experts
    - Responsible for development of strategy, CQA's, CPP's
- Risk Based Approach
  - Quality Risk Management (QRM)
    - Focus on 'Risk to Patient' by managing and mitigating risks to product quality

Why a Science & Risk Based Approach?



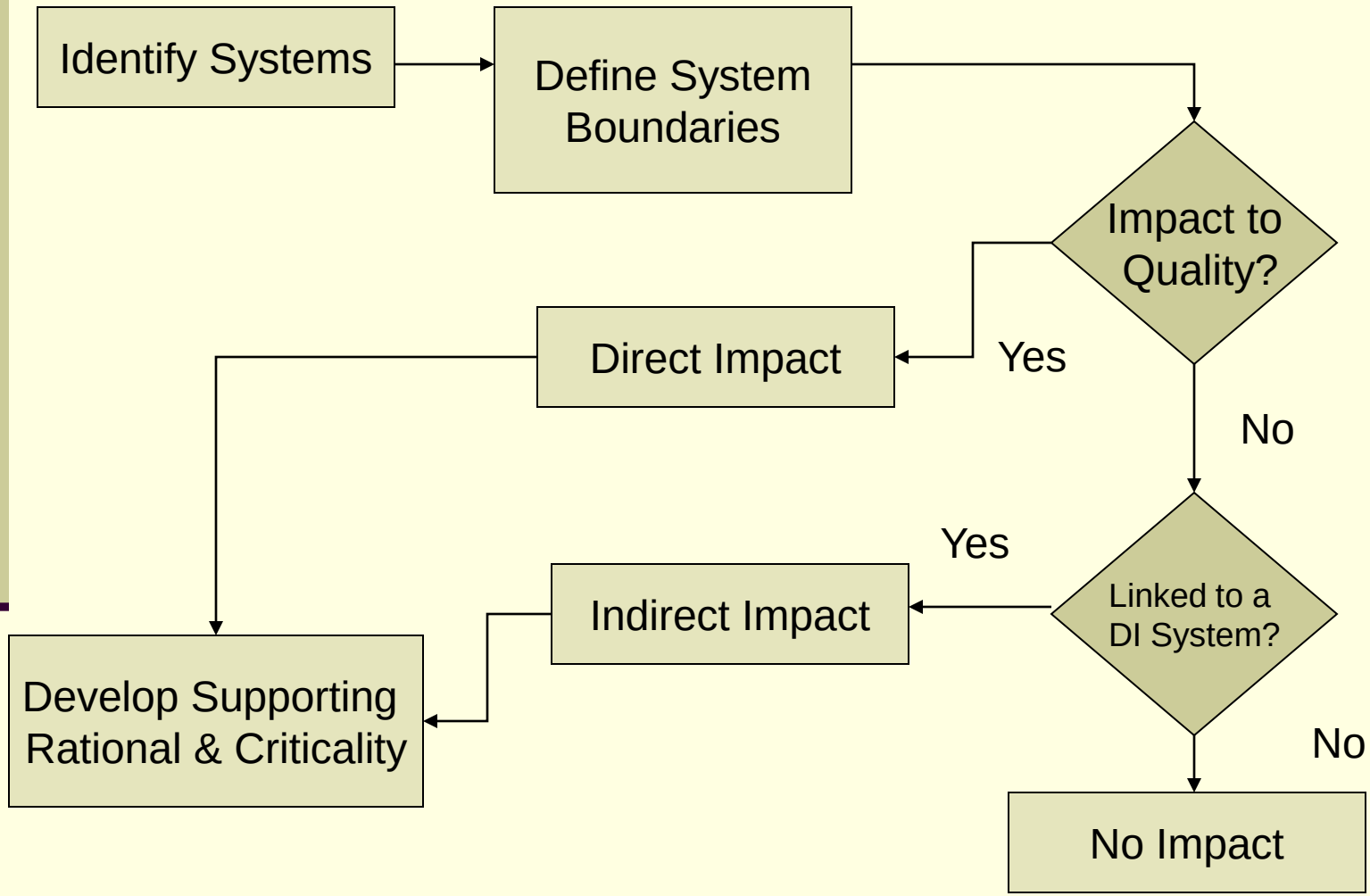
Definitions

- System
  - An organization of components that have a defined operational function
- System Boundary
  - A limit drawn around a system to logically define what is and what is not included
- Impact Assessment
  - The process of evaluating impact of the operating, controlling, alarming and failure conditions of a system

Definitions (Continued)

- Direct Impact
  - A system, change or failure that has, or can have a direct effect on product quality or patient safety
- Indirect Impact
  - A system, change or failure that has or can have an indirect effect on product quality or patient safety
- No-Impact
  - A system, change or failure that has no effect on product quality or patient safety

Impact Assessment Flowchart



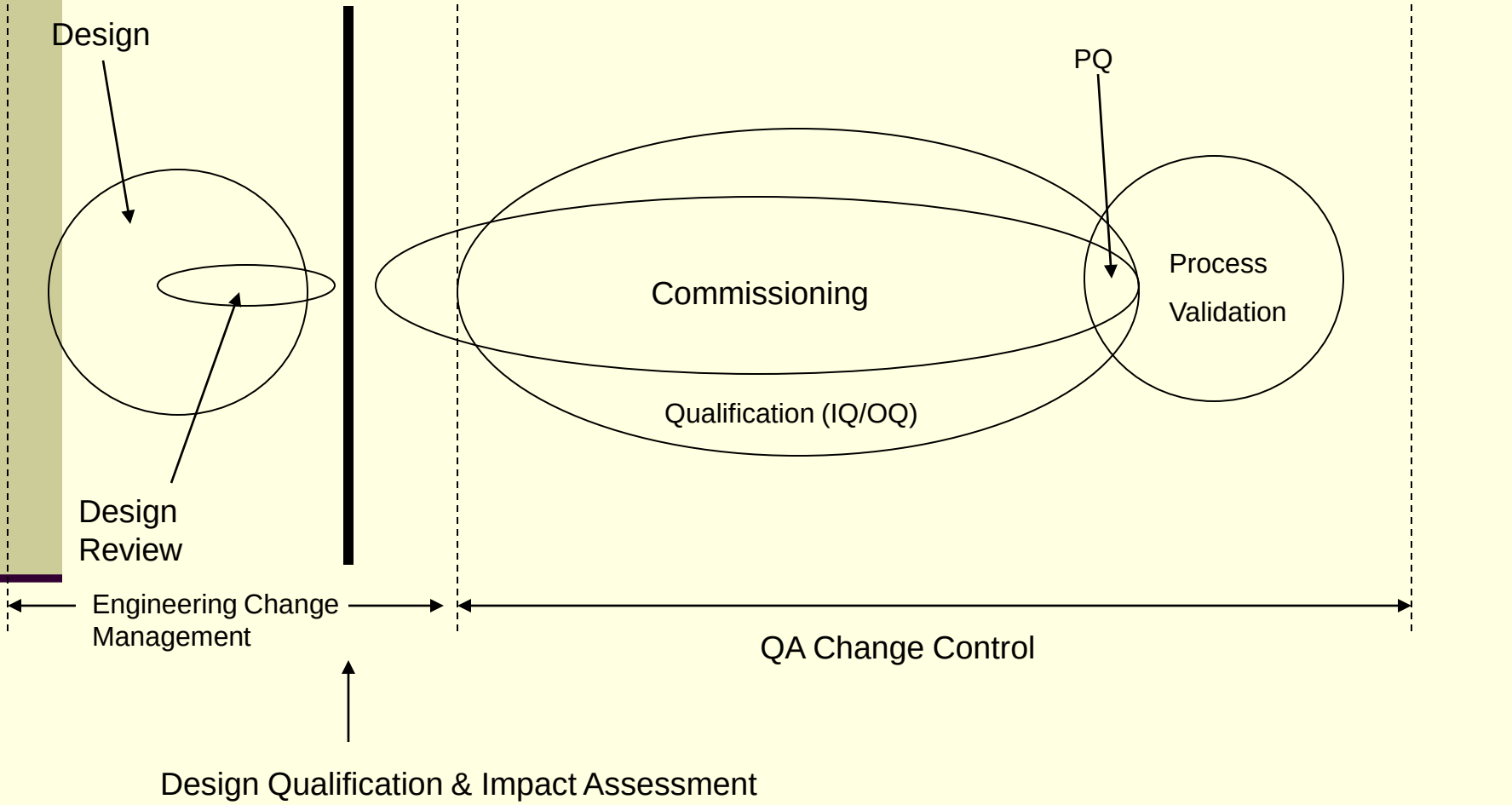
Tools for Criticality Assessment

- Failure Modes and Effects Analysis (FMEA)
- Fault Tree Analysis
- HACCP
- Cause and Effect
- Qualitative
- Quantitative

Where is Impact Assessment Used?

- Design Review
- Change Control
- Adverse Events
  - Deviations or discrepancies
  - Incidents involving system, component or process failure

Designing for Impact



Change Management

- Impact Assessment is a key part of the Change Management process
  - Assists with the defining the change
  - Identifies risk to quality and patient
  - Determines testing/verification of change to assure suitability

Adverse Events

Adverse Events

- Impact Assessment process should be integral in the deviation or discrepancy process to define what happened, determine the root cause and apply corrective and/or preventive action eliminate the go-forward risk

Example for Discussion # 1

- Compressed Air System in a Non-Sterile OSD facility which feeds product contact processes:
  - What are the CQA's?
  - What are the CPP's?
  - What is Direct Impact? Indirect? No Impact?
  - Where would you set the system boundaries?
  - What would the challenge strategy be?

Potential Answers for Example # 1

- Compressed Air System in a Non-Sterile OSD facility which feeds product contact processes:
  - What are the CQA's?
    - Cleanliness of the CA only at the product contact areas, usually Viable particle, oil mist and non-viable particulate IAW ISO standards
  - What are the CPP's?
    - Pressure dew point
  - What is Direct Impact? Indirect? No Impact?
    - Direct Impact: Final filters, dew point monitoring
    - Indirect: Primary filtration, dryers
    - No Impact: Anything upstream of primary filtration
  - Where would you set the system boundaries?
    - Around direct impact components
  - What would the challenge strategy be?
    - Verify monitoring equipment, dryers and filtration
    - Recurring CA testing

Example for Discussion # 2

- HVAC system supplying a Non-Sterile OSD processing room (manufacturing or packaging)
  - What are the CQA's?
  - What are the CPP's?
  - What's Direct Impact? Indirect? No Impact?
  - Where would I set the system boundaries?
  - What would the challenge strategy be?

Potential Answers for Example # 2

- HVAC system supplying a Non-Sterile OSD processing room (manufacturing or packaging)
  - What are the CQA's?
    - Room air cleanliness
    - Room T&RH conditions
    - Room pressurization control
  - What are the CPP's?
    - HVAC filter selection and DP
    - HVAC Leaving Air Temperature
    - Room pressurization control
  - What's Direct Impact?
    - HVAC AHU and distribution ducting
    - T&RH monitoring equipment
  - Where would I set the system boundaries?
    - Around AHU, excluding utilities like steam, HHW, electric, CHW, clean-steam for humidification, BAS, etc.
  - What would the challenge strategy be?
    - Verify direct impact equipment, commission utilities, recurring room air quality testing