Best practices for Process Validation

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- ✓Define Validation
- ✓Discuss Validation Requirements
- ✓Define Risk
- ✓Discuss Validation Pre-Requisites
- ✓Discuss the Validation Life Cycle
- ✓Discuss Common Validation Issues

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“Validations are akin to scientific investigations in which the hypotheses are formulated, experiments are designed and conducted, data are collected and analyzed, and conclusions are reached.

And like scientific discoveries, validations must be questioned and retested for the life of the process they cover.”

D.M Carlberg

Carlberg, D.M., 2005, Cleanroom Microbiology for the Non-Microbiologist 2nd Ed., CRC Press, New York.

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Validation Requirements

The importance of validating readily apparent in FDA regulations, ISO standards, and GHTF guidance documents

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Definitions

- *"Establish"* means define, document (in writing or electronically), and implement
- “can” indicates a possibility or a capability
- “should” indicates a recommendation
- “shall” indicates a requirement
- “may” indicates a permission

Validation Activities

- ✓ Commissioning
- ✓ Installation Qualification (IQ)
- ✓ Operational Qualification (OQ)
- ✓ Performance Qualification (PQ)
- ✓ Process Performance Qualification (PPQ)

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QSR Requirements

820.75 Process Validation

"Where the results of a process cannot be fully verified by subsequent inspection and test, the process shall be validated with a high degree of assurance and approved according to established procedures"

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QSR Requirements

820.250 Statistical Techniques

"Where appropriate, each manufacturer shall establish and maintain procedures for identifying valid statistical techniques required for establishing, controlling, and verifying the acceptability of process capability and product characteristics.

Sampling plans, when used, shall be written and based on a valid statistical rationale"

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QSR Requirements

820.70 Production and Process Controls

"Each manufacturer shall develop, conduct, control, and monitor production processes to ensure that a device conforms to its specifications"

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Guidance Documents

GHTF - Quality Management Systems - Process Validation Guidance

FDA - Process Validation: General Principles and Practices

FDA - General Principles of Software Validation

http://www.imdrf.org/docs/ghtf/final/sg3/technical-docs/ghtf-sg3-n99-10-2004-qms-process-guidance-04010.pdf

http://www.fda.gov/downloads/Drugs/Guidances/UCM070336.pdf

http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm085281.htm

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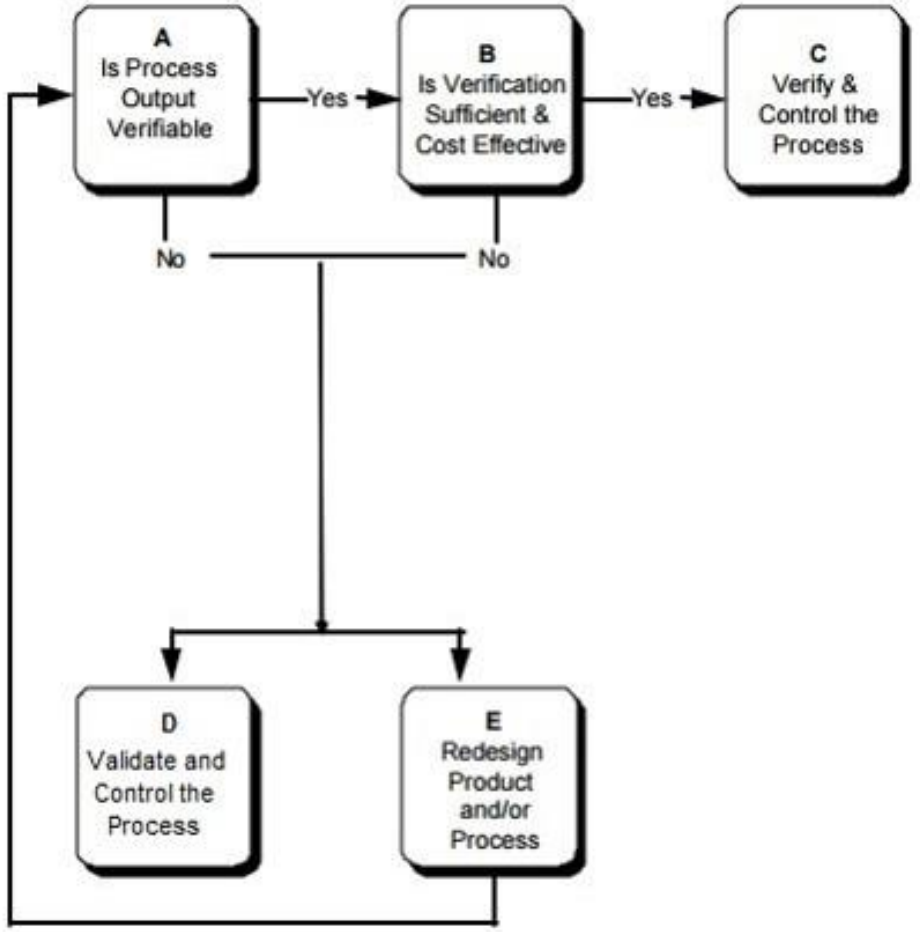
GHTF Process Validation Decision Tree



Adapted from GHTF Study Group 3
Quality Management Systems Process Validation Guidance
January 2004

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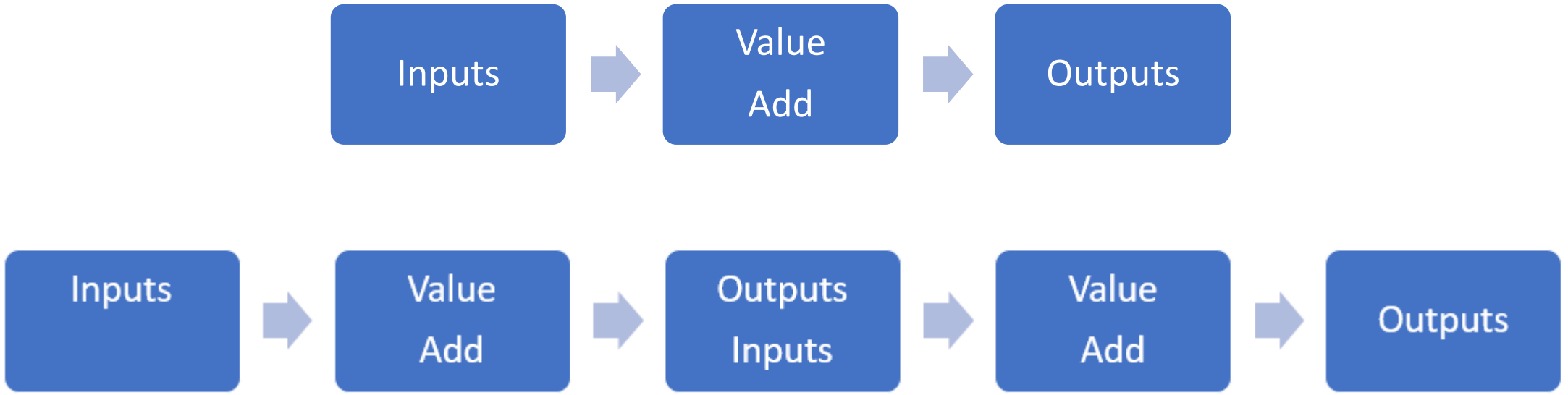
Process and System Validation

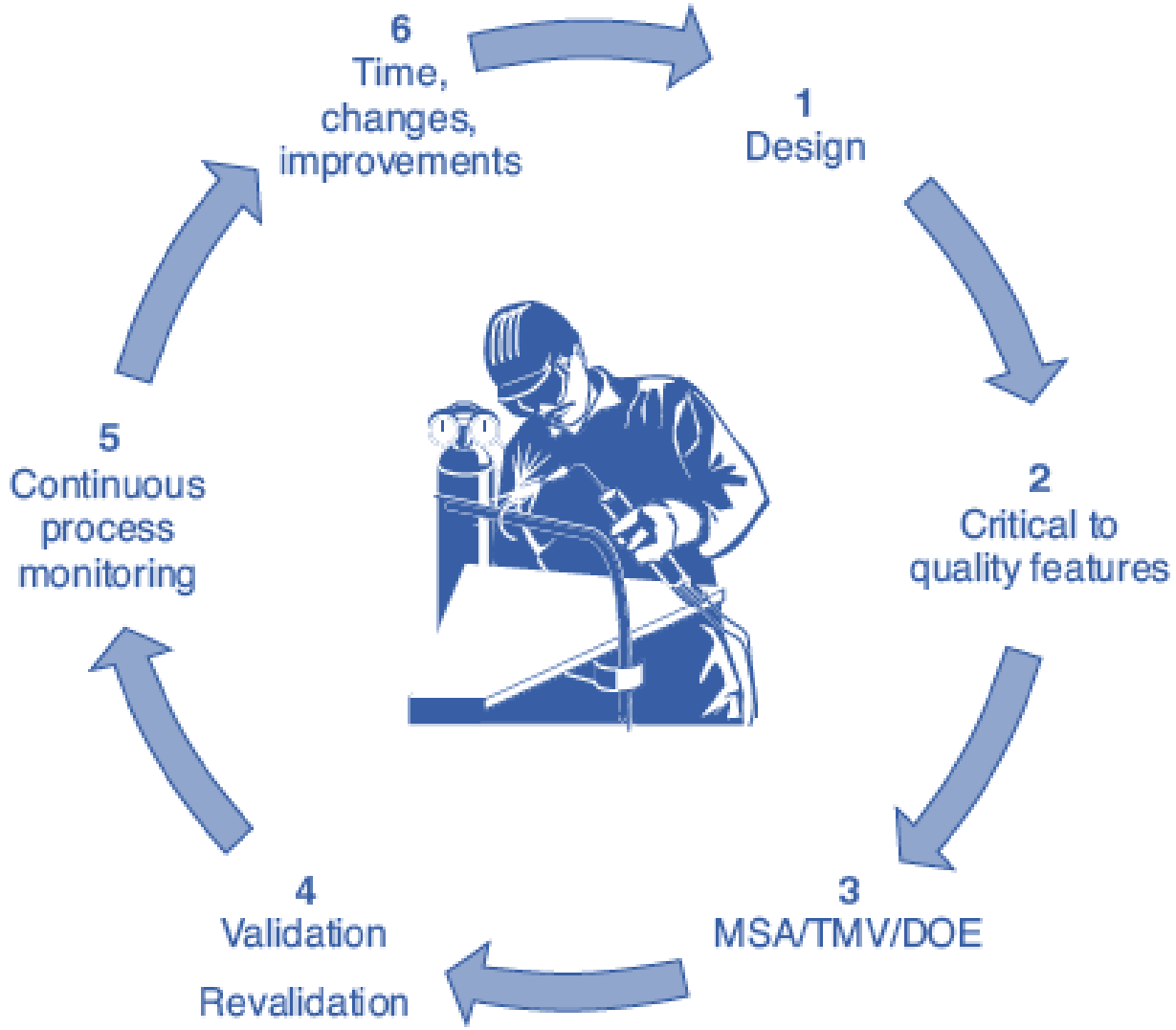



iDENTiFY
ASSESS
ANALYZE
RiSK
MANAGEMENT
REDUCE
CONTROL
TRANSFER

Validation Prerequisites

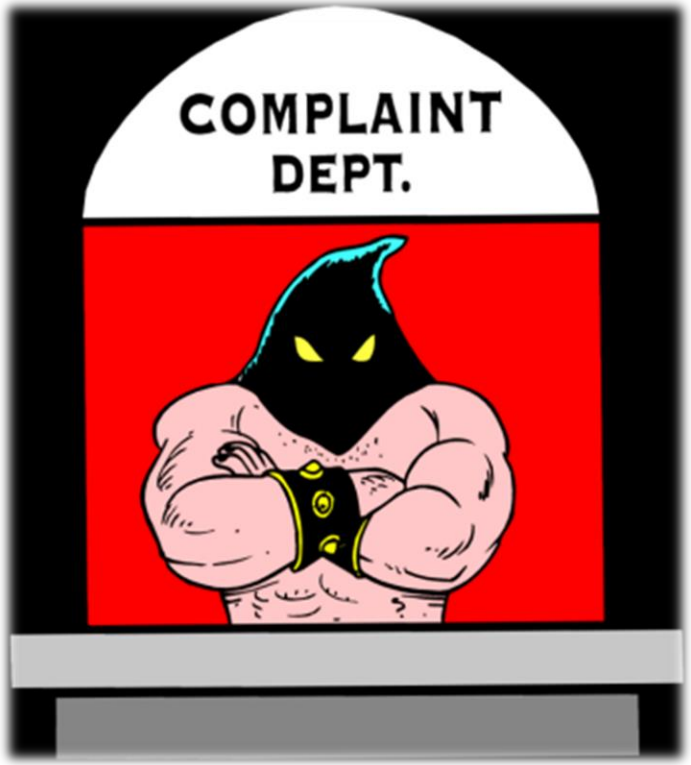
The Process Validation Life Cycle

May 31-June 1, 2017



Source: Durivage, M.A. and Mehta B., 2016, *Practical Process Validation*, Milwaukee, ASQ Quality Press

Retrospective and Re-Validation Activities



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Retrospective Validation

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Re-Validation Activities

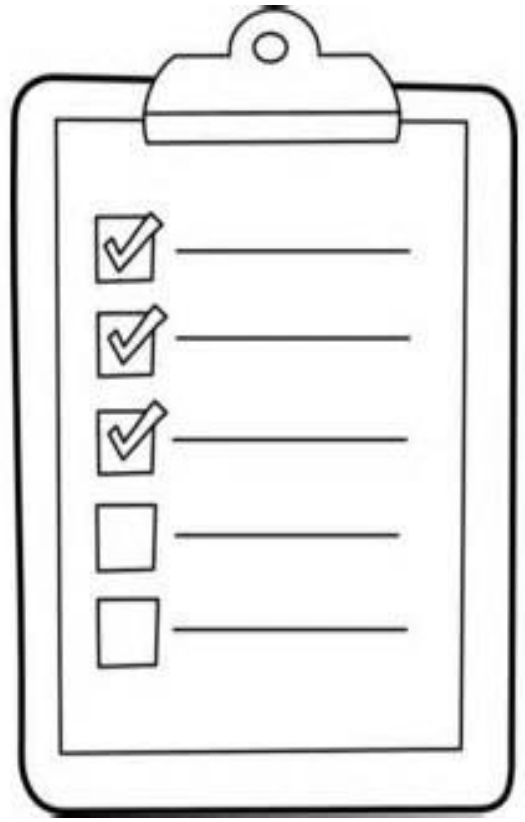
May 31-June 1, 2017

FDA Warning Letters Summary (Validation)

- Missing rationale for the comparison of data from old and new PQ runs
- Failure "maintaining the process in state of control"
- Missing "root cause analysis" as required in the validation plan for evaluating inadequate results
- Missing rationale for the number of PQ runs
- Arbitrary sampling plan

Source: http://www.gmp-compliance.org/eca_news_2025_6374,6246,6247,6418.html

Common Validation Issues



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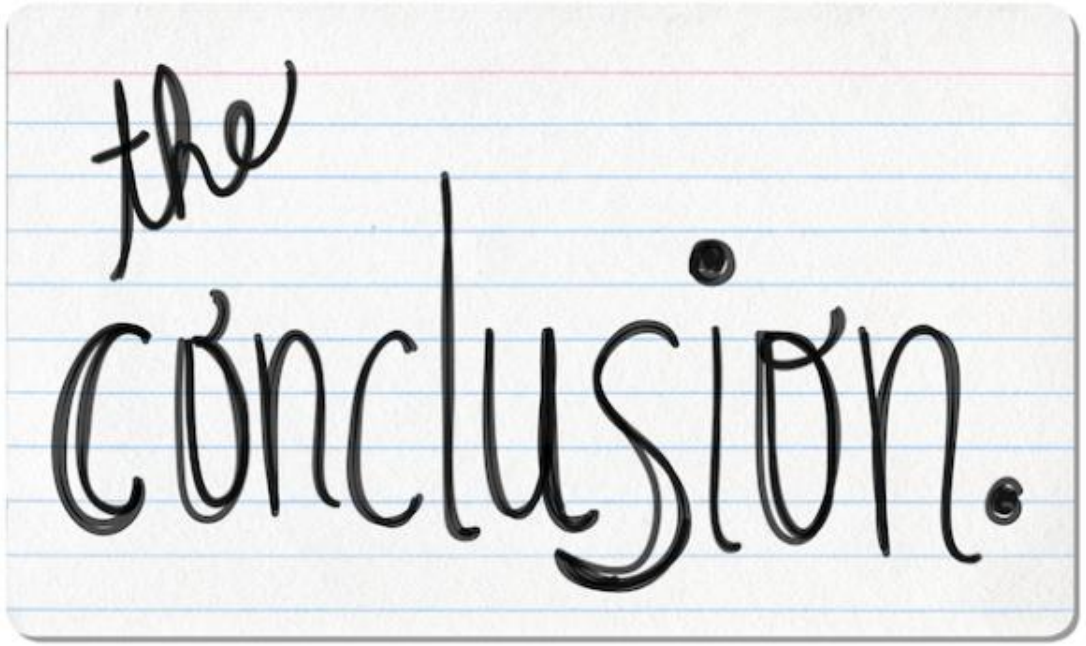

- Use a Risk-Based Statistical Rationale
- Keep Apprised of Current Industry Trends
- Under Promise – Over Deliver on Validation Commitments
- Perform Continuous Process Monitoring
- Document Your Plan, Actions, and Results

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Questions

THANK YOU!

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