

Validating a Clinical Data Management System: A Practical Guide



Matt Ferdock, DataCeutics, Inc.

Presented to the **3rd Annual Validating Clinical Data Management**
Conference July 27-28, 2000 - Park Hyatt, Philadelphia, PA
Sponsored by the Institute for International Research



Agenda

- Introductions
- Dictionary/Background
- Methodology
- SDLC Tie-in
- Regulations Tie-in
- Examples
- Ongoing



Introductions

- DataCeutics
 - Founded 1993
 - Leader in Clinical Systems Validations
 - Experts in 21 CFR 11 Assessments
 - Leader in cGCP SOP writing
 - Clinical Systems Experts (SAS, Oracle Clinical, Documentum)



Speaker

- Matt Ferdock
 - President, DataCeutics, Inc.
 - 15 Years' Experience in Health Research
 - Last 11 years spent in Rx industry
 - Managed or Performed 30+ CSVs
 - Expert in Corporate 21CFR11 Compliance Strategies



Validation Methodology

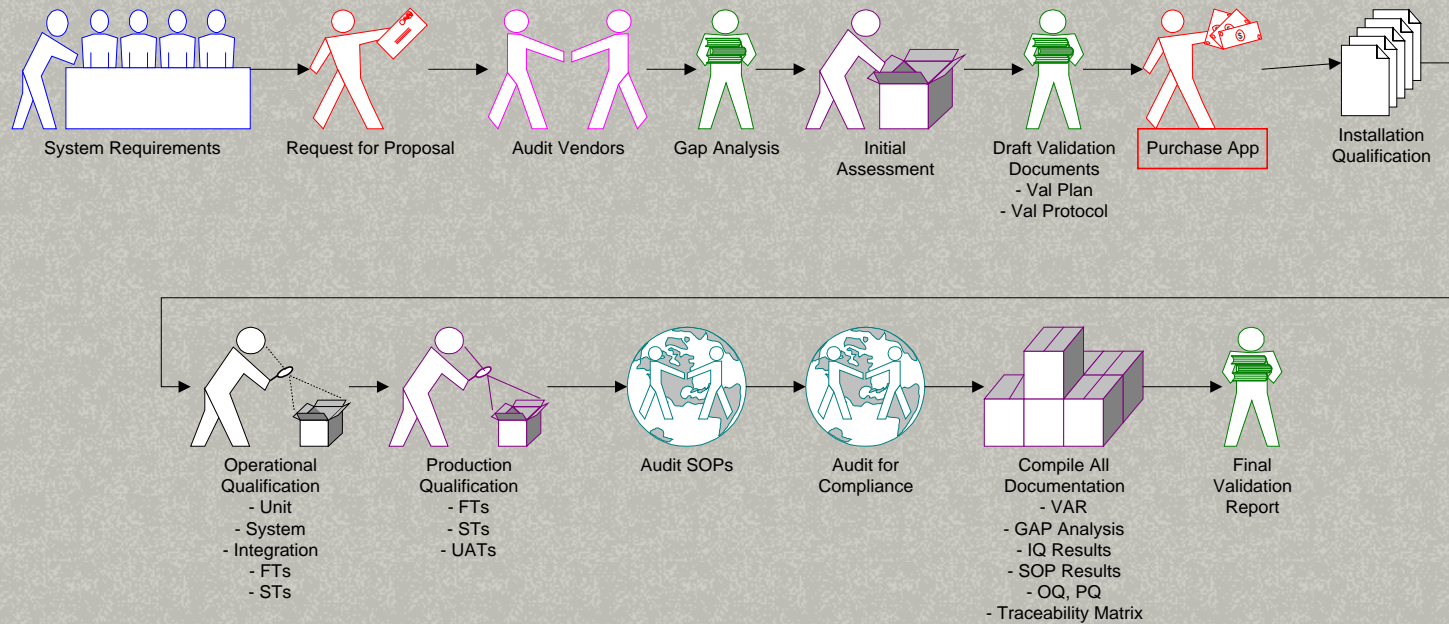


07/28/2000

Copyright 2000 by DataCeutics

5

Validation Methodology





Validation Dictionary





Validation Dictionary

- **Key terms** (refer to The Validation Dictionary, by the Institute for Validation Technology, 1998; “A Globally Harmonized Glossary of Terms for Communicating Computer Validation Key Practices”, Pharmaceutical Manufacturers Journal, ##, ##)
 - Systems Validation is *establishing evidence that a computer system does what it purports to do and will consistently do so in the future.*
 - Validation Committee is *A cross-functional group of qualified individuals representing each major division in a company (including business area representatives, QA, R&D) that is assembled to review, evaluate and approve all Validation activities.*



Validation Dictionary (cont.)

- Validation Plan is *The collection of activities that include, and are specifically related to, computer system validation itself.*
- Validation Protocol is *2) A prospective experimental plan that, when executed, is intended to produce documented evidence that a system has been validated.*





Validation Dictionary (cont.)

- Installation Qualification (IQ) is 2)
Establishing the documentary evidence that a sub-system or equipment is installed in compliance with the technical specifications.... 3)
Documented evidence that all key aspects of hardware installation adhere to appropriate codes and approved design intentions and that the recommendations of the manufacturer have been considered.





Validation Dictionary (cont.)

- Operational Qualification (OQ) is *The documented evidence that the equipment/system performs per design criteria over all defined operating ranges.* OQ is typically performed in developmental areas on developmental computers.





Validation Dictionary (cont.)

- Performance Qualification (PQ) is *Documented verification that equipment, systems or processes operate the way they are purported to do. This operation must be reliable and reproducible within a specified, pre-determined set of parameters, under **normal production** conditions and must be in a State of Control (sic).*





Validation Dictionary (cont.)

- Prospective Validation is *Establishing evidence that a system does what it purports to do based on a written and approved, preplanned protocol. The validation is performed prior to the manufacture of clinical or marketable product, and the product is not sold until equipment, system and process meet the validation acceptance criteria.*





Validation Dictionary (cont.)

- Retrospective Validation is *Establishing documented evidence that a system does what it purports to do based on a review and analysis of historical data and information obtained during the production of clinical or marketable product.*





Validation Dictionary (cont.)

- Revalidation is *The repetition of the Validation sequence, or a specific portion of it, to assure that the system is suitable for use after modification, repair or maintenance that could alter the product characteristics or performance. Revalidation is also required periodically (e.g. annually) on critical processes even if modifications or repairs are not made. This is done to insure that the process or system is not undergoing some subtle undetectable changes or degradation.*





Validation Dictionary (cont.)

- Test Case is *A specific set of test data and associated procedures for a specific objective.*
- Validation Change Control is *A formal monitoring procedure during which qualified members of a Validation Committee review the affect of proposed or actual changes on the manufacturing process to determine the impact on the Validation status. These representatives may initiate corrective action to restore the system to a validated state.*





Validation Dictionary (cont.)

- Final Report is *A document summarizing the results derived from the execution of a protocol. The final report shall include a conclusion, which indicates validation success or failure and designates proven acceptable ranges for all critical process parameters as determined by the execution of the Validation Protocol.*





Validation Dictionary (cont.)

- Validation Capability/Maturity Model (refer to The Capability Maturity Model: Guidelines for Improving the Software Process, Carnegie-Mellon University, Paulk, M ed., 1995.) is *A model used to describe the level of knowledge of Validation.*
 - Level 1 - Validation Unaware: No knowledge of the Theory of Validation
 - Level 2 - Validation Aware: Basic knowledge of the Theory of Validation
 - Level 3 - Validation Active: Forced to participate by regulation or customer demand
 - Level 4 - Validation Enthusiast: (aka masochist) Experienced in practice, recognizing the benefits and limitations and encouraging others to participate.





Validation Methodology

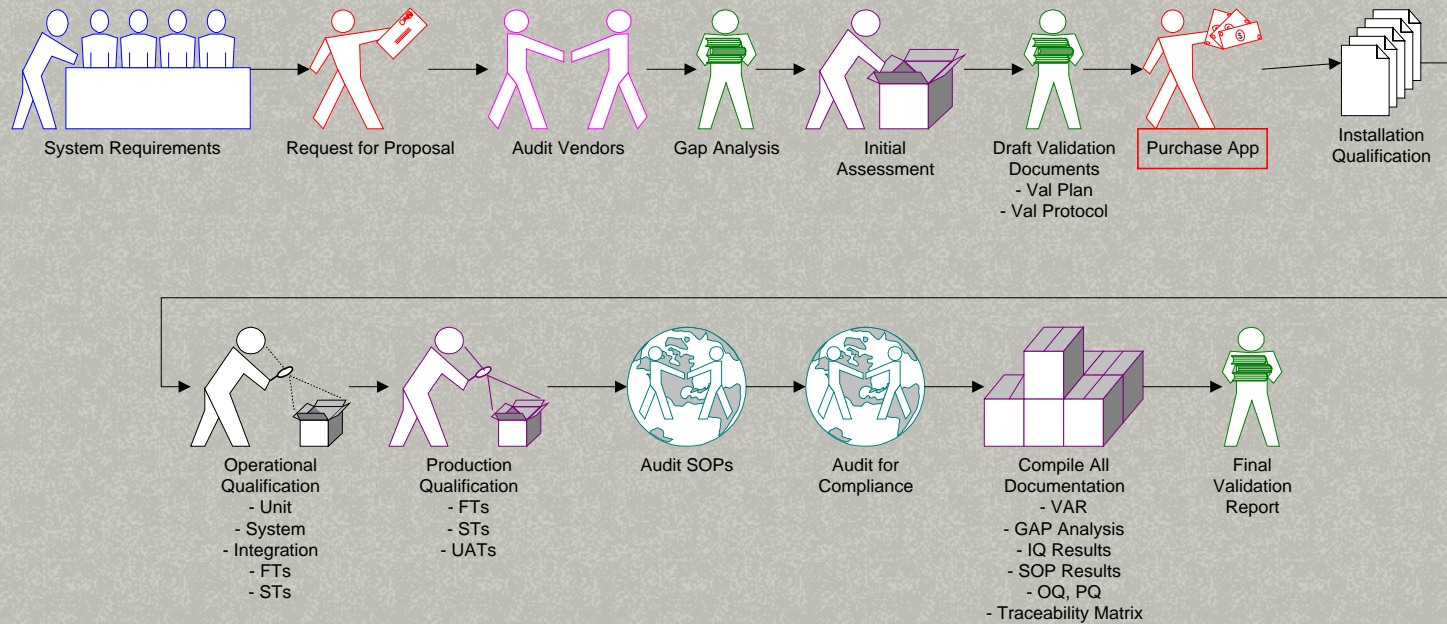


07/28/2000

Copyright 2000 by DataCeutics

19

Validation Methodology

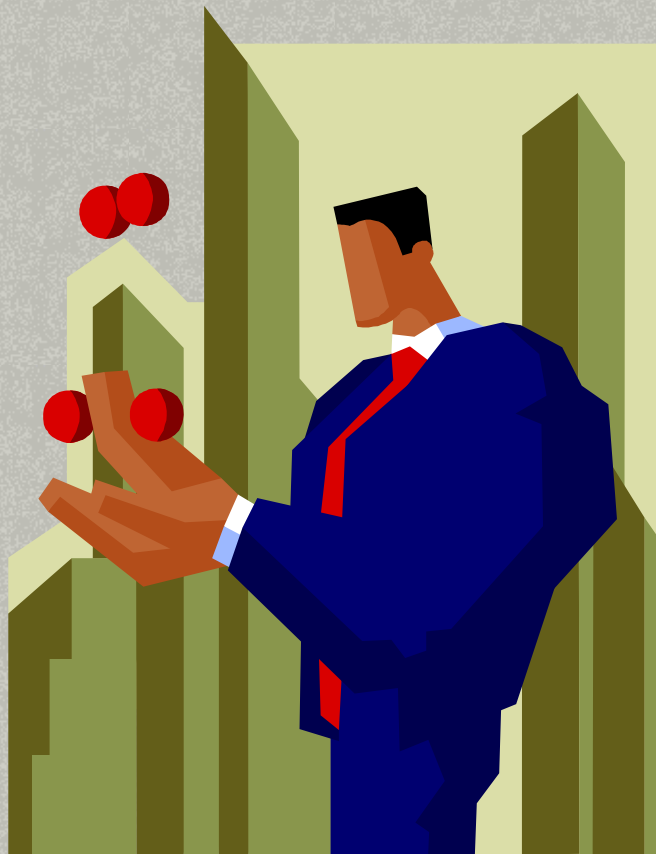


Requirements



- First part of SLC
- Business Need
- Affected Areas
- Rationale
- May assess costs & Impact

RFP



- Developing in-house
- Buying
- Send RFP

Vendor Audit

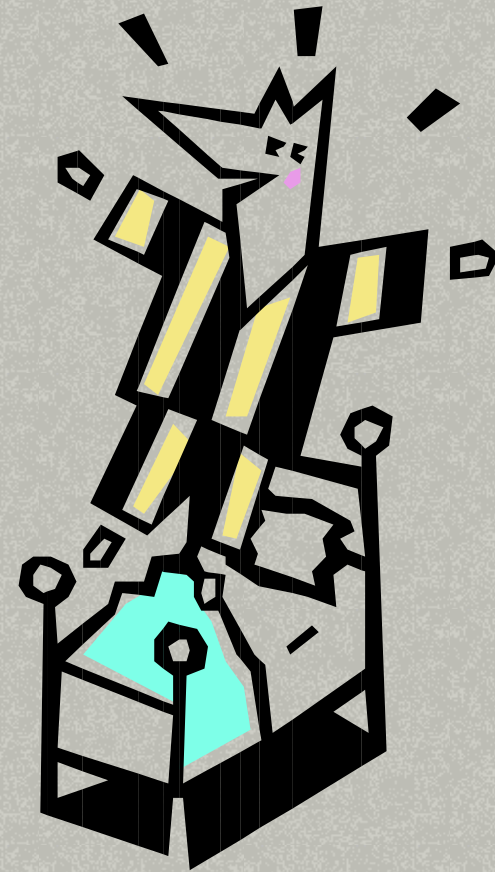
- Is vendor stable?
- How long in business?
- Do they follow an SLC?
- Are their people trained?
- Is their process documented?
- Have they built compliance into their software?





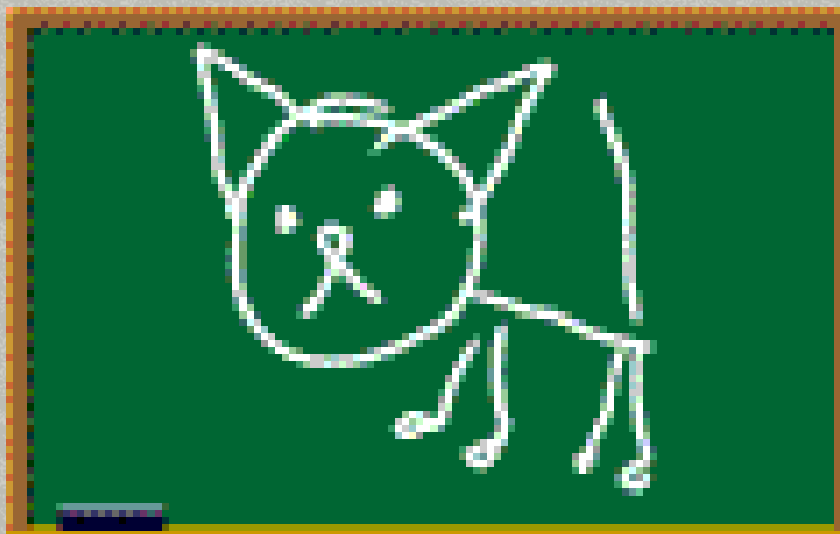
GAP Analysis

- Where does the app fall short of regs?
- Where does it fall short of your requirements?
- Either VETO vendor OR write a GAP Analysis
- How will you close the Gaps?
- Do you need to develop an audit trail, etc?





Initial Assessment

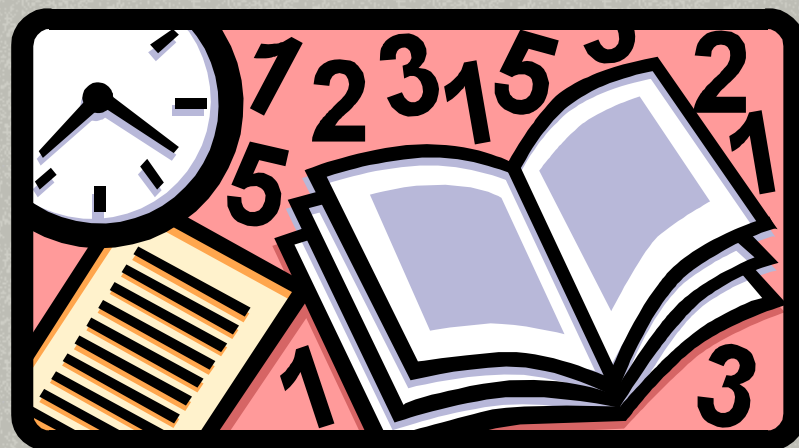


- Determine early on where your business and support groups are with SOPs?
- Does your group understand the regs?
- Is there a cGCP Validation SOP?
- Does IT have documented processes?
- Is the computer room qualified?
- Where are your SOPs?
- What process will you follow to develop OR purchase an App?
- How will you validate it?



Validation Documents

- Validation Plan
 - High Level
 - Contains Timeline
- Validation Protocol
 - Specific Areas
 - Purpose
 - Evaluation Method
 - Acceptance Criteria





Purchase Application

- Contact vendor
- Initiate Software development





Installation Qualification



- IQ Server
- IQ Middle Tier
- IQ PC
- IQ Server OS
- IQ Middle Tier OS
- IQ PC OS
- IQ RDBMS or back end
- IQ Middle Tier of App
- IQ Client
- Document that the system was installed according to vendor requirements

Operational Qualification



- Tests done in a development environment
- Unit
- System
- Integration
- Functional
- Boundaries/Stress
- Document that the system performs as expected



Production Qualification

- Testing done in a Production Environment
- May include
 - Functional Tests
 - User Acceptance Tests
 - Stress Tests
- Must demonstrate each requirement has been met and follows SLC through SOP & normal usage
- Traceability Matrix



Audit of all Relevant SOPs



- Are all business & support areas fully documented
- Are details adequate
- Document that users have been trained
- Document that users are following them
- Are they compliant

Is system Compliant?

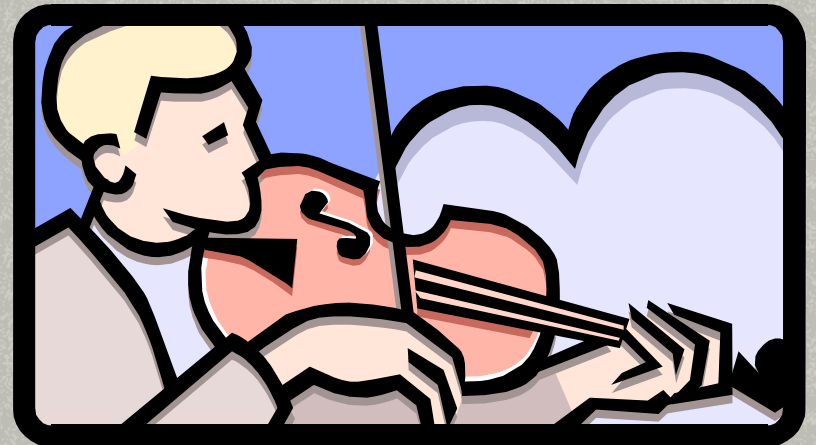


- Apply 21 CFR 11 Checklist
- Document where the system is and where the system is not compliant
- Have a written plan for bringing it inot compliance



Compile all Documentation

- Requirements
- RFP
- VAR
- IQs
- OQ/PQ
- SOP Audit
- 21 CFR 11 Audit
- GAP Analysis
- Traceability Matrix





Final Validation Report



- System is ready for production when:
 - Compliance has been addressed
 - All supporting documentation is complete
 - Your next review is due



System Life Cycle Tie-ins

- Requirements
- RFP
- Functional Specifications
- Design Specifications
- Unit, System, Integration, Functional Testing
- IQ
- Training
- OQ/PQ



Regulatory Tie-ins

- System in order to be in compliance with 21 CFR 11 must:
 - ❖ Have an audit trail
 - ❖ Make accurate and complete copies of records
 - ❖ Provide security
 - ❖ Users must be trained
 - ❖ System must be documented
 - ❖ Does system enforce step sequencing?



Ongoing

- How to Maintain Validated State
 - Keep documentation on all systems upgrades
 - Hardware & Software
 - Perform Training regularly
 - Audit SOPs at least annually
 - Amend Validation Documents as needed
 - Assign a Resource