Welcome

Computer System Validation Training Delivered to FDA

ISPE – Boston Area Chapter
February 20, 2014

ISPE®

Background

- **Training Conducted on April 24, 2012**
- **Food & Drug Administration**
  Division of Manufacturing & Product Quality
  Rockville, MD
- **20-30 General Inspectors**
- **Range of Experience and Background**

Training Agenda

- **CSV Fundamentals**
- **Data Integrity Considerations**
- **Electronic Batch Record Requirements**
- **Emerging Technologies**

CSV Fundamentals

- **Review of Guidance Documentation**
- **21 CFR Part 11 Guidance on Enforcement**
- **System Validation Objectives**
- **System Life Cycle Approaches**
- **GAMP®5 & ASTM E2500 Risk Assessment**

Regulatory Guidance

- **Relevant Regulations**
  - **21 CFR Part 11 (Electronic Records; Electronic Signatures)**
  - **Predicate Rules (21 CFR Part 211, 820, 58)**
  - **Eudralex 4 Annex 11**
- **Guidance to Industry**
  - **General Principles of Software Validation,**
  - **Computer Systems**
  - **Electronic Source Documentation,**
  - **Off-the-Shelf Software**
  - **Cybersecurity**

21 CFR Part 11 e-Records

- Validation of Systems
- Generate Accurate and Complete Copies
- Protection of Records
- Limit Access to Authorized Individuals
- Secure Audit Trails
- Operational System Checks (Sequencing)
- Authority Checks
- Device Checks
- Qualification of Resources
- E-Sig Policies
- System Documentation Controls
  - Distribution, Access, Use
  - Revision and Change Control

21 CFR Part 11 e-Signatures

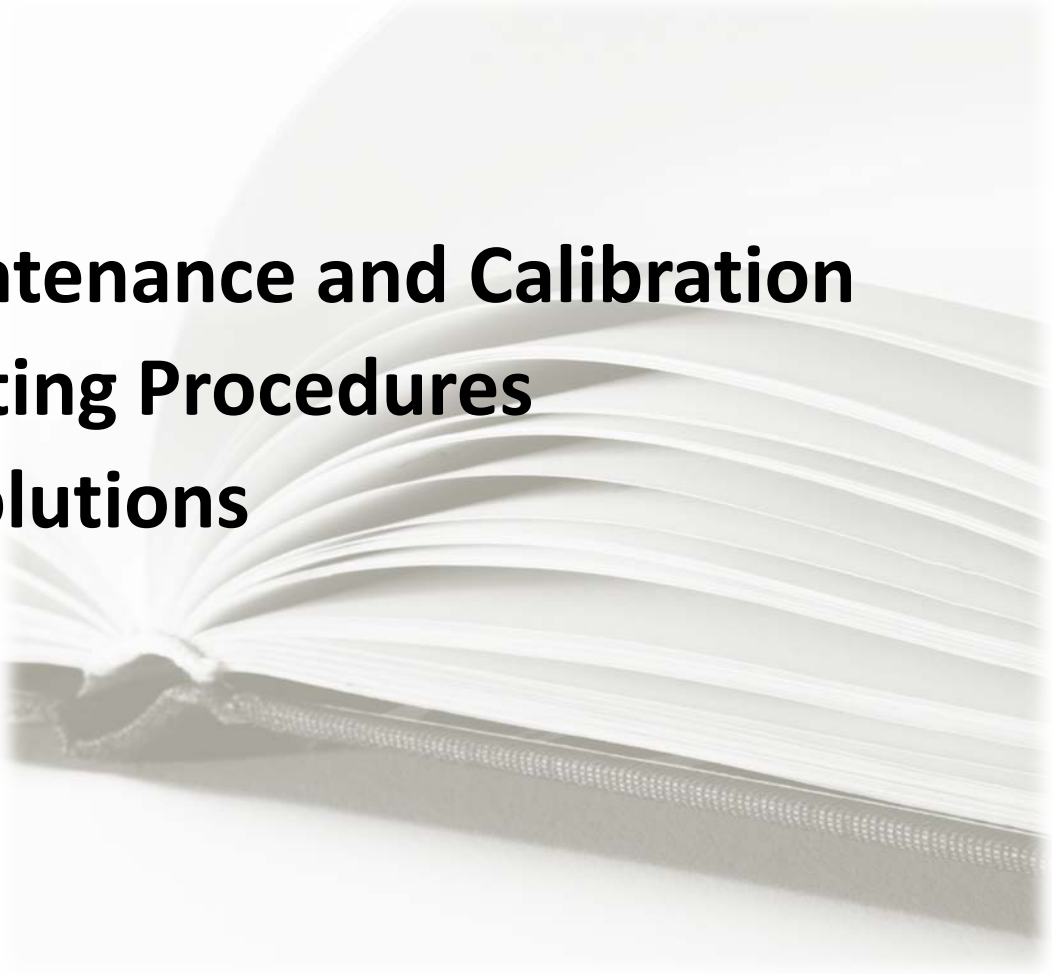
- **Clear Indication Of:**
  - **Printed Name of Signer**
  - **Date and Time of Signature Execution**
  - **Meaning Associated with Signature**
  - **Items Subject to Same Controls as E-Records**
  - **Included as Part of Human Readable Form of Electronic Record**
- **Signatures Linked to Electronic Records**
- **Signature Cannot be Excised, Copied or Otherwise Transferred**

Guidance on Part 11 Enforcement

- **Part 11 will be interpreted narrowly; we are now clarifying that fewer records will be considered subject to part 11**
- **For those records that remain subject to part 11, we intend to exercise enforcement discretion with regard to part 11 requirements for validation, audit trails, record retention, and record copying in the manner described in this guidance and with regard to all part 11 requirements for systems that were operational before the effective date of part 11 (also known as legacy systems)**
- **We will enforce all predicate rule requirements, including predicate rule record and recordkeeping requirements**

GLP –Record Requirements

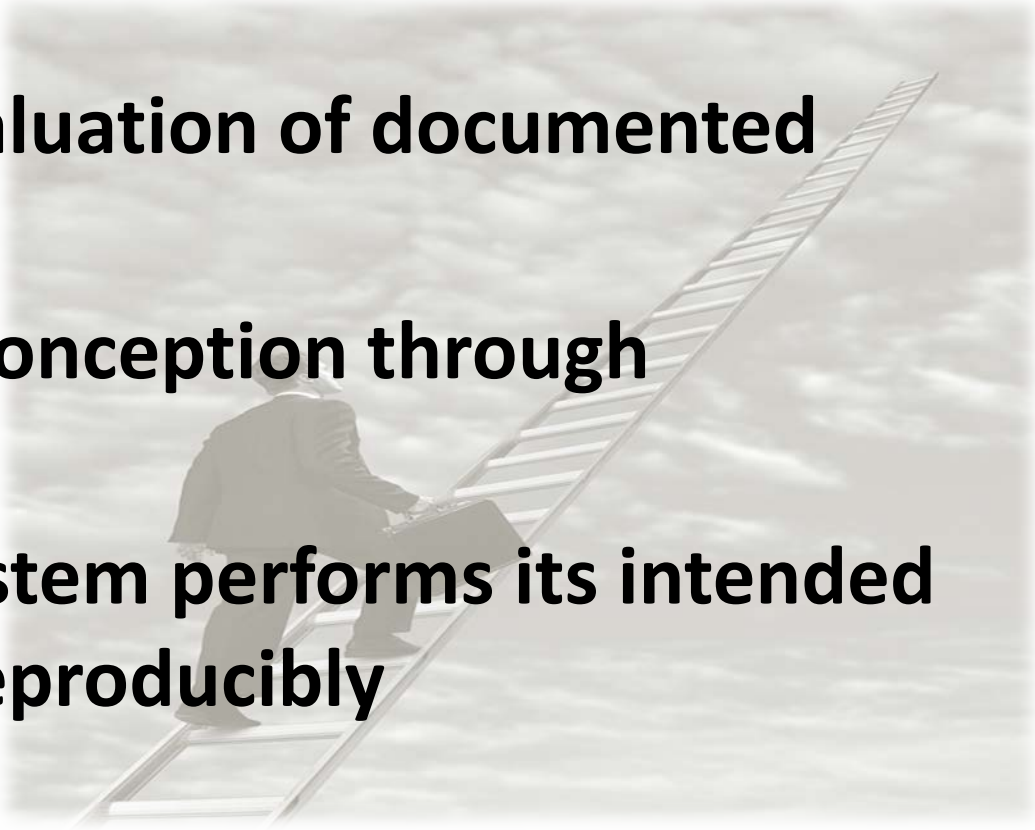
- **Raw Data**
- **Equipment Maintenance and Calibration**
- **Standard Operating Procedures**
- **Reagents and Solutions**
- **Test Results**
- **Animal Care**
- **Study Protocols**



GMP - Predicate Rule Records

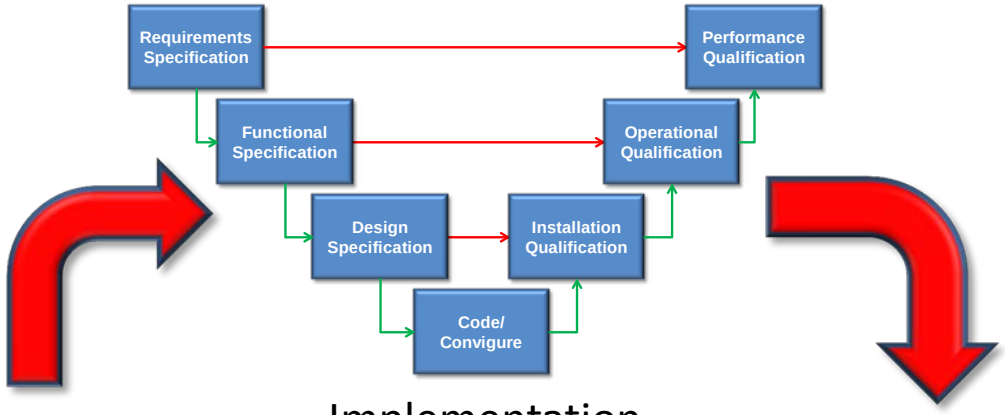
- **Equipment Cleaning and Maintenance**
- **Written Procedures, Deviations**
- **Testing and Approval or Rejection of Components, Drug Product Containers, and Closures**
- **Equipment Identification**
- **Sampling and Testing of In-Process Materials and Drug Products**
- **Calculation of Yield**
- **Charge-in of Components**
- **Materials Examination and Usage Criteria**
- **Drug Product Inspection**
- **Packaging and Labeling Operations**
- **Stability Testing**
- **Reserve Samples**
- **Master Production and Control Records**
- **Batch Production and Control Records**

System Validation Objectives

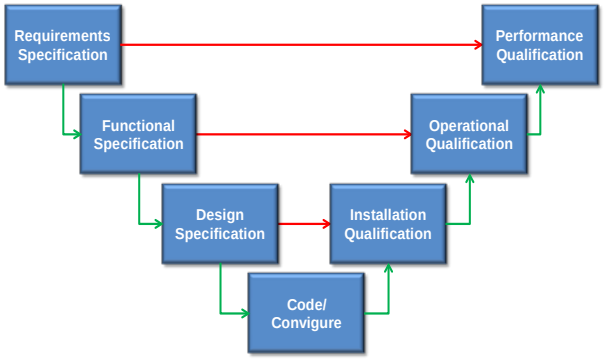


- **Collection and evaluation of documented evidence**
- **Covering system conception through retirement**
- **Demonstrating system performs its intended use reliably and reproducibly**

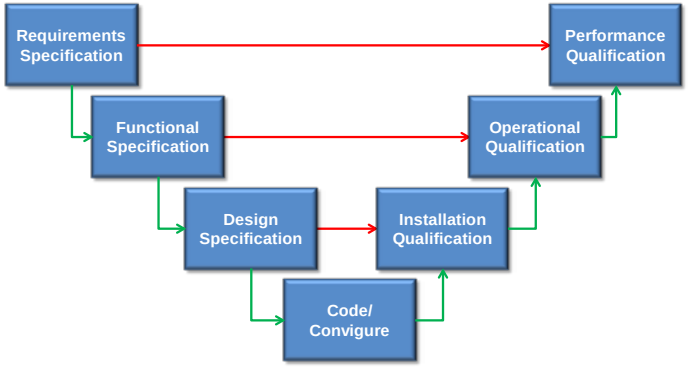
Full System Life Cycle



Implementation



Retirement



New Releases

Common Concepts – GAMP5 and ASTM E2500

- **Decisions are Science and Risk-based**
- **Science Based Quality System**
  - **Focus on Criticality (CQA, CPP)**
- **Product/Process Understanding**
- **Focus on the Patient**
- **Scalable Activities**
- **Good Engineering Practices**
- **Subject Matter Experts**
- **Use of Vendor Documentation**

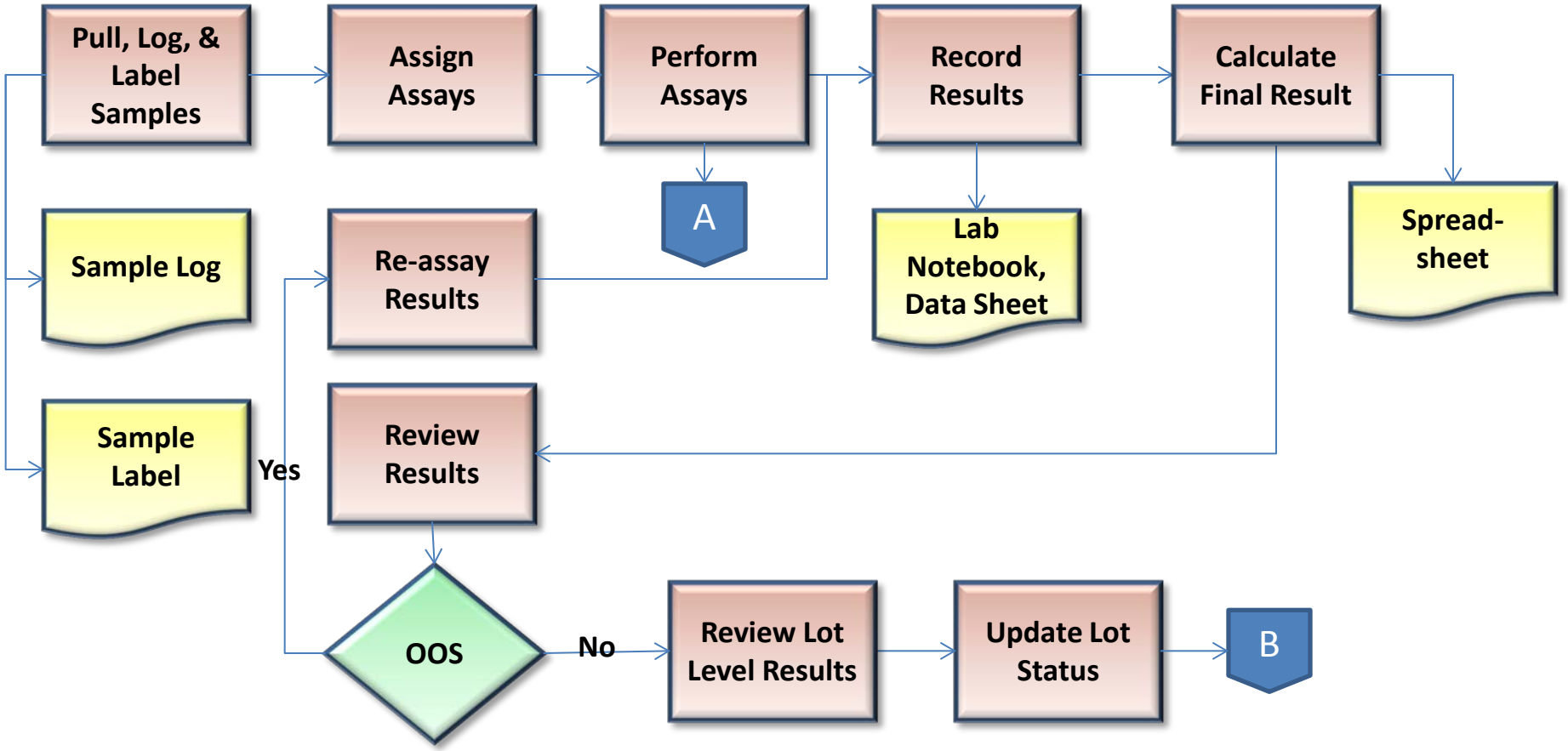
Training Agenda

- CSV Fundamentals
- Data Integrity Considerations
- Electronic Batch Record Requirements
- Emerging Technologies

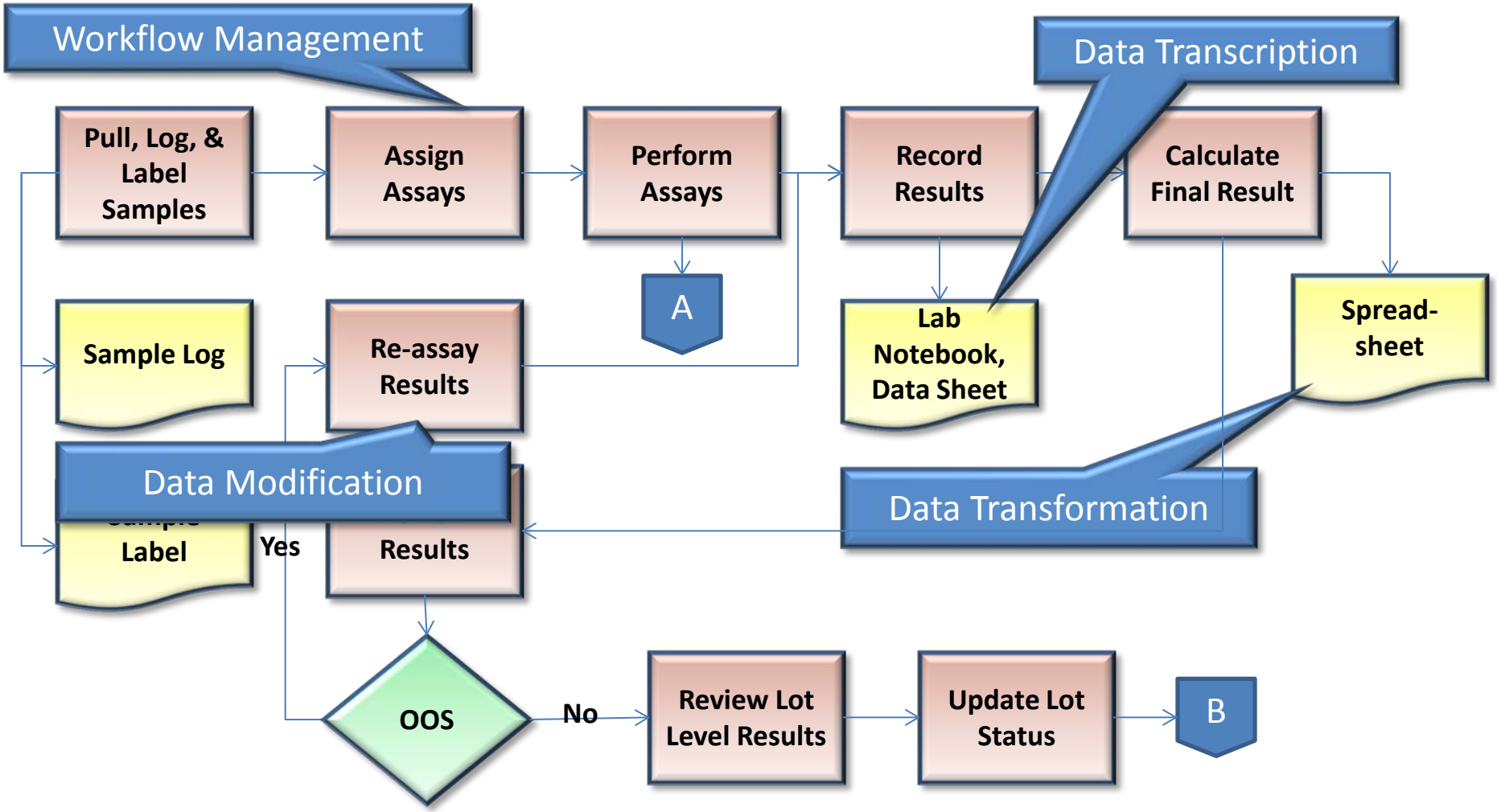
Data Integrity Considerations

- **Sources of Variation in Information Management**
- **Intentional Data Falsification**
- **Accidental Data Loss and Corruption**

Understanding Information Flow

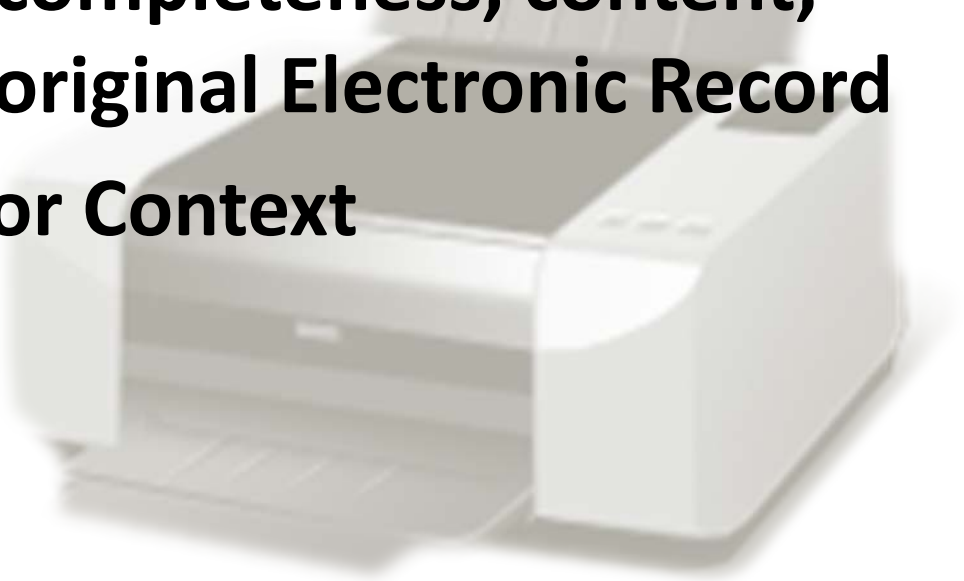


Sources of Variance

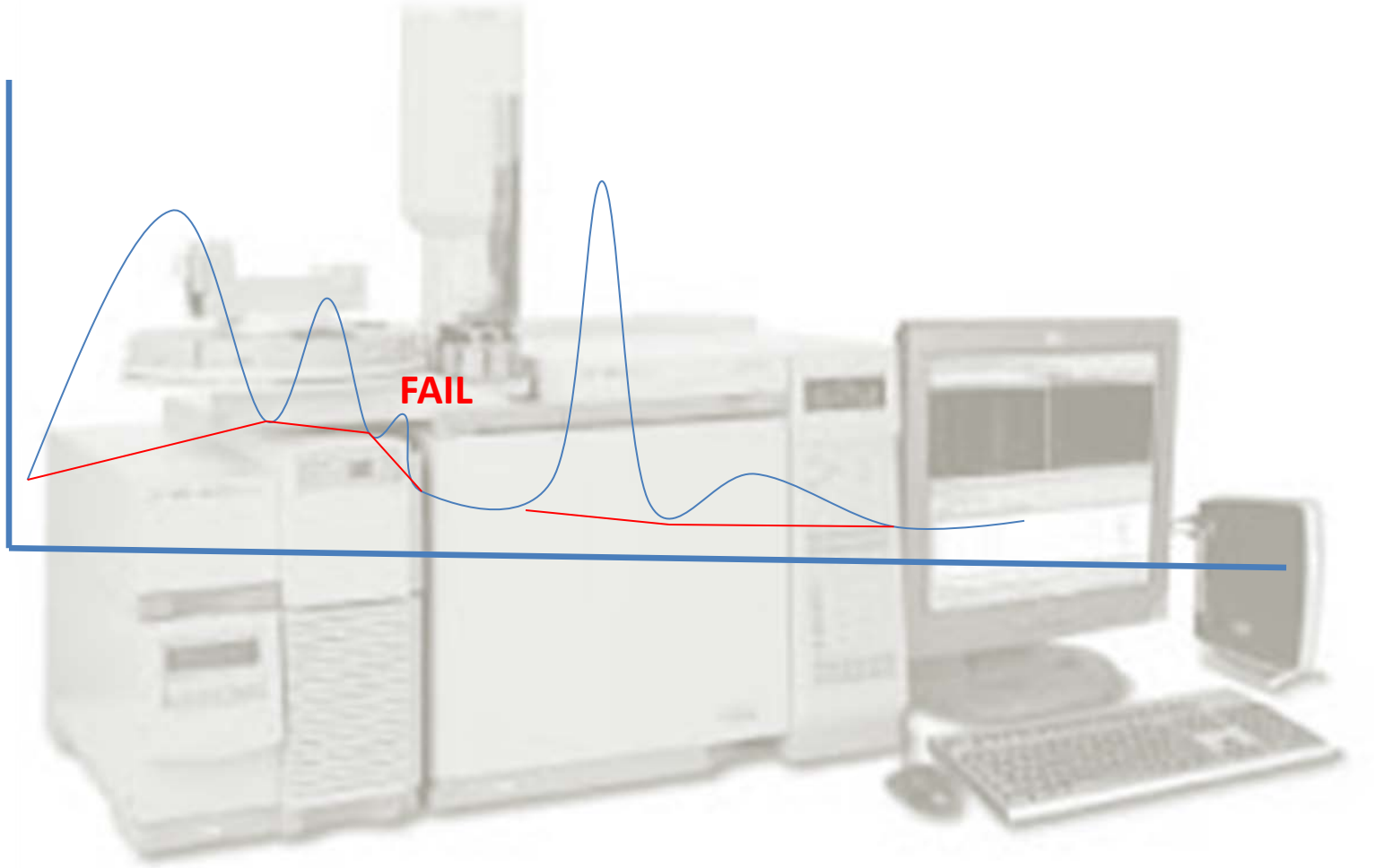


Use of Printed Copies

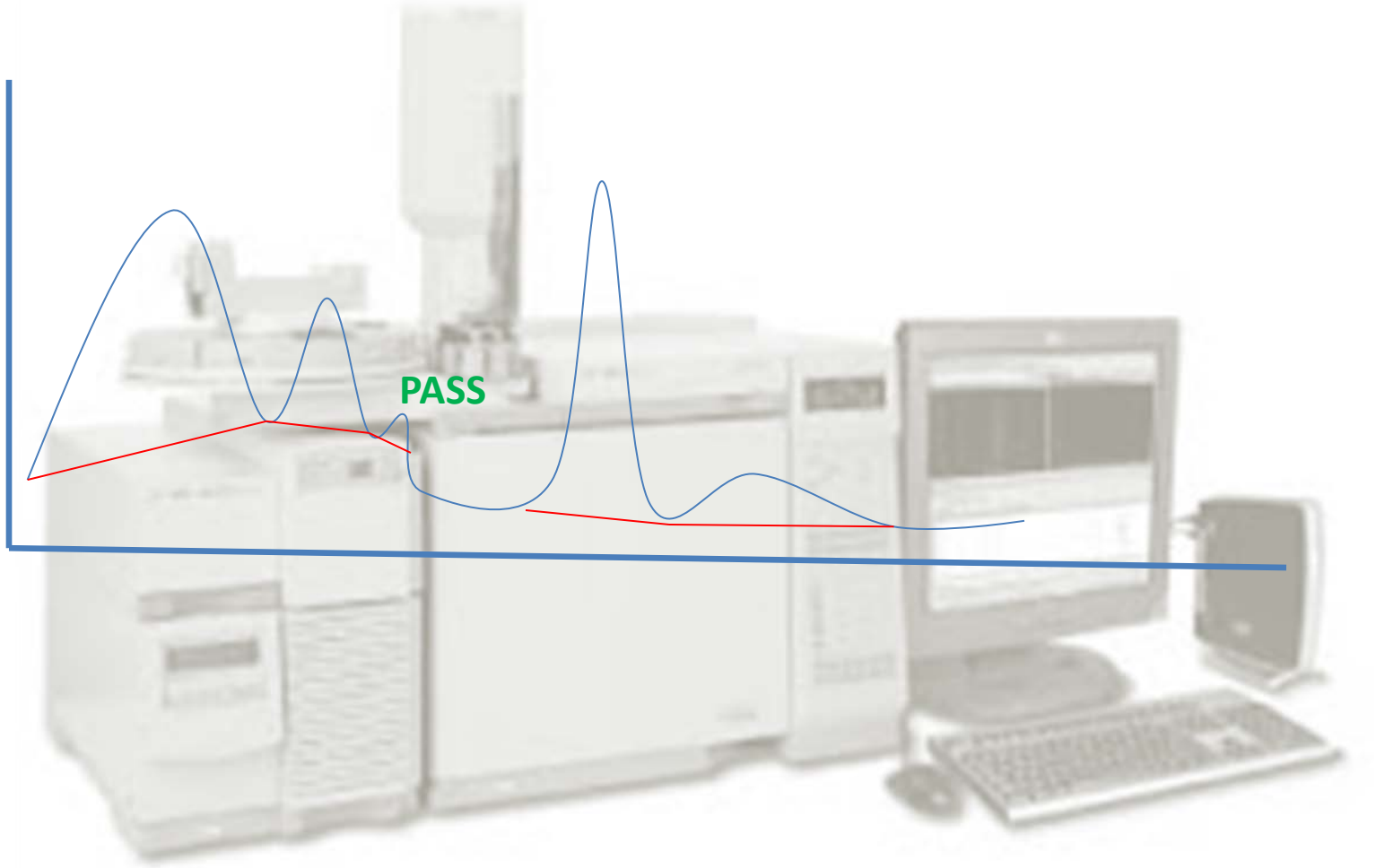
- **When the accuracy, completeness, content, and meaning of the original Electronic Record**
- **Includes Metadata for Context**



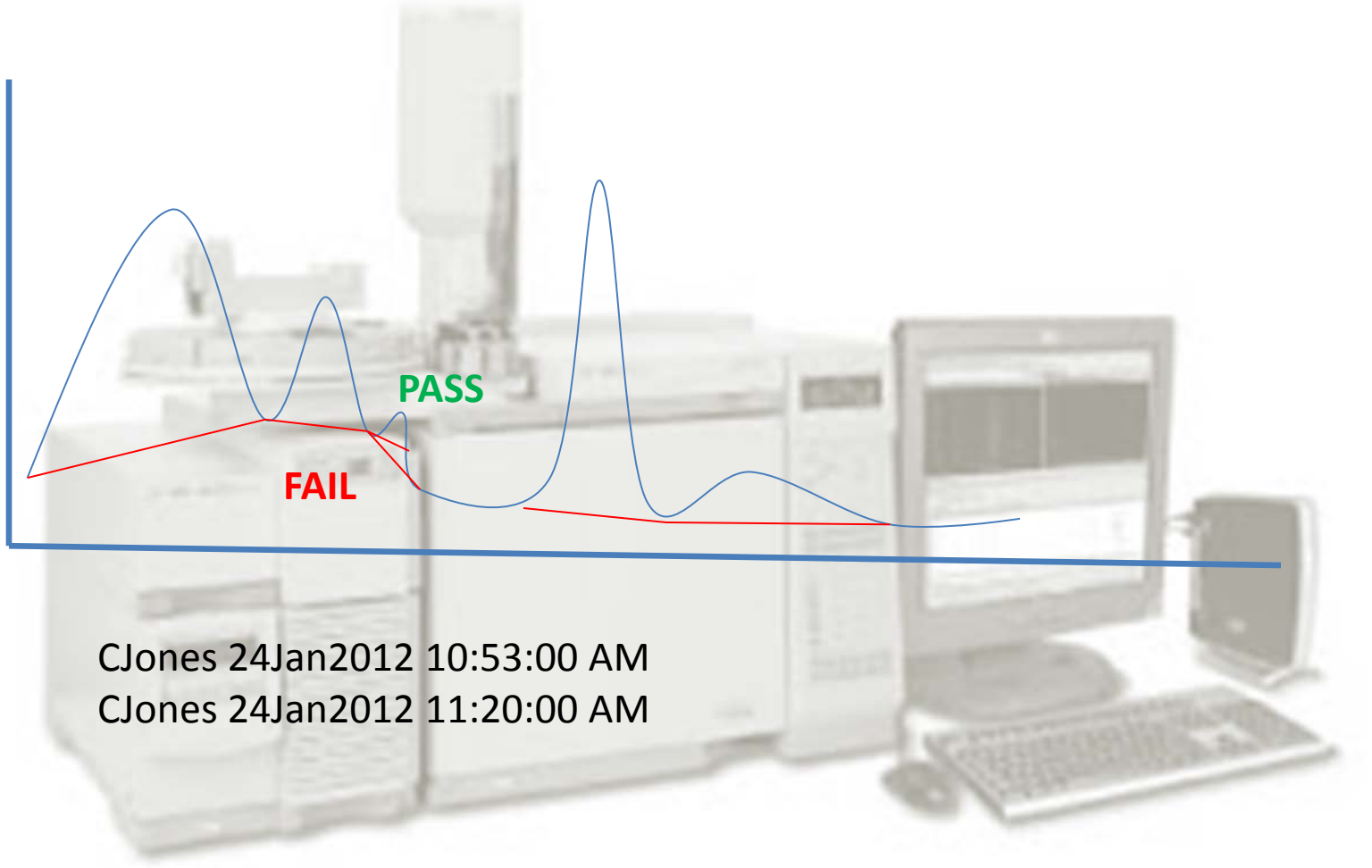
Data Presentation
Chromatographic Printout



Data Re-Processed
New Print Out



Review of Electronic Source Data



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Preventive Actions

- **Documented and Approved (SOPs)**
- **Testing and Verification**
- **Backup and Recovery Procedure**
- **Disaster Recovery and Business Continuity**
- **Periodically Reviewed**

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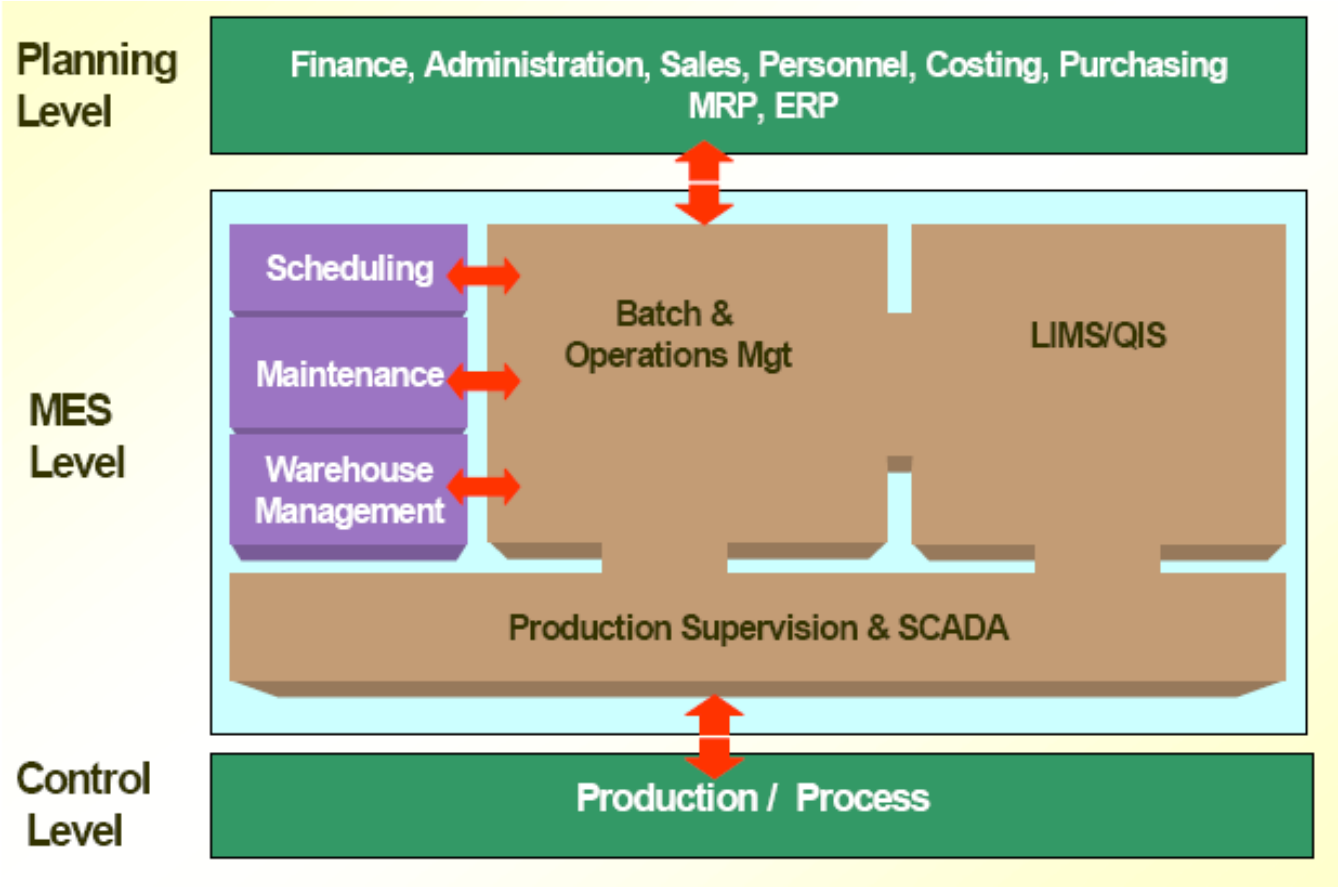
Electronic Batch Record Requirements

1. **Accurate Reproduction of Appropriate Master Production or Control Record**
2. **Documentation of Completed Steps**
3. **Dates**
4. **Identification of Equipment and Lines Used**
5. **Batch Component/In-Process Identification**
6. **Component Weights and Measures**
7. **In-Process and Laboratory Control Results**
8. **Area Inspection**
9. **Actual Yield, Percentage of Theoretical Yield**
10. **Labeling Control Records**
11. **Containers and Closures**
12. **Sampling Performed**
13. **Personnel Identifications**
14. **Investigations Performed**
15. **Deviations from Standard Operating Procedures**

Manufacturing System Architecture



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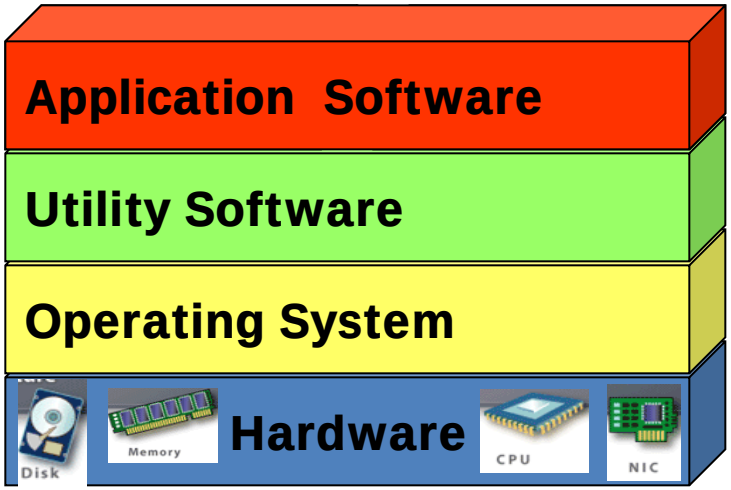
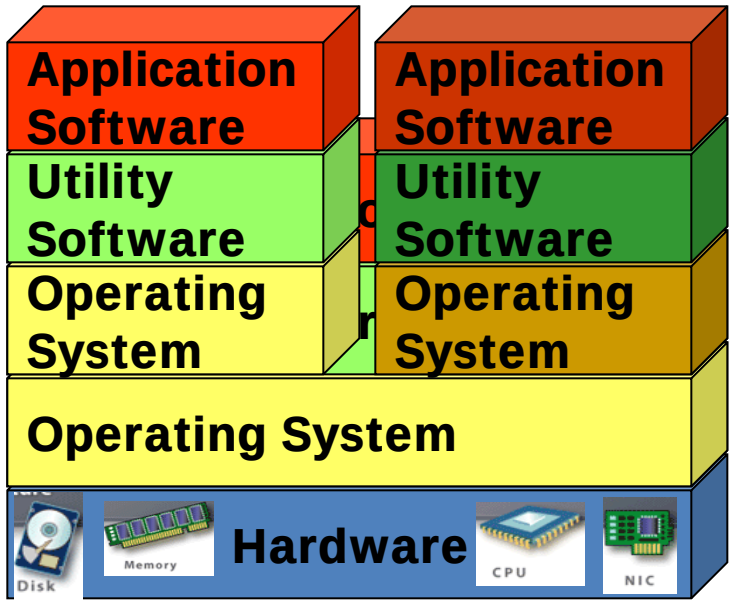
Virtualization

Physical Machine Environment



Virtual Machine Environment



Qualification Factors

- **Installation Qualification**
  - **Hardware**
  - **Operating Software & Utilities**
  - **Virtualization Software**
  - **Application Software**
- **Virtualization Functions**
- **Virtual Machine Configuration**

Cloud Computing

- **General term for various virtual and managed IT services**
- **Progression of outsourcing scenarios**
- **On-demand computing services covering infrastructure and applications**
- **IT services provided over the Internet without the user knowing details**

Cloud Service Models

- **Software as a Service (SaaS)**
- **Platform as a Service (PaaS)**
- **Infrastructure as a Service (IaaS)**

CSV and the Cloud

- **Policy – Applications and infrastructure in the cloud aren't exempt from requirements to qualify, validate and control.**
- **Vendor and contract audits**
- **Leverage some of the "good" in the cloud:**
  - **Availability and load balancing**
  - **Proven Images**
  - **Rapid setup and change of test and validation environments**
  - **Per machine or per environment security controls**

Mobile Devices

- **Multiple Hardware and Operating Systems**
- **Multiple Network Connections**
  - **Wireless Ethernet**
  - **Cellular**
  - **Bluetooth**
- **Camera, camcorder, microphone, GPS, touch screen, storage**
- **Apps**

CSV Challenges

- **Personal devices or corporate issue**
- **Asset control**
- **Configuration management and control**
- **OS and application control**
- **Network connectivity**
- **Authentication**

Thank You!

Questions?