



43rd
Annual Meeting



Atlanta - 2007

A Layered Approach To Managing Computer Validation Risks

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Overview of the Presentation

- **Overview Of Risk-Based Approach In Pharmaceutical Industry**
- **Computer Validation Risks & Challenges**
- **Introduction Into A 4-Layer Model Validation Methodology**
- **A Case Study – Layered Approach**
- **Conclusions**



Overview Of Risk-Based Approach To The Industry

- **cGMPS FOR 21th CENTURY: A RISK-BASED APPROACH, August 2002**
 - Merging Science-based Risk Management With An Integrated Quality Systems
- **INDUSTRY RESPONDED WITH OVERWHEMING ENTHUSIASM**
 - Issued White Papers through Various Associations (ISPE, PDA, DIA etc.)
- **ICH CONSENSUS GUIDELINE QUALITY RISK MANAGEMENT (Q9), NOVEMBER 2005**
 - Implementation (Step 5)
 - EU: To be notified.
 - MHLW: Adopted on September 1, 2006
- **FDA GUIDANCE FOR INDUSTRY - Q9 QUALITY RISK MANAGEMENT, JUNE 2006**
 - FDA: Published in the Federal Register, June 2, 2006



Principles Of ICH Q9 Guideline

- ICH Quality Risk Management Scope: “Risks Related To Product Quality”
- Define A Standard Framework For Risk Management
- The Evaluation Of The Risk To Quality Should Be Based On Science & Linked To Patient Safety
- The Level Of Effort, Formality And Documentation Of The Quality In Risk Management Process Should Commensurate With The Level Of Risk
- A List Of Non-exhaustive Risk Evaluation Methods



FDA Guidance For Industry Of ICH Q9

- **What's In ICH Q9 Guidance**
 - Q9 Has Broad Risk Concepts And Principles
 - Principles For Implementation
 - Elements Of Risk Assessment/Management Processes
 - Risk Management Tools
- **What Is Not In ICH Q9 Guidance**
 - A “Cookbook” For Risk Management
 - A Specific Prescription For A Risk Management Program
 - An Exhaustive Treatment Of Theory
 - An Exhaustive List Of Methods & Tools



Risk And Evaluation Methods

- **Risk Is Defined As A Function Of Likelihood And Severity**
- **Q9 Listed A Variety Of Risk Analysis Tools And Defined By:**
 - Quantitative Method
 - Qualitative Method
 - Expert Judgment



Computer Validation Risks & Challenges

- **Computer Systems Are Becoming More And More Complex**
 - Distributed Computing
 - Web-Based Application
 - Network Computing
 - Software Components Are Distributed In Different Machines To Collectively Provide Required Functionality
 - Each Component Operates In Its Own Hardware Platform & Operating System



System Design Challenge

- Network Infrastructure Design
- Data Storage Design
- Components Distribution Design
- Security Design
- Network Control & Monitor Design



Deployment Challenge

- Physical Network
- Database Server
- Application Server
- Security
- Network Traffic Control & Load Balancing



Dynamic Configuration Challenge

- Network Connectivity Configuration
- Security Configuration
- Application Configuration
- Data Service Configuration



System Validation - Scope

- Infrastructure
 - Network Infrastructure
 - Data Service
 - Security
- Application
 - Application Server
 - Application Client



System Validation - Methods

- System Development Life Cycle
 - User Requirement Specifications
 - Functional Specifications
 - Design Specifications
 - Implementation
 - Testing
 - Change Control

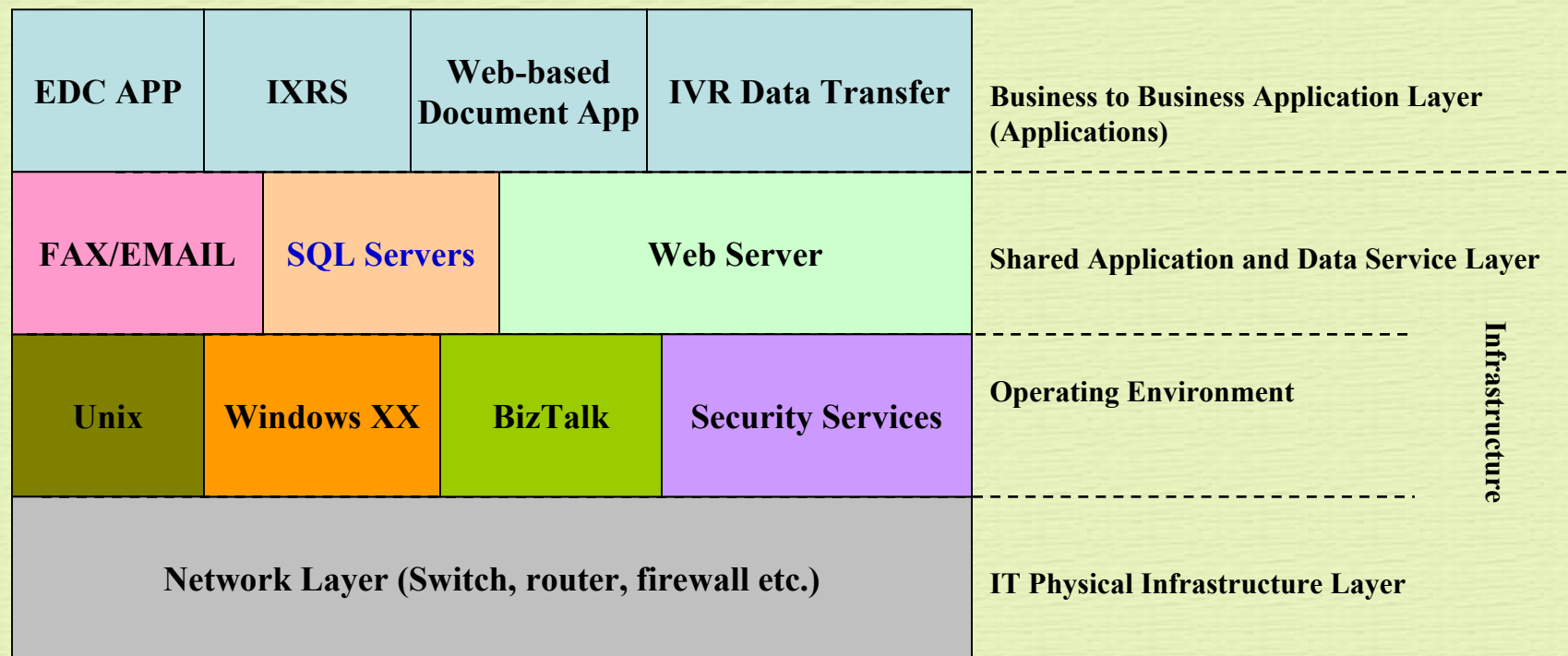


4-Layer Model Approach To Computer Validation

- What Is & Why Layered Approach?
 - Divide And Conquer
 - Separate Infrastructure From Application
 - Separate Network From Data Service
 - Separate Data Service From Applications



Layered View Of Distributed System



IT Physical Infrastructure Layer

- IT Physical Layer Components:
 - Networking Switches & Routers
 - Load Balancing Device, Firewall/Security Device
 - Cabling & Physical Connectivity
 - Network Monitoring & Controlling Device
 - Physical Servers
- Validation Focus:
 - Vendor Qualification And Standards



Operating Environment

- Operating Environment Components:
 - Operating System
 - Directory Service
 - Object Name Service
 - User Authentication Service
 - Integration Service - MS BizTalk
- Validation Focus:
 - Dynamic Configuration



Shared App and Data Service Layer

- Application Servers
 - Web Services
 - Database Services
 - Document Management Services
 - FAXING/EMAIL Services
 - Data Reporting Services
- Validation Focus:
 - Installation Qualification And Operational Qualification



Application Layer

- Business Applications
 - IVRS Applications
 - ePRO Applications
 - Web Based Application
 - Distributed Applications Such As Data Transfer, Web Reports, etc.
- Validation Focus:
 - Full Life Cycle System Validation



Advantage of Layered Model

- Reflects Technical Architecture
- Reflects Organizational Structure
- Separates & Isolates Issues In Different Universe Of Problems
- Well Defined Interface Between Layers
- Applies SDLC In Each Layer With Different Risk Focuses



Case Study-Case Description

- **Almac Clinical Technologies Is An IVR/EDC System Vendor Which:**
 - Provides IVR/EDC Consulting Services
 - Develops IVR/EDC Systems
 - Hosts Clinical Trial Data
 - Reports/Transfers Data To Sponsors



Case Study - Host Environment

- 20 Network Switches & 5 Routers
- 4 Firewall Devices
- 10 Database With 3 Replicates By SAN
- 5 Web Servers
- 2 BizTalk Services
- Over 200 IVRS/EDC Applications
- More Than 86000 Users Worldwide



Analyze and Prioritize Risk

- **Most Important Assets**
 - IT Infrastructure
 - IVRS/EDC Systems
 - Clinical Research Data
 - Institution Knowledge
- **Inventory Assessment Of Computer Systems**
 - Regulated vs Non-regulated System
 - Infrastructure vs Clinical Trial Applications
 - Standard vs Non-standard Hardware
 - Standard vs Non-standard Software
 - Disaster Recovery Solution



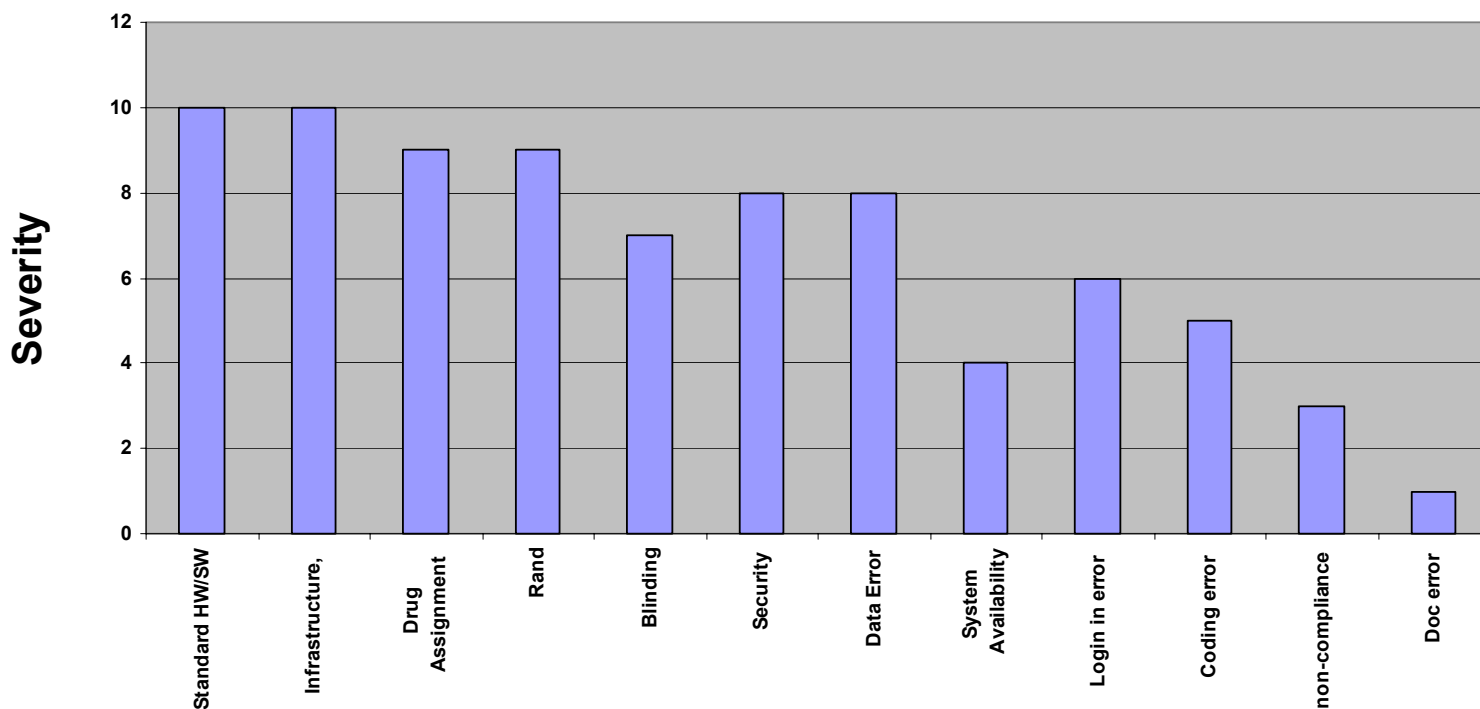
Risk Measurement

- **Frequency Of Risk Event – Statistical Methods**
 - Track Actual Hazard Events (Incident Report)
 - Analyze The Causes Of Hazard Events (Link To Asset)
 - Calculate The Frequency Of The Occurrences
- **Severity Of Risk Event – Mixed Methods**
 - Severity Of Risk By Quantitative Measurement
 - Severity Of Risk By Qualitative Measurement
 - Severity Of Risk By Expert Judgment Measurement
- **Normalize All Three Measurements - Quantitative**
 - For Example Scale 1-10
 - Loss In Dollar Or % Of Total Revenue Loss



Organizational Risk Map

Risk Frequency/Severity Chart



Risk Factors In The Order Of Frequency



Case Study - Validation Strategy

- **Infrastructure Qualification Plan - Bottom 3 Layers**
 - Vendor Assessment
 - Standards
 - Customer Support
 - Maintenance – Configuration Management
 - IQ/OQ
- **IVRS/EDC Application Validation Plans – Clinical App**
 - System SDLC
 - Patient Safety
 - Data Integrity
 - Data Security
 - Compliance



Case Study – Org. Structure

- Assign Validation Staff At Infrastructure Level
- Qualify The Bottom Three Layers By IT Organization
- Validate Business Application By End Users
- Perform PQ By The Combination Of User & IT Organizations



Case Study - Milestone & Deliverables

- Qualification Plan and Validation Plans
- Project Tasks And Responsibility Matrix
- Conceptual And Physical Design Document
- Hardware/Software Inventory
- IQ/OQ For Each Component
- PQ For Integrated System



Case Study - Milestone & Deliverables

- Vendor Audit/Assessment Reports
- System Life Cycle SOP
- System Maintenance SOP
- Change Control SOP
- Physical & Logical Security SOP
- Application Deployment SOP
- Infrastructure Qualification Summary Report
- IVR/EDC System Validation Summary Report



Conclusions

- Clearly Defined Layers Of Computing Environment
- Quantitatively Associated Risks To Different Layers
- Developed Risk Maps To Major Business Asset
- Defined Risk-Based Validation Strategy For Computer System Validation Based On Layered Approach
- Developed Repeatable Process To Execute The Strategy
- Significantly Improved Efficiency Of Validation Task
- Enjoyed The Highest Audit Rating Among Competitors

