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Worldwide Compliance & NDS Services Manager
10. December 2002

Validation Strategies for Equipment from Multiple Vendors

Time:	3.00 pm Central European Time
Telephone Number:	+44 20 8240 8243
Chairperson:	Ingrid Ginnutt

Agilent Technologies

Content

- FDA guidelines and inspectional observations
- Validation Approaches
- Instrument Qualification in Multi-Vendor Environments
- Network Qualification

Regulatory Requirements

GLP - 58.63 Maintenance and Calibration of Equipment

- Equipment shall be adequately inspected, cleaned and maintained. Equipment used for the generation, measurement, or assessment of data shall be adequately tested, calibrated and/or standardized.

- Written SOP shall set forth methods, testing, etc. and include remedial action in event of failure. Must also designate responsible individual (s) for each position.

- Written records shall be maintained of all activities and shall indicate when non-routine repairs are required. Records shall document nature of defect, how discovered and corrected and remedial action taken.

Warning Letters - Laboratory Related

- There were **no written procedures for the HPLC system on validation**, on HW & SW change control, revalidation, user operations, data and system security, disaster recovery, back-up and audit trail archive.

Procedures

- The functional, operational and security features of the data acquisition and storage **HPLC software** have **not been challenged or validated** for accuracy or for reliability.

Validation

- **The HPLC system was not validated** to show that info was accurately exchanged between the hardware (HW) and the software (SW).

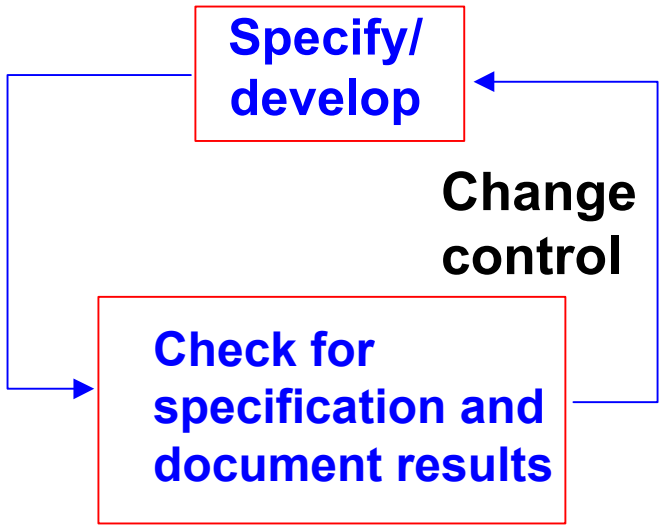
Validation

Definition

.. establishing documented evidence which provides a high degree of assurance that a specific process will consistently produce a product meeting its predetermined specification.

Source: FDA guidelines on General Principles of Validation, March 1986

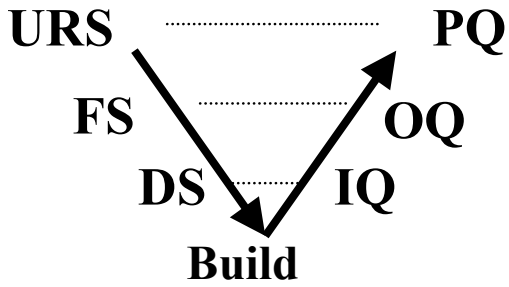
Continuous process

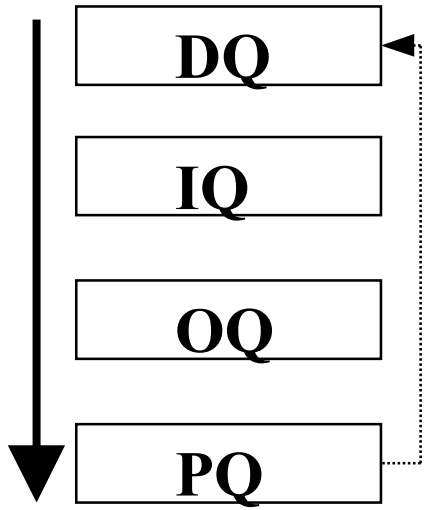


Validation means nothing else than well-organized, well- documented common sense (Ken Chapman, 1985)

Validation Master Plan

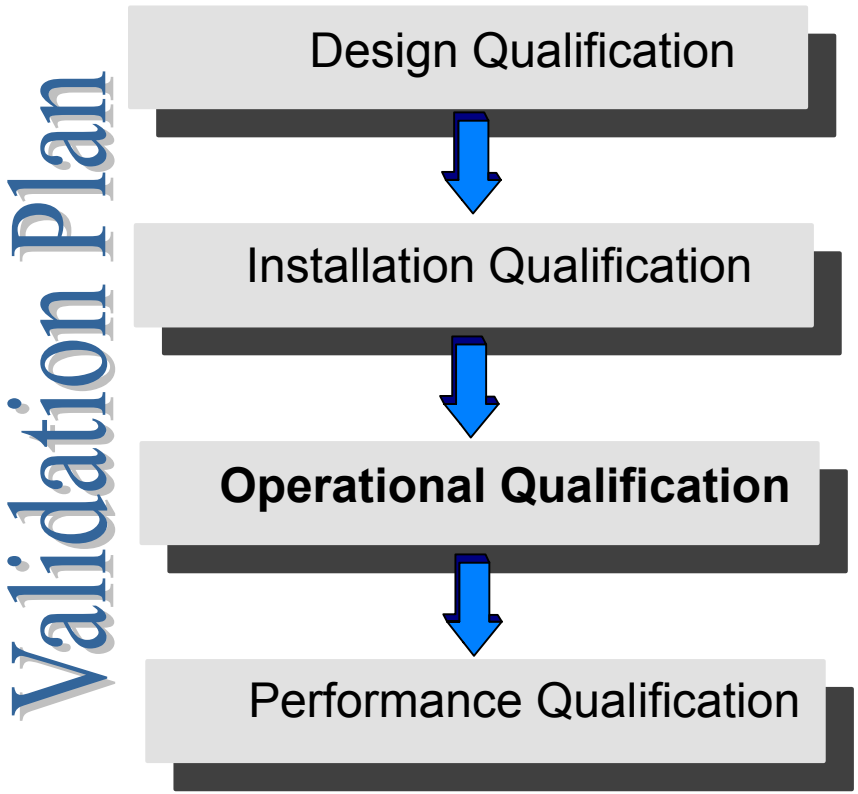
- Scope, e.g., for all regulated environments
- Glossary, e.g., validation
- Responsibilities, e.g., validation team
- Steps for validation, e.g., V or 4Q model
- Procedures for tests and acceptance criteria
- Release procedure, e.g., who has to approve
- Content of validation report
- Documentation and archiving
- Discontinuance





Example masterplan for equipment - computers - networks
www.labcompliance.com/books/masterplan.htm

Validation Phases - Steps



- User requirement specifications
- Functional specifications
- Operational specifications
- Vendor qualification

- Check arrival as purchased
- Check installation of hardware and software

- Test of key operational functions
- Test of security functions

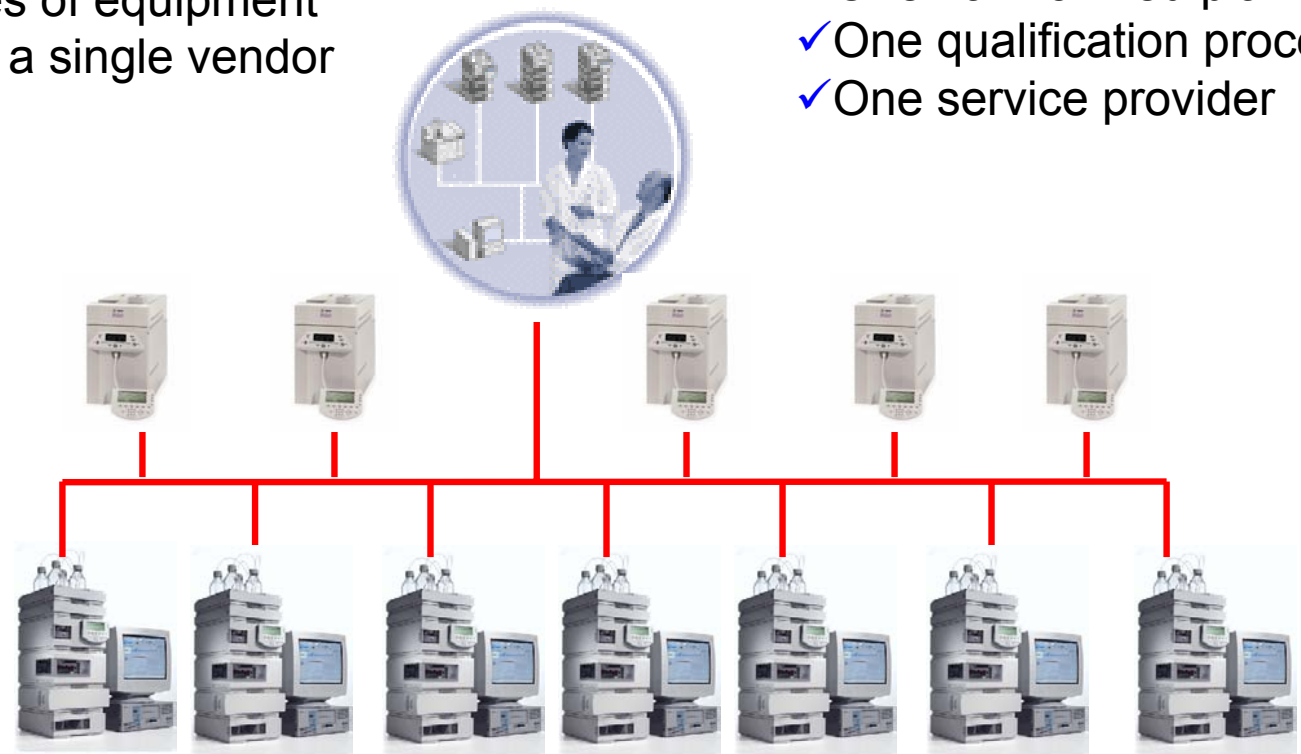
- Test for specified application
- Preventive maintenance
- On-going performance tests

Reference: L.Huber,
Validation of Computerized Analytical and Networked Systems, 2002, Interpharm Press

The Homogeneous Laboratory Environment

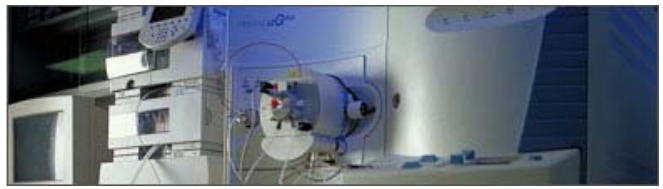
- ✓Limited types of equipment
- ✓Supplied by a single vendor

- ✓One harmonized plan
- ✓One qualification procedure
- ✓One service provider



The Typical Laboratory Environment

Chromatography equipment from multiple vendors



Mixed Vendor LC/MS

Chillers/Heaters

Dissolution

Refrigerators/Freezers

pH meters

Instrument Qualification in the Typical Lab Environment

- Multiple qualification procedures for similar types of equipment
- Multiple testing conditions…
- Multiple reports types…
- Multiple service providers…

- Increased time and effort
- Increased difficulty justifying procedures for regulatory audit
- Increased cost

Typical HPLC Qualification Situation

	Instrument 1	Instrument 2	Instrument 3
Manufacturer	A	B	C
Column Temp.	40 C 60 C	50 C	NONE
UV Accuracy	Caffeine Uracil	Holmium Oxide	Uracil
Upward/Backward Testing	Yes	No	Yes
Injector Repr.	10 uL 50 uL 100 uL	20 uL	50 uL

Agilent's Harmonized Compliance Service

- A single, **consistent approach** to instrument hardware qualification that is **vendor-neutral** in scope.
- Agilent offers a full complement of **preventative maintenance** (PM) and **operational qualification** (OQ) services
- **Broad availability** backed by Agilent Technologies
- **Reduction of costs** associated with audit preparation or challenged audits

Focus on your mission, not on compliance

Harmonized Qualification Service

Multi-Vendor, Multi-instrument Equipment List

UV Spectrophotometer
Liquid Chromatograph (LC)
LC/MS
Gas Chromatograph (CG)
GC/MS
Dissolution Tester
Capillary Electrophoresis

LabMetrix Technologies
LabMetrix® Group

UV Spectrophotometer	Timer	Freezer
Liquid Chromatograph (HPLC)	Flowmeter	Melting Point Apparatus
LC/MS	Thermometer	Flash Point Apparatus
Gas Chromatograph (GC)	Hygrometer	Autoclave
GC/MS	Water Bath	Furnace
Dissolution Tester	Oven	Stability Chamber
Capillary Electrophoresis (CE)	Refrigerator	Centrifuge
IR spectrophotometer	Densitometer	Refractometer
Polarimeter	Nitrogen Analyzer	Milli Q Water System
Heated Magnetic Stirrer	Burette	Titrator

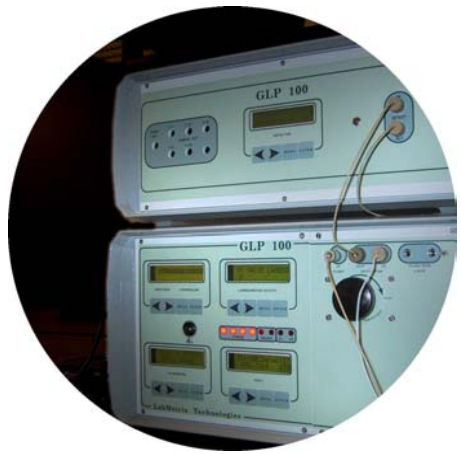
Qualification Master Plan

- Scope of Performance Verification
- Calibration System, the GLP100
- Systems concerned with the Validation
- Documentation Related to the Validation
- Conformity Specifications (Standards & Customer)
- Amendments

A Consistent Metrology-Based Approach

- Modular control/measurement device that connects to test and measure all defined parameters (temperature, flow, pressure, electrical signals, ...)

- Tests defined in Qualification Master Plan (QMP)
- Instrument controlled by native data system (or controller)
- Report generated for the specific system
- NIST/COFRAC traceable, metrology based (COFRAC for Europe and NIST for USA)



LabMetrix Technologies
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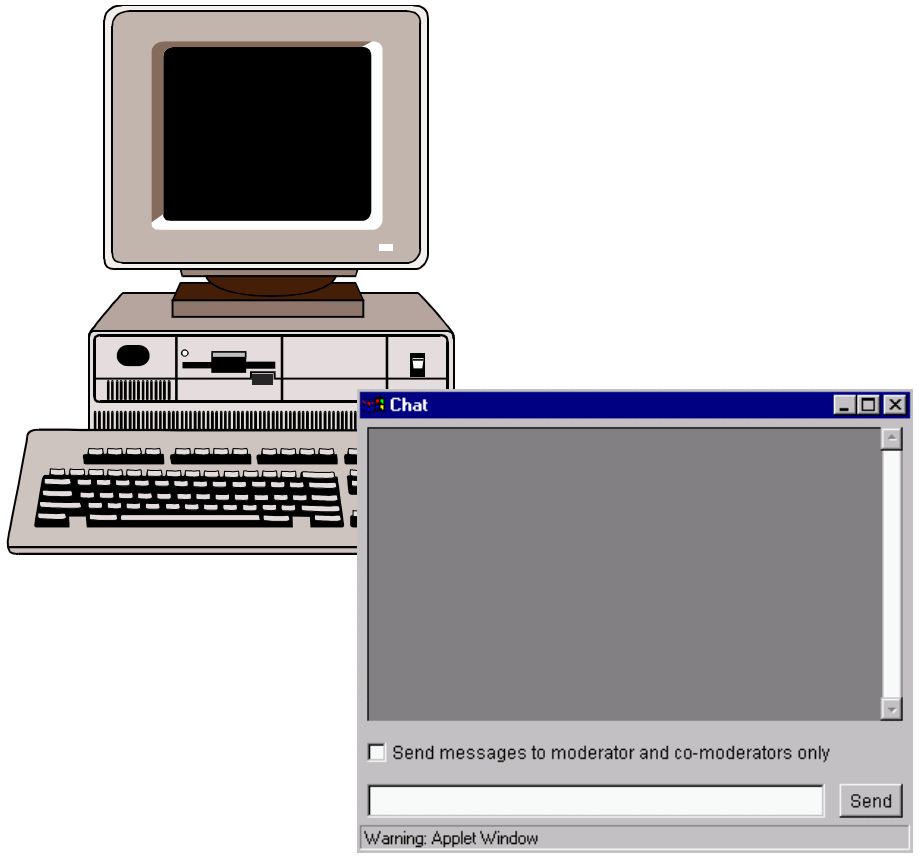
Multi-Vendor Approaches

Feature	Typical Multi-Vendor Option	Agilent Multi-Vendor Option
Validation Master Plan	No	Yes
Unified Protocols	No	Yes
Customized testing	No	Yes
Different Techniques	?	Yes
Traceability	?	Yes
Document Management	?	Yes
Unified Reports	No	Yes

Consitent, reliable, auditable

Break Number 1

Please type your question into the Chat Box at any time during the presentation.



Network Qualification

- The **network** ... module design limitations, which can only support up to four chromatographic acquisition systems, had up to five chromatographic systems connected. There was **no validation** showing this configuration to be acceptable

Wrong specs

- **System testing** was not conducted to ensure that each system as configured **could handle high sample rates.**

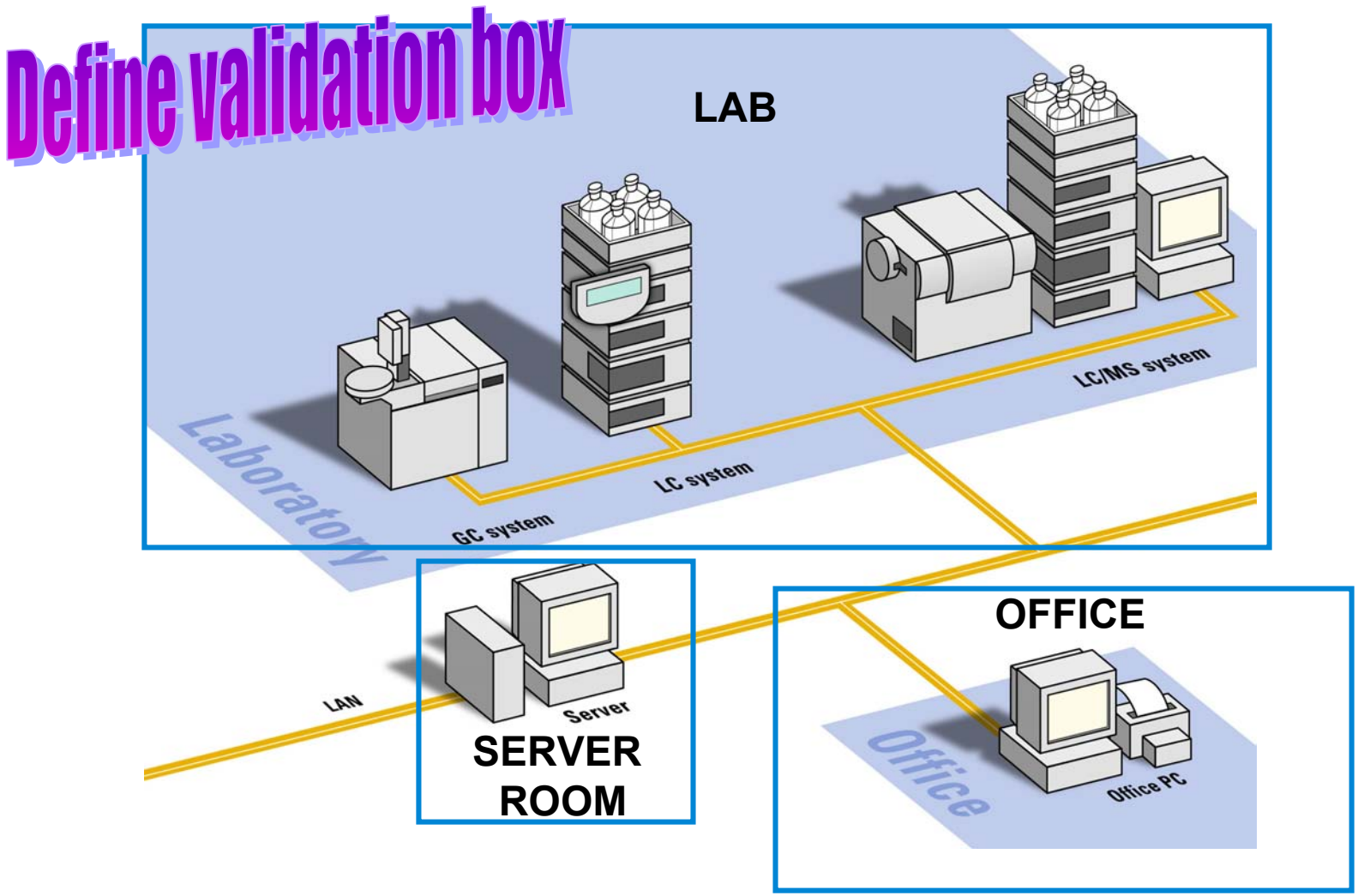
High Load

- **Validation** of the system **did not include critical system tests** such as volume, stress, performance, boundary, and compatibility

Stress testing

Ref: www.fdawarningletter.com

Laboratory Network Qualification



Specifics about Networked Systems

- Networks heterogeneous: They include a multitude of hardware components and communication protocols
- A change to a network component has the potential to affect many all other components and applications
- Many people (with “business tasks”) who may not be trained on GXP’s will have access to the network
- The network requires frequent changes, additions, and repairs, but it can not be taken out of service

Holistic Network Qualification

"Validating networked systems not only requires qualifying individual networked components (for example, applications running on each computer), but it also means qualifying authorized access to the networked system and qualifying the data transfer between related computers, as in qualifying the interfaces of components at both sites. The "whole system" (i.e., including the network) is validated by running typical day-by-day applications under normal and high load conditions and verifying correct functions and performance with a previously specified criteria." L. Huber, Validation Book

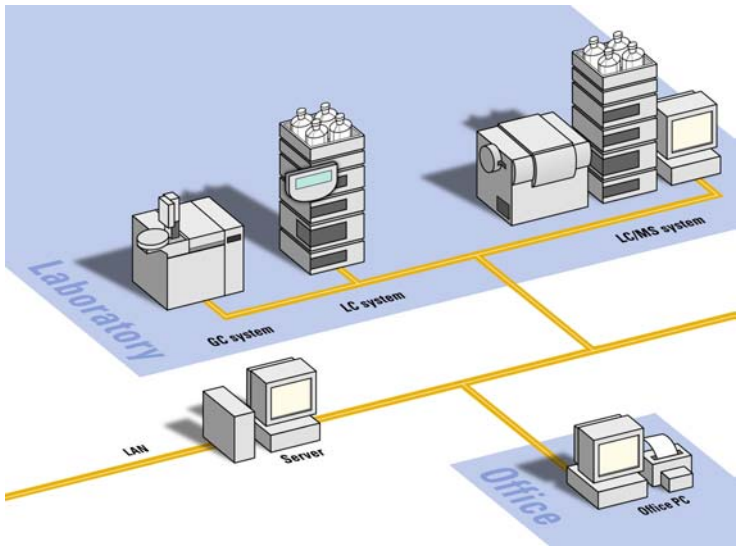
Network Specific Tests

- Start and shut down
- Security tests, log on with correct and incorrect password
- Correct password administration (e.g., PW with 4 characters)
- Session unlock
- (User specific) automated time-outs
- Access to task / file permissions
- Backup and restoration
- Recovery from system failures
- Audit trail of network transactions
- Correct data transfer under normal and high traffic

Network Qualification using Modern Networking Tools

- Instruments may be viewed as nodes on the network
- Instruments and their controllers may be accessed through network monitoring tools
- Diagnostic information may be obtained from analytical instruments through standard network protocols
- Instruments may be monitored throughout the enterprise in much the same way that servers and computers are monitored for status conditions

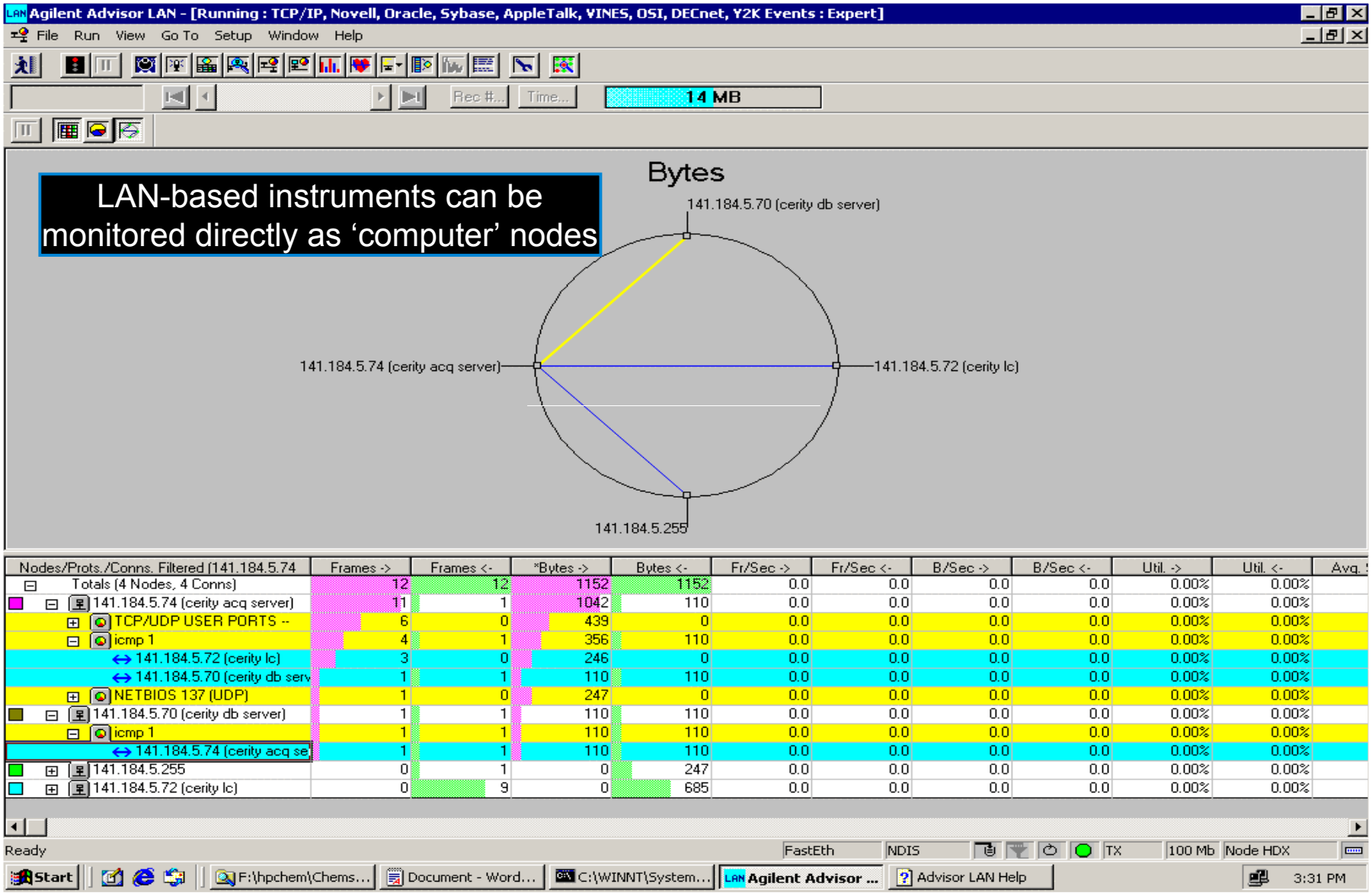
Agilent Network Qualification Service



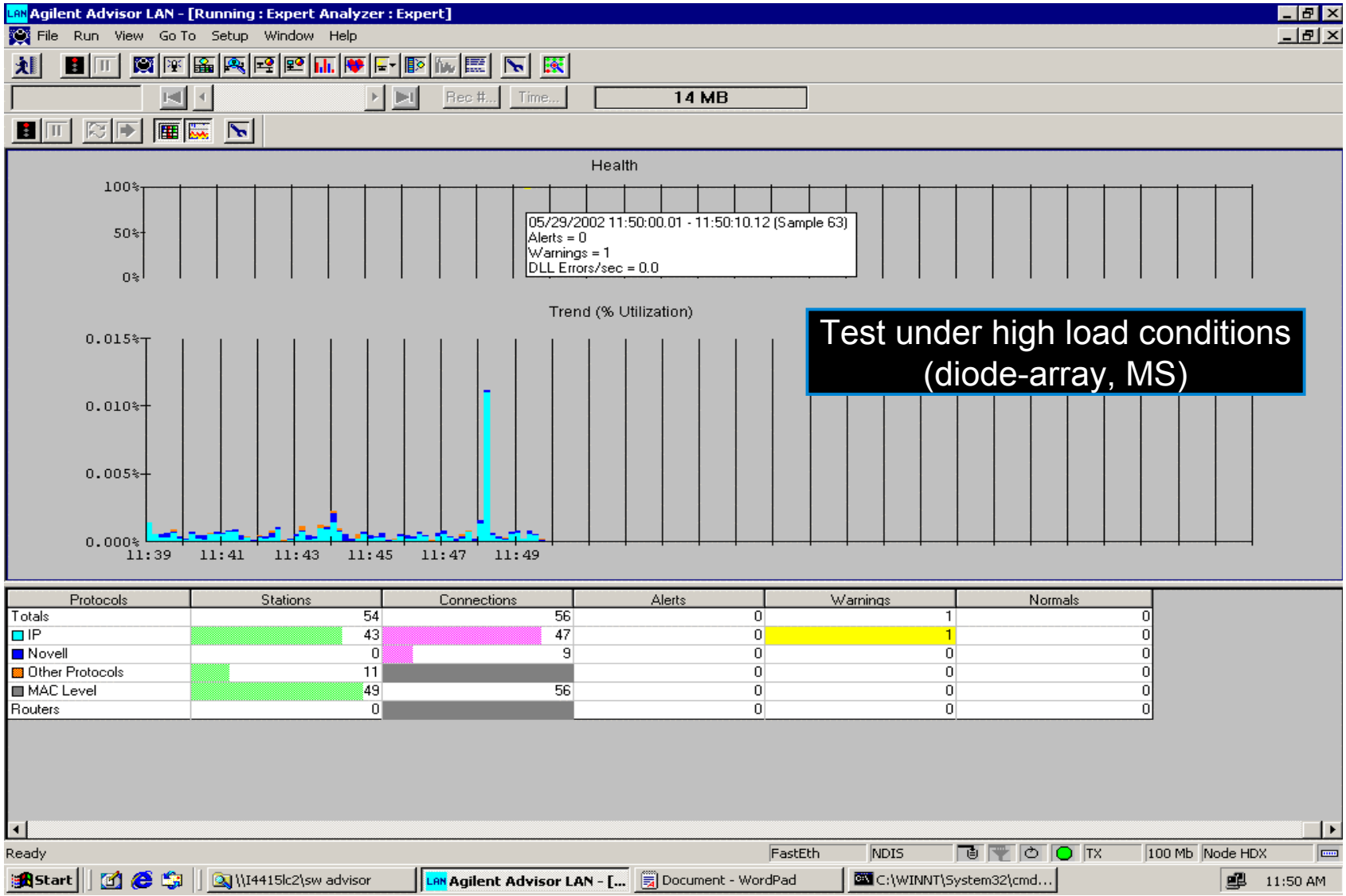
Agilent expertise in laboratory equipment, data systems, and networking:

- Map network topology
- Determine network bandwidth
- Assess network utilization
- Continuous Monitoring of network health

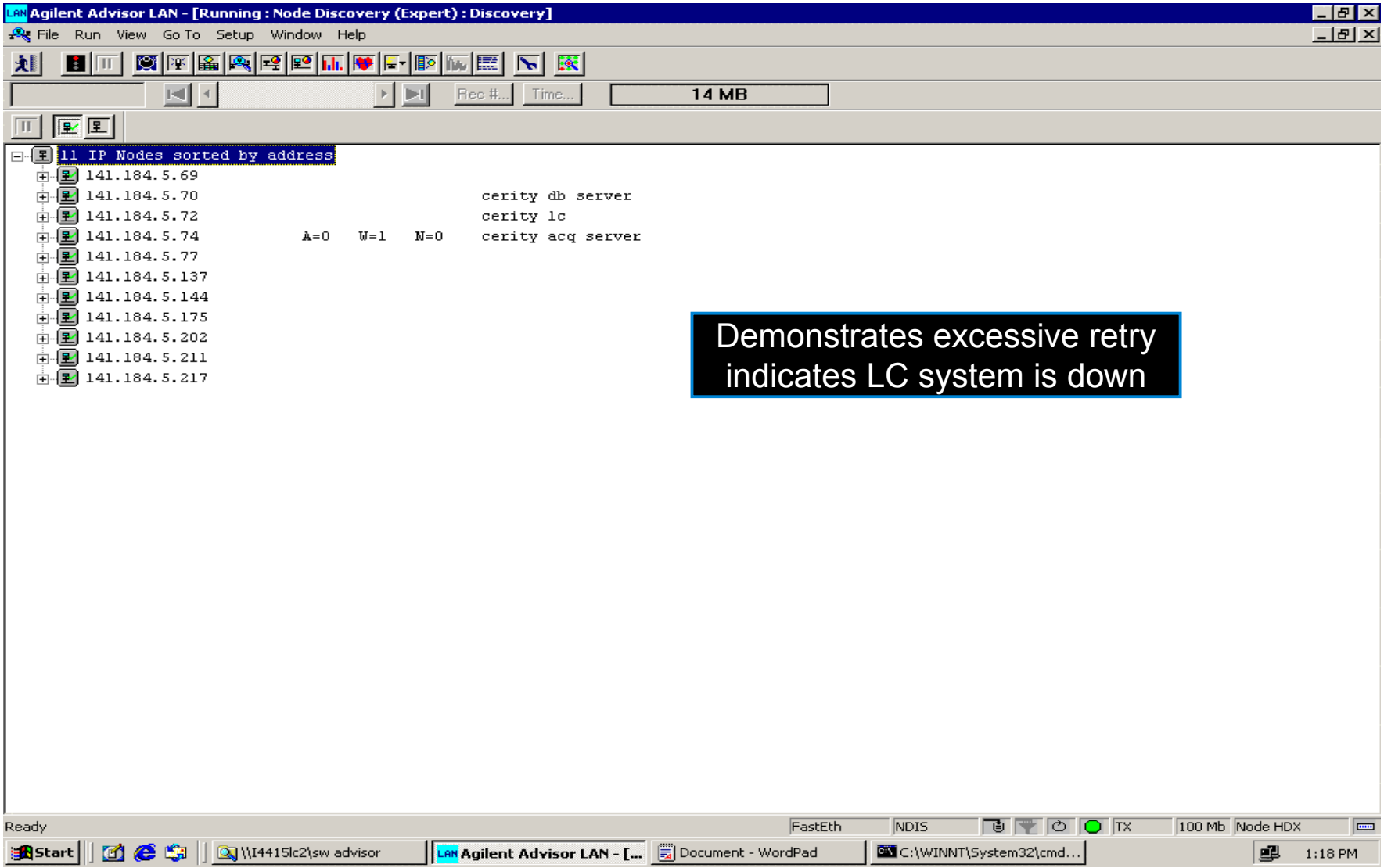
Mapping Topology



Monitoring Network Bandwidth



Monitoring Warnings

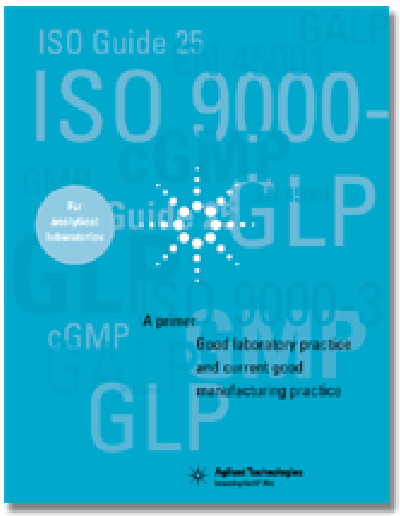


Summary Recommendations

- Form a validation team (include IT!)
- Develop validation (master) plan
- Define user requirements and functional specifications
- Qualify the vendor
- Perform and document qualifications
- Evaluate the need for retrospective evaluation and develop a plan
- Document

Resources

GLP/GMP Primer from Agilent Technologies

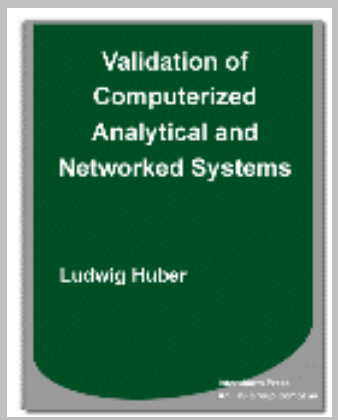


- Basics of GLP/cGMP
- Impact on Laboratories
- Equipment validation/qualification
- Computer validation
- FDA 21 CFR Part 11
- Method validation (ICH, USP)
- Vendor contributions
- Glossary

Agilent Publication 5968-6793E

Compliance Services Brochure Brochure 5988-6910EN

Resources



L.Huber
Validation of Computerized Analytical and Networked Systems

Interpharm Press

www.labcompliance.com

www.labcompliance.com

- **Global on-line resource for validation&compliance issues in laboratories**
- **Regulatory news**
- **Discussion forum**
- **Monthly newsletter**
- **Usersclub with free downloads**
- **Links to literature, documents and other websites**
- **Several pages dedicated to 21CFR11**

Agilent's Compliance Solutions

- Agilent was independently rated #1 for Compliance expertise
- Vendor-independent, global solution for all laboratory analytical instruments
- Advanced laboratory network qualification services
- A responsive, experienced team focused on helping you succeed
- Reduced validation costs

Wrap-up E-Seminar Questions

Thank you for attending today's Agilent e-Seminar.

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Related e-Seminars

Agilent Cerity for Pharmaceutical QA/QC: Real world examples for Part 11 technical controls

23. January 2003, 3:00pm - 4:00pm ECT

23. January 2003, 5:00am - 6:00pm ECT

Automated Analytical Method Validation and Regulatory Compliance

12. February 2003, 3:00pm - 4:00pm ECT

19. February 2003, 5:00am - 6:00pm ECT

Monitoring the Health and Status of a Networked Chromatography Data System

13. March 2003, 3:00pm - 4:00pm ECT

13. March 2003, 5:00am - 6:00pm ECT

Design Qualification (DQ) and Re-Qualification (RQ) for Data Systems

16. April 2003, 3:00pm - 4:00pm ECT

17. April 2003, 5:00am - 6:00pm ECT