GLP Computerized Systems – Updates from OECD Guidance

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28 JAN 2016, NAICC, Orlando

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Validation – EPA GLP Obligation

Expectations of the EPA for Computers in GLP (40 CFR 160 - FIFRA GLPs)

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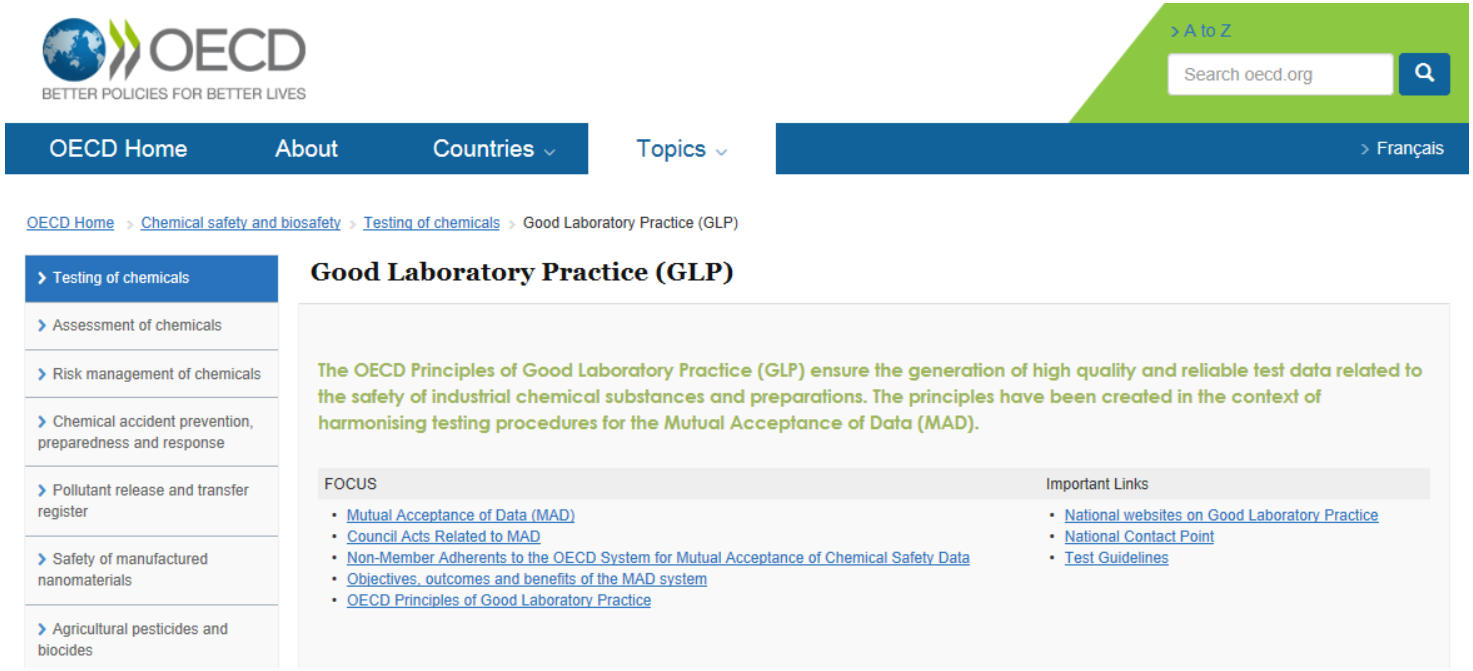
- Computers are **recording raw data** (§160.130(e))
  - "Sign and date" replaced by GLP audit trails
- Computers are **essential equipment** (§160.63)
  - Design, calibration, and maintenance is termed Validation (CSV, Computerized System Validation)
- Computers must be governed by **SOPs** (§160.81)
  - Equipment SOPs, raw data definitions
  - Personnel training on computers (§160.29)
- Computers will **archive data** (§160.190)
  - Paper archiving will be supplemented with media storage and electronic records

OECD GLP Working Group



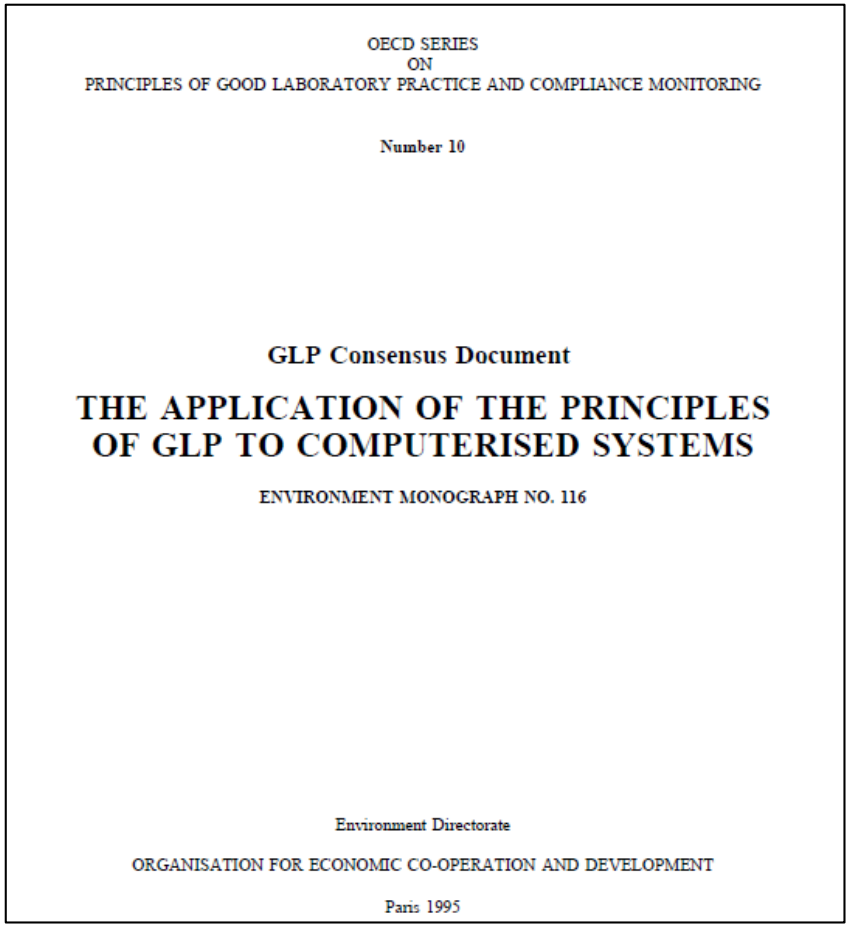
Citation: http://www.oecd.org/chemicalsafety/testing/goodlaboratorypracticeglp.htm

OECD GLP WG – IT Subgroup

- **Austria –** Ronald Bauer (Chair)
- **Belgium –** Guido Jacobs
- **Ireland -** Marie O'Mahony
- **Italy -** Francesco De Blasio
- **Switzerland -** Christoph Moor
- **United States (EPA) –** Francisca Liem

Doc 10

- OECD GLP Consensus Document 10
- “The Application of the Principles of GLP to Computerised Systems”
- 1995



OECD SERIES
ON
PRINCIPLES OF GOOD LABORATORY PRACTICE AND COMPLIANCE MONITORING

Number 10

GLP Consensus Document

THE APPLICATION OF THE PRINCIPLES OF GLP TO COMPUTERISED SYSTEMS

ENVIRONMENT MONOGRAPH NO. 116

Environment Directorate

ORGANISATION FOR ECONOMIC CO-OPERATION AND DEVELOPMENT

Paris 1995

Doc 10 History

- **1995** OECD GLP Consensus Document 10 (15 pages)
- **2012** OECD IT Subgroup formed to rework guidance
- **2014 Sep** draft revision for public comment (23 pages)
- **2014 Nov** comments from Society of Quality Assurance (Greg Furrow, Michael Regehr)
- **2015 Sep** Ronald Bauer presentation on current revision (DGGF, Ulm, Germany)
- **2015 Dec** linguistic review by UK/MHRA (Andrew Gray)
- **2015 or early 2016** anticipated publication

References for Revised Doc 10

- **OECD GLP Doc 10** (1995)
- **PIC/S 11-3** "Good Practices for Computerised Systems in Regulated GxP Environments," 2007
- **OECD GLP Doc 15** "Establishment and Control of Archives that Operate in Compliance with the Principles of GLP," 2007
- **GAMP 5** "Good Automated Manufacturing Practice," ISPE, 2007
- **Annex 11** EU GMP Guidelines, Annex 11: Computerised Systems
- **Red Apple II** "Computerized Systems used in Nonclinical Safety Assessment: Current Concepts in Validation and Compliance," 2008, DIA

Key Additions / Clarifications

- Scope (simple to complex system)
- Systems Inventory
- Risk Assessment
- Life Cycle
- Periodic Review
- Audit trails
- Electronic signatures
- Change management
- Vendors

OECD DRAFT ADVISORY DOCUMENT 16[1]

THE APPLICATION OF GLP PRINCIPLES TO COMPUTERISED SYSTEMS

FOREWARD

1. The following draft Advisory Document will replace the 1995 OECD GLP Consensus Document number 10 - *The Application of the Principles of GLP to Computerised Systems.* The original Document 10 was developed by the OECD Working Group on GLP, based on a document emanating from a 1992 workshop held in Switzerland. The current Draft Advisory Document, also developed by the Working Group, retains all of the key text from the original Consensus Document 10 where changes were unnecessary, but also includes new text to reflect the current state-of-the art in this field. This draft will be revised based on the input received during the public comment period.

Nomenclature introduced

- **Validation Director** – delegated person responsible for a validation project
- **COTS** - commercial off-the-shelf software or hardware provided by a vendor to the general public
- **Vendor** – Supplier, third parties, internal IT departments, service providers, hosted service providers

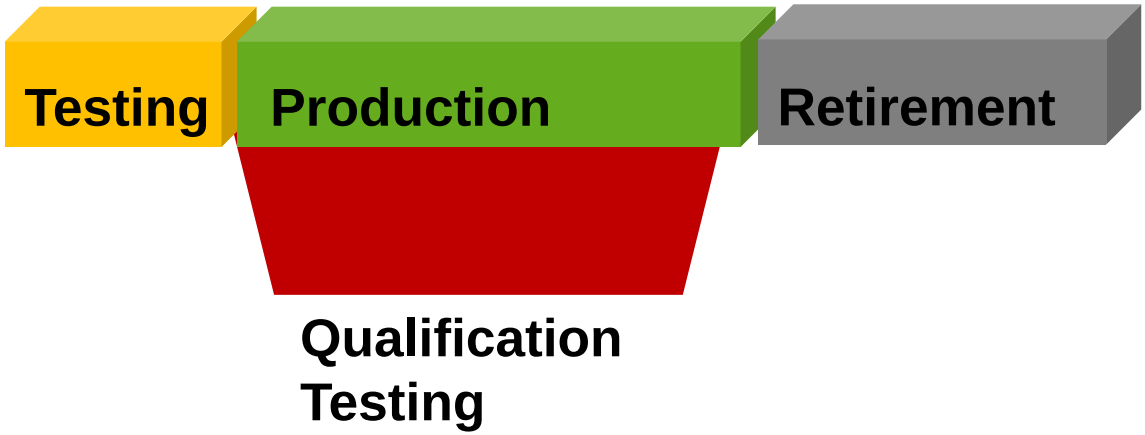
Scope

- From balances to LIMS
- Simple systems: COTS, automated equipment of low complexity (balances, freezers)
- Complex systems: multi-user, multi-site (laboratory information management systems)
- Prospective (only retrospective if changed to GLP relevant)
- Mixed systems: if both GLP and non-GLP uses, validation applies, testing limited to GLP functions

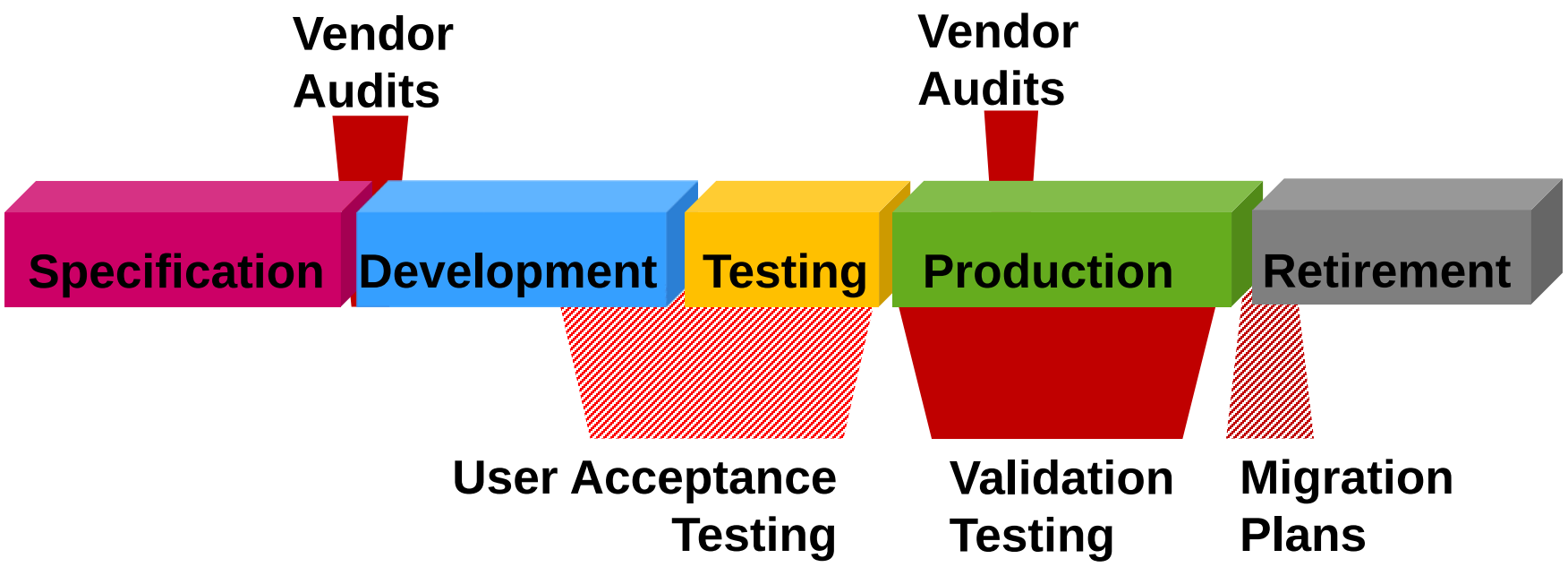
System Life Cycles

- Life cycles are to be chosen and defined by the user
- All phases should be documented (e.g., specification, purchase, design, development, testing, integration, qualification, implementation, release, operation, retirement)
- Life cycle and validation activities should be scaled based on documented risk assessment

Life Cycle – Simple Systems



Life Cycle – Complex Systems



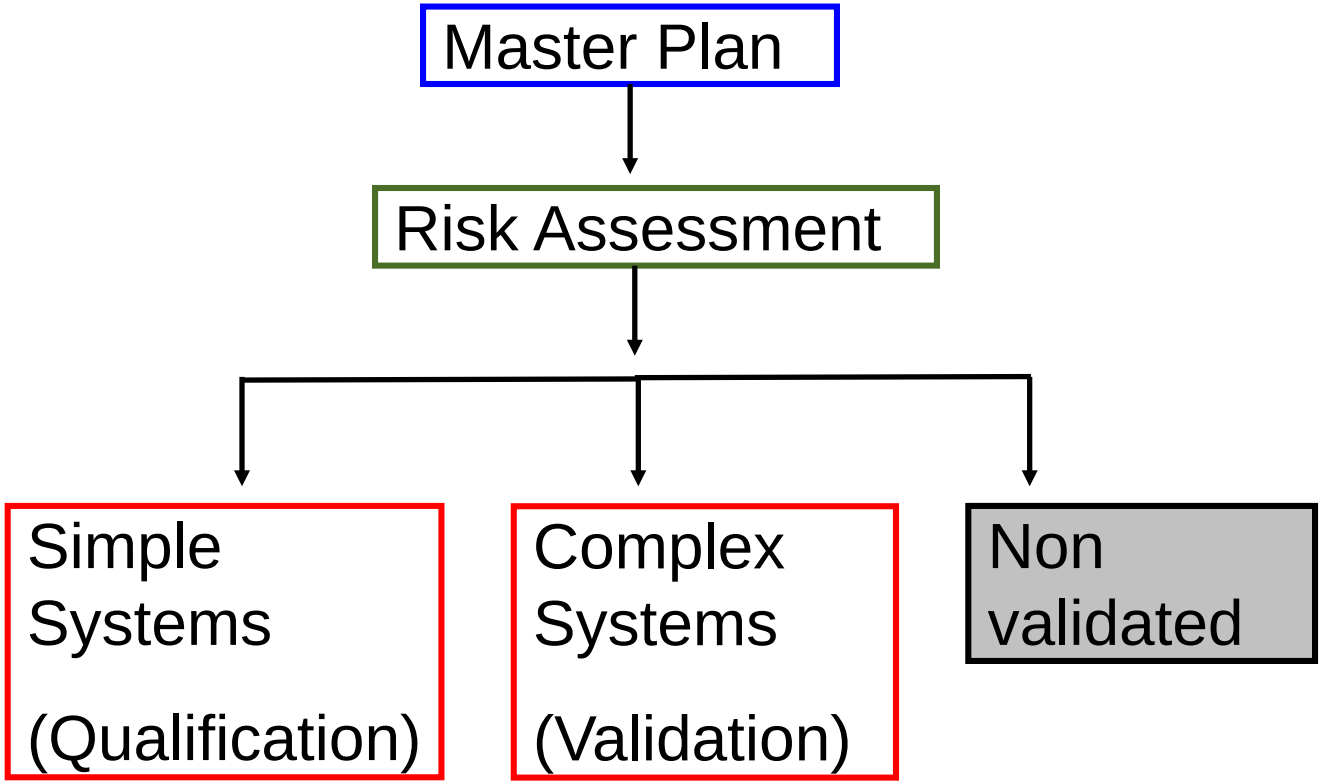
Inventory

- up-to-date listing of all GLP-relevant computerized systems
  - validation status
  - make, model, or version
  - Business system owner, IT owner, and validation director
  - System functionality
  - Test Facility specific

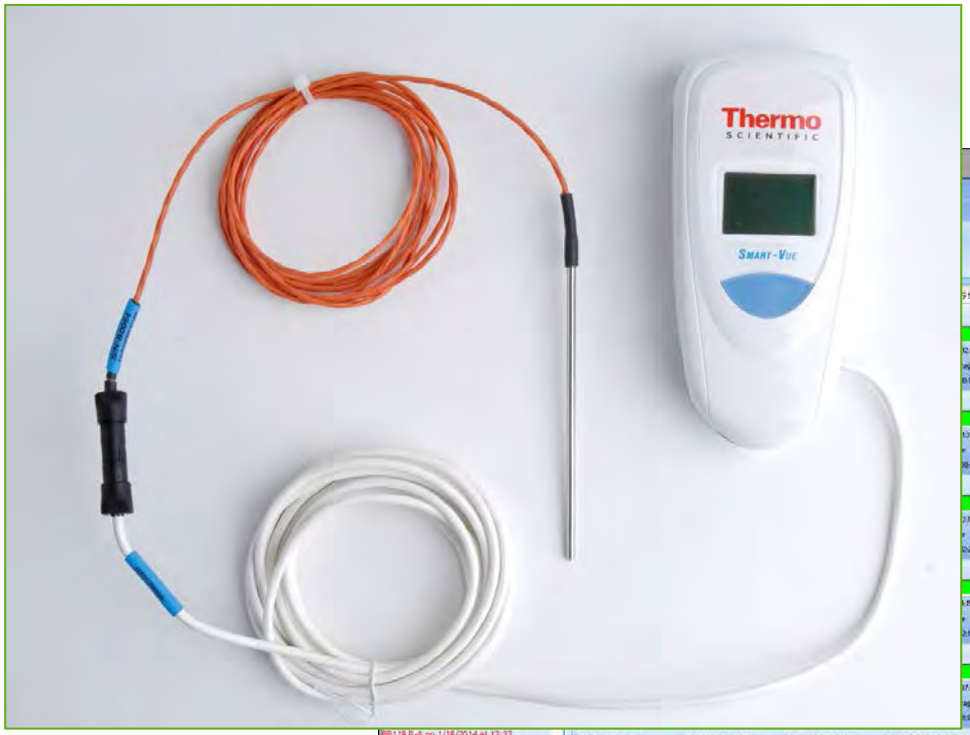
Risk Assessment

- Risk Management:
  - Risk Identification, Assessment, Mitigation, Control
- Results in an appropriately scaled validation strategy based on intended use and potential risks to data integrity
- Assess simple and COTS systems as lower risk
- Defines need or extent of a vendor assessment
- Defines frequency and depth of periodic reviews

Risk Assessment



Simple vs Complex Systems



Citation: Smart-Vue Software; Thermo Scientific www.thermoscientific.com (2014)

Periodic Review

- Review current use, performance, validation history, upgrade history
- Review deviations, incidents, unexpected events
- Review user access and roles
- Justify choice of personnel performing the periodic review (e.g. TFM, Study Director, QAU, IT, vendor)
- Review audit trail system (recorded information, user behavior)
- Document periodic review results and remedial actions

Personnel - Test Facility Management

- Overall responsibility to ensure validated computerized systems (facilities, equipment, personnel, and procedures)
- Delegate specific responsibility to designated trained personnel
- Maintain a computerized system inventory
- Evaluate vendors based on risk assessment and complexity. Evidence of vendor assessment.
- Ensure global systems provided within the company are operated and maintained **locally** in accordance with GLP

Personnel - Study Director

- Sufficient training to understand the relevant procedures with the computerized systems
- Confirmation of the validation status of the systems used should within a study
- Traceability from study protocol or relevant method to the inventory for computerized systems used in a GLP study

Personnel - QAU

- Aware of GLP-relevant computerized systems
- SOPs for QAU responsibilities regarding computerized systems
- Sufficient training to understand the relevant procedures with the computerized systems
- Monitor validation, operation, and maintenance of a system (delegate to experts as needed)
- Direct read-only access to systems for data and audit trail reviews

CRO Expectations

- SOP for general Risk Assessment, Life Cycles, Validation
- SOPs for specific computerized systems
  - Access granting, training, maintenance, roles
- Inventory of computerized systems
  - Instruments, PCs, networked applications, and sponsor-hosted systems
- Risk assessments, validation documentation, and TFM release for each class or individual system

System Release Authorization - complex

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System Release Authorization

ALADIN - RTP

Eingang APD/Q
17. Mai 2004

Approvals

Head of Validation Team RTP — Diane G. Travis — Date: 5/6/04

Project Management RTP — Dr. Philip A. Brindle — Date: 05/06/04

Global System Validation Leader — Dr. Michael F. Regehr — Date: 6May04

Document Version: 1.0, Date: 6MAY2004

Original to: RTP GLP Archives

Copy to: RTP Quality Assurance Unit
Limburgerhof Quality Assurance Unit
System Validation Director
Global System Validation

TRUE COPY OF ORIGINAL
INIT MK DATE 11 May 04
TOTAL PAGES 2

Version: 1.0
Date: 6MAY2004

Page 1 of 2

System Release Authorization

ALADIN - RTP

Initial ALADIN System Release Authorization

APD's global laboratory data system, ALADIN, was validated as a joint project between Limburgerhof and RTP. ALADIN was formally released for production in Limburgerhof on August 1, 2003. ALADIN was formally released for production use in RTP as of October 1, 2003.

Users have been trained, manuals are available, and access rights have been assigned to users. All future APD studies and work, as appropriate, must be performed using ALADIN.

The initial ALADIN System Release Authorization for RTP was communicated by an RTP-All-Users email on October 1, 2003.

Restated ALADIN System R

The production system is sche
with version 3.2.2 of the ALAD
reconfigurations. The upgrad
control and revalidation proce
(CHEM 12.03.00), the ALADI
Plan.

Revalidation at both sites is s
Management approves the c
without additional work proce
Oracle databases and other c
test environment was impract

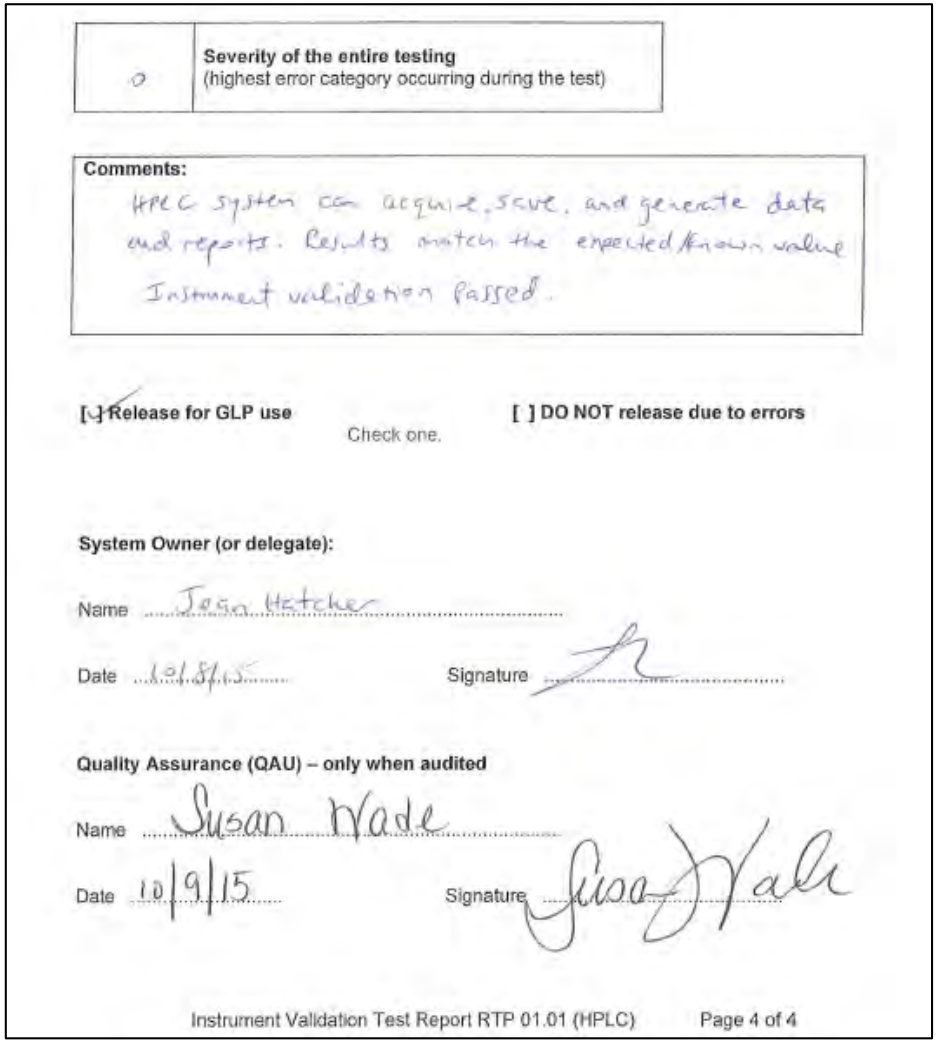
Acceptance testing and instal
ALADIN Validation Plan and
each of the two sites, all the s
installation is verified as funct

If issues are found during rev
Automated audit trails, ongoi
change control of the ALADI
or reversion to earlier ALADI

Authorization is given to relea

Version: 1.0
Date: 6MAY2004

System Release Authorization - simple



0	**Severity of the entire testing** (highest error category occurring during the test)

Comments:

HPLC system can acquire, save, and generate data and reports. Results match the expected/known value. Instrument validation passed.

[✓] **Release for GLP use** [ ] **DO NOT release due to errors**

Check one.

System Owner (or delegate):

Name Jason Hatcher

Date 10/8/15 Signature

Quality Assurance (QAU) – only when audited

Name Susan Wade

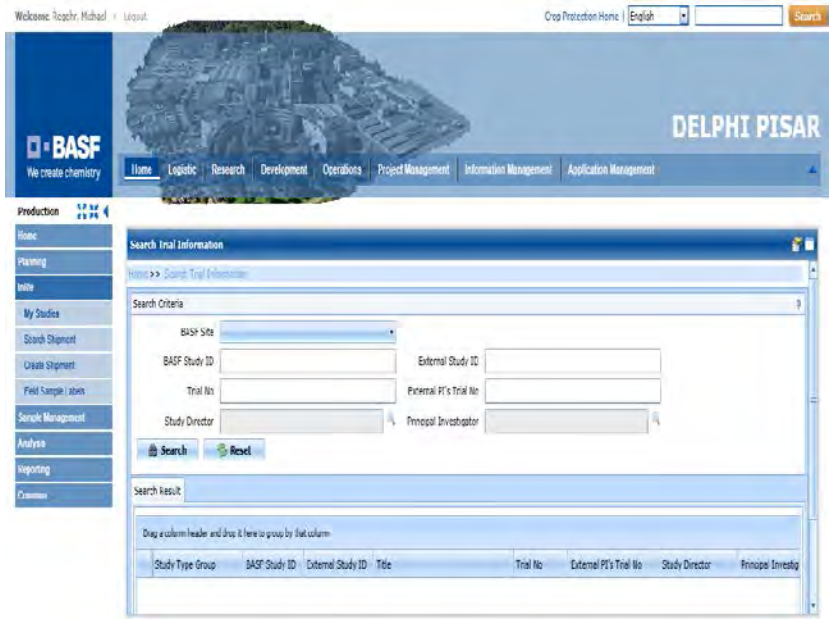
Date 10/9/15 Signature

Instrument Validation Test Report RTP 01.01 (HPLC) Page 4 of 4

Situation of a Sponsor Supplied System

PISAR example

- Vendor – BASF
- Business owner – D.Anspaugh
- User access – J.Jordan
- PISAR System SOP



- PISAR Risk Assessment (vendor assessment)
- User connection – PC to sponsor-hosted system via Citrix

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