CONCEPT
HEIDELBERG

GMP Compliance for
Computerized Systems Validation
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Supplier Assessments / Audits

Dr.-Ing. Guenter Generlich
guenter@generlich.de

Audit / Auditing

The independent examination of a sample of records, activities and/or systems to assess the state of governance, to ensure compliance with established controls, policies and procedures, and to recommend control improvements where judged necessary to reduce risks.

Role performed by Internal and External Auditors and, for computer systems, Computer Auditors.

What are the Reasons for an Audit?

An audit will be
- expensive
- labor intensive
- not wanted by our management
- not necessary

so what's the point?

An audit can help reduce the validation risk - the risk that an IT supported business system does not comply with regulatory requirements.

Assessment Goals

- Ensure compliance to technical, commercial, and regulatory requirements and directives
- Develop relationships with supplier, clarify expectations, and identify misunderstandings and risks
- Learn how the supplier´s organization works
- Local managers and professionals should want to improve their own operation
- Identify major problems before they create unjustified costs
- Enroll the supplier´s opinion leaders in the change process

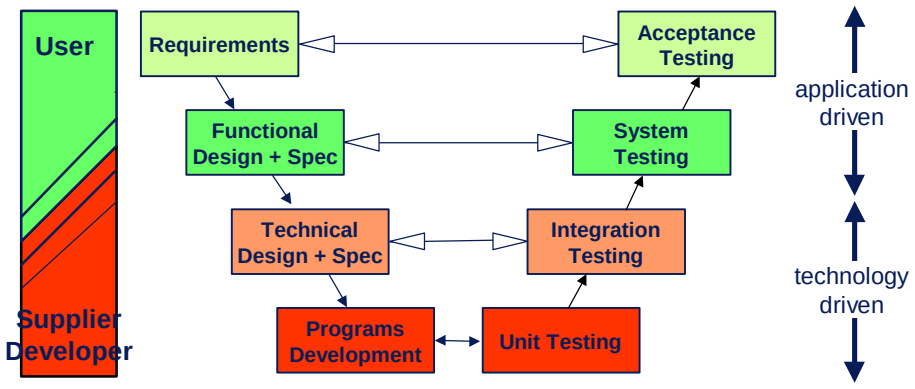
Typical ?

Management is often so focused
on finding solutions
that it fails to define the problems

* * *

“I don’t want to hear your problems,
I want to hear your solutions”

Who Does What



Suppliers We Need to Assess

- Standard packages
- Custom systems / bespoke solutions
- Customized / configurable systems
- Technology products
- Service providers

Audit new vendors, and don't forget old vendors!

Types of Audits

- 1st party audits
  - internal audits by the pharmaceutical manufacturer on itself
- 2nd party audits
  - by the user company on its suppliers (which can be an internal or an external organization)
- 3rd party audits
  - of suppliers by an organization acting independently of the pharmaceutical manufacturer(s)

Joint Audits

- Reduced time and effort to both users and suppliers
- Increased co-operation between user companies
- Summing-up the expertise
- Better base to realize changes, improvements
- Progress towards common auditing standards

Maturity Scale

1 Pharmaceutical companies auditing infrequently or at the wrong time
2 Individual pharma companies maintaining their own audit schedule and performing independent audits
3 Multiple companies visiting a single supplier for the same product
4 Pharma companies pooling resource to audit a supplier, but with each producing their own report
5 Pharma companies requesting a third party to audit a supplier and produce a single report
6 Pharmaceutical user groups in conjunction with suppliers manage joint audit process

Supplier Audit Cycle

Preliminary Assessment	initial evaluation , pre-qualification, pre-audit questionnaire
Detailed Audit	in-depth, full quality, pre-contract (!)
Follow-up Audit	re-audit, monitor audit
Surveillance Audit	periodic audit

GAMP Software Categories

Categ.	Software Type	Validation Approach
1	Operating System	Record version, including service pack; operating system challenged indirectly by the functional testing of the application.
2	Firmware	Non-configurable firmware: record version; configurable firmware: record version and configuration, calibrate instruments, verify operation against requirements; manage custom/bespoke firmware as categorie 5 software.
3	Standard Software Packages	Record version (and configuration of environment) and verify operation against requirements; consider auditing the supplier for critical and complex applications.
4	Configurable Software Packages COTS	Record version and configuration, verify operation against requirements; normally audit the supplier for critical and complex applications; manage any custom/bespoke programming as categorie 5 software.
5	Custom (Bespoke) Software	Audit supplier and validate complete system

Audit Planning

- Prerequisites
- Preparing for the Audit
- GAMP or PDA Technical Report 32
- Conducting the Audit
- After the Audit
- Audit Report
- Follow-up

PDA - ARC

PDA Parenteral Drug Association www.pda.org
ARC Audit Repository Center www.auditcenter.com

Advantages

- Highly professional contents
- Cost savings
- Immediately available
- Reliably suppliers

Issues

- Less contact with supplier
- Relevant aspects covered?

Prerequisites

- Objectivity
  - The auditor must be unbiased
  - Gather factual evidence
  - Avoid personal judgements
  - Keep an open mind
- Independence
  - No conflict of interest
  - Avoid the appearance of conflict
- Courtesy
  - Be prompt and timely with all communication
  - Behave like a guest
  - Observe all site safety and security provisions
  - Establish a professional report

Preparing for the Audit

- Pre-work requirements
- Audit team selection
- Planning and scheduling
- Preparing tailored audit criteria

Pre-Work Requirements

- Supplier profile
  - commercial focus, market position
  - financial stability
  - organizational set-up & complexity
  - focus quality management
- Product profile
  - description: what is it
  - market it was designed for
  - consistence: s/w, h/w, …
  - related things: what's included
  - target use
  - related risks
- Specific client needs

Previous Audit Info

- Past performance is a good measure of future performance
- Good lead for problematic areas
- Communicate intra/inter company
- Check confidentiality agreements if results were provided by other clients
- Input for surveillance program

Audit Team

- Experienced lead auditor (certified ?)
- Skill assessment & fulfillment
- Individuals with different skill sets, e.g.
  - Users and QA members — testing procedures, change management, adherence to stated QA/QC standards
  - IT professionals and engineers — product development, software/ hardware standards, security, technical documentation

Planning & Scheduling

- Communication with supplier
  - preliminary scheduling: phone, e-mail
  - formal letter and schedule
  - negotiated best fit for execution
  - confirm dates and schedules
- Audit questionnaire
  - according to GAMP or PDA Technical Report 32
  - lead time at least 2 weeks
- Tailored audit criteria

PDA Technical Report 32

1. Quality System
2. Project Management
3. Methodology
4. Testing
5. Configuration Management
6. Manufacturing
7. Documentation and Records Management
8. Security
9. Training and Education
10. Maintenance

PDA Technical Report 32

1. Quality System
2. Project Management
3. Methodology
4. Testing
5. Configuration Management
6. Manufacturing
7. Documentation and Records Management
8. Security
9. Training and Education
10. Maintenance

Checklist Example from TR32

#	Question	Answer	Objective Evidence
24.	Do testing documents exist for:		
24.1	Unit level testing?	Y	Unit level testing corresponds to the software item testing. See procedure "Software Item Testing", SIT002A.
24.2	Integration testing?	Y	Integration level testing is performed in the test phase software item test. The stepwise composition of system components up to the complete system is integrated into this test phase. See procedure "Software Item Testing "SIT02B and C.
24.3	System level testing?	Y	System level testing covers complete system functionality, including system interfaces to other systems; it includes the test phases "System Test" and "Interface Test".

Conducting the Audit

- Opening
  - review purpose, scope, objectives
  - agree on common goal
  - schedule
  - supplier presentation (limit 30', facility tour?)
- Collecting Evidence
  - audit guide, criteria checklist, follow-up list
  - interviews: establish rapport, confirm/verify results, suspend judgement, no debate
  - document and record findings
- Wrap-up
  - meeting review
  - follow-up list
  - preliminary observations list
  - obtain supplier acknowledgement

After the Audit

- Draft Report published within 10 working days
- 10 working days for supplier's review and formal comment
- 30 days for Response and Commitment Report
- Request for extensions ?
- Supplier status reports
- Metrics?
- Follow-up
  - quick hits/easy fixes and extended term
  - set due dates

Report Access & Distribution

- Establish who will receive copy of final report and source material
- Minimal distribution
- Intranet not recommended

Content of Report

- Cover Page
- Assessment/ Audit History
- Table of Contents
- Introduction: purpose, scope, team members
- Description of Suppliers Business
- Summary: key audit areas, key observations (+ & -)
- Response and Commitment
- List of Evidence: documents reviewed, referenced (no copies)
- Detailed Results: audit checklist

Some Typical Areas of Concern

- Documentation generally weak
- Testing
  - test cases not defined under GxP
  - review of results
- Change control system missing
- Subcontractors not under control
- Not familiar with pharmaceutical regulations / guidelines

Supplier Acceptance or Rejection

Based on the outcome of the audit you may decide

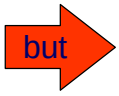
- to use the supplier unconditionally
- to use the supplier for certain products or versions only
- to use the supplier subject to specific corrective actions
- to agree with the supplier on the application of a documented QMS for the purposes of the contract
- to prohibit the use of the supplier

The Verification Process May . . .

Look good:	Does not look good:
• Validation would be the same as for in-house developed systems	• Do not purchase !! • Extensive validation required with large number of test cases • Consortium with other users

Vendors with ISO 9000

- Not recognized by regulatory bodies
- ISO 9000 Validation
- ISO 9000 process oriented
- Validation product oriented

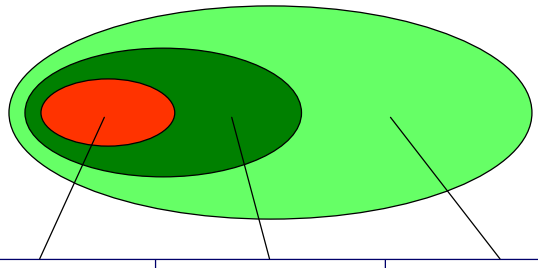


an ISO-certified vendor will (most probably) deliver a better product and documentation

Postal Audits

- No substitute to visiting a supplier
- Part of tendering process - further consideration justified?
- Preliminary info to focus effort on critical areas during the detailed audit
- Follow-up audit to review outstanding corrective actions
- Means of re-assessing on-going suppliers or service providers
- Auditing other premises of supplier with same QMS

Configurable Standard Packages



	Base Documentation	Kernel Documentation	Implementation Validation
Perform	Supplier Developer	Kernel Team	Owner User
Approve	ROCHE Q	ROCHE Q	ROCHE Q

Hints and Tips for Your Supplier Assessment

- Contact or join user group
- Visit reference customers
- Perform shared audits with other companies
- Operation ? documentation ??
- Plan for pilot installation
- Use your own license template
- Negotiate escrow agreement
- You cannot buy a validated system

Escrow Agreement

"An Escrow is a deed, a bond, money, or a piece of property held in trust by a third party to be turned over to the grantee only upon fulfillment of a condition."

from http://www.webster.com/

Auditor Code of Ethics (1)

1. I will be honest, impartial, and candid and will demonstrate freedom of mind and approach that will ensure objective viewing of the operation being audited.
2. I will conduct myself in a dignified manner that reflects well upon my profession and my company.
3. I will inform my company of any personal involvement (business connections, financial interests, employment history, or personnel or family affiliations) that might influence, or appear to influence, my judgement ort jeopardize my independence in my ability to assess the suitability of the operation being audited.

Auditor Code of Ethics (2)

4 I will undertake only those audits compatible with the degree of training, experience, and proficiency I hold with regard to the operation being audited.

5 I will issue reports that clearly, factually, and accurately describe the operation being audited, and that are constructive in nature.

6 I will not disclose information concerning the business affairs or technical processes of the client/ supplier without obtaining prior written consent to do so from the client's/supplier's management.

Auditor Code of Ethics (3)

7 I will not disclose any proprietary information or confidential data provided by a company being audited without obtaining consent to do so from that company's management.

8 I will strive to contribute to the development of improved audit techniques and methods within the quality audit profession and the PDA Process Model.

Hot Buttons of CSV

Essential key points that characterize
a sound validation approach, such as:

- Four eyes principle
- Team approach
- Owner is responsible
- Validation plan
- Predefined test results
- Independent approval
- Change management
- Ongoing training
- Requirements traceable
- Expert judgement
- Documentation of results
- Operation ? documentation
- Development method
- Ongoing evaluations
- Supplier assessment not delegated
- Archive well organized
- Risk assessment
- Standard Operating Procedures
- System access defined
- Never touch a standard source code

Frequent Misconceptions of CSV

- Long-time use = validation
- One-off activity
- Not needing documentation
- Documentation will always be voluminous
- Just software testing
- Not necessary to know requirements/ user needs
- Just paper generation
- CSV is a job for IT or QA/QC
- Regulatory bodies don't care about IT systems
- We bought a validated system