Current Practices of COMPUTERIZED SYSTEM VALIDATION

The less manual the better
The more automated the better
Less transcripts the better
Electronic documentation
Electronic Signature

- Basics of Computerized System Validation
- Life Cycle of Computerized System
- Life Cycle Approach
- Electronic Records and Electronic Signatures: Compliance Point of View
- Data Integrity
- Testing as Per Gamp 5 Guidelines
- Auditor's Perspective
Dear Customers / Friends,

Kevin has an impressive legacy of partnership with its customers in successfully applying technology-based solutions and supporting their competitiveness. We are proud of our reputation as a reliable & trustworthy solutions provider for factory automation as well as Regulatory Compliance Services.

Our corporate culture is one of dedication, respect, and continuous improvement. We measure our success by our customers’ successes.

In a time marked by rapidly changing customer expectations, I am enthusiastic about the opportunities available for us to address the emerging requirements of our customers.

Yours Sincerely,

Ketan Khambhatta,
Managing Director

Founded in 2000, Kevin Technologies is a leader in Automation for Life Sciences, Starch & Edible Oil, Consumer Packaged Goods & MES (Manufacturing Execution Systems) solutions. We are also one of the largest companies, in the area of Regulatory Compliance & Validation for FDA approved facilities across pan India.

We specialize in conceptualization & development as well as engineering of automation and supervisory control systems. Kevin helps clients meet their business objectives by providing effective project management capabilities and expertise in state-of-the-art technologies including Regulatory Compliance & Validation Services.

Our Mission
To provide technical excellence through innovation teamwork and commitment.

Our Ultimate Vision
To be the number one company in the area of expertise that we operate in, especially Factory Automation & Regulatory Compliance Services.
Basics of Computerized System Validation

In recent years, we have observed an upwards trend in the use of computerized systems in the pharmaceutical industry. If we talk about guideline-driven industries, pharmaceutical industry will lead the list. These guidelines pull towards validation and documentation at different stages.

Computerized systems are also not exempted from it. They are required by USFDA, EMA, GMP, GCL, GLP. CSV also helps to increase system uptime and reduce failure rates and identify defects at initial stages which cost heavily once systems go live. It also ensures product and data quality through precise documentation processes. USFDA and EU have given guidelines for handling Electronic records & Electronic signature through a guideline like 21 CFR part 11 and EU annex 11, respectively.

We show v-model approach of Good Automated Manufacturing Practice version 5 (GAMP 5) is a guideline developed by ISPE.

Foremost, we have shown here a few general questions to understand the requirement of validation for systems:

- Does the system create regulated records?
- Does the system maintain regulated records?
- Does the system modify regulated records?
- Does the system archive regulated records?
- Does the system retrieve regulated records?
- Does the system transmit regulated records?
- Does the system support product release?
- Does the system handle data that could impact product purity, strength, identity?

If any answer turns to yes in the above table, then it triggers computerized system validation.

Life Cycle of Computerized System

Now we will understand the V-model from GAMP 5, which will be implemented in the project and operation phases.

As per guidelines given in GAMP 5, Risk Assessment is involved at different stages of Project and Operation phases of Life cycle approach.

**Life Cycle Approach**

*Life cycle activities should be scaled according to:*

1. **RISK ASSESSMENT**
   - System Impact on Patient Safety
   - System Impact on Product Quality
   - System Impact on Data Integrity

2. **RESULT OF SUPPLIER ASSESSMENT**

Regulated companies should seek to maximize supplier involvement throughout the system life cycle in order to leverage knowledge, experience, and documentation, subject to satisfactory supplier assessment.

3. **SYSTEM CATEGORIZATION**

System Complexity & Novelty.

One has to understand that specific V-Model will be decided as per software categories.
SOFTWARE CATEGORIES (EACH CATEGORY HAS ITS OWN APPROACH OF VALIDATION).

Apart from these guidelines, one should also be aware of 21 CFR Part 11 and EU Annex 11—Electronic Records and Electronic Signatures (ER & ES):

**Electronic Records and Electronic Signatures:**
Compliance Point of View

Following are the sequential stages to achieve the compliance:

STAGE-A: EDUCATE TEAM

Educate project teams in the new company approach, ensuring an understanding of how compliance and benefits are to be achieved, and a commitment to resolve any non-compliance.

STAGE-B: DETERMINE WHETHER ER & ES REGULATIONS APPLY

If they do apply, ensure the User Requirements Specification contains requirements for electronic records and signatures that meet current company policies and standards. An initial identification of which electronic records and signatures will exist within the system should be included in the URS.

STAGE-C: ASSESS SYSTEM

The assessment should consider:
- The business processes that create and update records
- The purpose of any electronic signatures which records are being signed
- Any data supporting the electronic records or signatures

Appropriate technological and procedural controls should be selected using GAMP standards.

<table>
<thead>
<tr>
<th>CATEGORY TYPE</th>
<th>TYPICAL EXAMPLES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Category-1 Infrastructure Software</td>
<td>![Windows Logo]</td>
</tr>
<tr>
<td>Category-3 Non-Configured Software</td>
<td>![Micro-Controller Logo]</td>
</tr>
<tr>
<td>Category-4 Configured Software</td>
<td>![HMI Logo]</td>
</tr>
<tr>
<td>Category-5 Customized Software</td>
<td>- Internally and Externally developed IT Applications &amp; process control Applications - Spreadsheets-Macro</td>
</tr>
</tbody>
</table>

*Logos displayed are the properties of respective companies.*
This shall include following types of controls:
- Type (automatic, manual, combination)
- Date and time stamped
- Identification of time zone
- Amount of information retained (who/what/when)
- Access control and security of the audit trail
- Retention of the audit trail
- Backup and restore of the audit trail
- Procedures for managing the audit trail
- Retention of previous versions of data
- Purpose: e.g., for auditing of planned authorized changes to data or for detecting unauthorized change (fraud attempts)

A combination of these controls may be necessary to adequately manage the risk. The selected measures should be implemented and documented.

"Validation is not destination, it's continues journey to achieve high quality"

- Mr. Vivek Chanpura - GM- Project

**FACTORY AUTOMATION**

**REGULATORY COMPLIANCE SERVICES**

**COMPUTER SYSTEM VALIDATION**
being present in the operational environment.

- Within the project phase, testing helps to demonstrate fitness for intended use by verifying the correct operation of GxP critical functions and effective implementation of controls identified during risk assessment.

- Within the operational phase, risk-based testing may be required following a system change to demonstrate that:
  - Any new functionality is correct
  - Remaining original functionality has not been adversely affected.
  - Required risk controls are still in place and effective.

- Within the retirement phase, testing of data migration and/or archive and retrieval methods may be required prior to decommissioning the system.

Testing is an area of the system life cycle in which these are potentially large efficiency gains to be made by the appropriate leveraging of supplier involvement; in particular through the:
- Avoidance of duplication in testing.
- Leveraging of supplier test activities and evidence to the maximum practical extent.

Testing of a system is a combination of:
- Testing conducted by the supplier during basic development of the standard product.
- Testing conducted by the supplier (or integrator) during application-specific development i.e. the development of a solution customized or configured to the customer’s business process.
- Testing conducted by the regulated organization.

### DATA INTEGRITY – ALCOA FACTORS

**ATTRIBUTE**
- Signed / dated
- Clearly indicates who recorded the data or performed the activity
- Who wrote it/when

**LEGIBLE**
- It must be possible to read or interpret the data after it is recorded
- Permanent
- No unexplained hieroglyphics
- Properly corrected if necessary

**CONTEMPO RANEOUS**
- Data must be recorded at the time it was generated
- Close proximity to occurrence

**ORIGINAL**
- Data must be preserved in its unaltered state
- If not, why not
- Certified copies

**ACCURATE**
- Data must correctly reflect the action / observation made
- Data checked where necessary
- Modifications explained if not self-evident

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**DATA INTEGRITY**

Data Integrity refers to maintaining and assuring the accuracy and consistency of data over its entire life-cycle, and is a critical aspect to the design, implementation and usage of any system which stores, processes, or retrieves data.

**TESTING AS PER GAMP 5 GUIDELINES**

To overcome the current issues related to audit/regulatory compliance Testing shall be done as per GAMP5 best practices.

As per GAMP 5, “Testing computerized systems is considered a fundamental verification activity. Appropriate testing is a regulatory expectation”

Also, as stated in EU Annex 11 [8]:
“Evidence of appropriate test methods and test scenarios should be demonstrated. Particularly, system (process) parameter limits, data limits and error handling should be considered”

The understanding of both product and process assists in determining appropriate test scope and strategy. Traceability between requirements, identified risks and test cases is an important part of demonstrating this fitness for intended use.

Testing plays a vital role in the project, operational and retirement phases of a computerized system life cycle:

- During all phases, the main purpose of testing is to discover defects. Therefore, avoiding those defects...
## GENERAL OBSERVATION:

<table>
<thead>
<tr>
<th>Topic</th>
<th>Observation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Calibration / Inspection Checking not done</td>
</tr>
<tr>
<td>2</td>
<td>Computer control of master formula records</td>
</tr>
<tr>
<td>3</td>
<td>Backup file not maintained</td>
</tr>
<tr>
<td>4</td>
<td>Input / Output verification</td>
</tr>
<tr>
<td>5</td>
<td>Written record not kept of program and validation data</td>
</tr>
<tr>
<td>6</td>
<td>Backup data not assured as exact and complete</td>
</tr>
<tr>
<td>7</td>
<td>Written calibration / inspection records not kept</td>
</tr>
</tbody>
</table>

Routine calibration, inspection, checking of automatic, mechanical, electronic equipment is not performed according to a written program designed to assure proper performance.

Appropriate controls are not exercised over computers or related systems to assure that change in master production and control records or other records are instituted only by authorized personnel.

Failure to maintain a backup file of data entered into the computer or related system.

Input to and output from the computer related systems of formulas records or data are not checked for accuracy.

A written record of the program along with appropriate validation data has not been maintained in situations where backup data is eliminated by computerization or other automated processes.

Backup data is not assured as exact complete secure from alteration, erasure or loss through keeping hard copy or alternate systems.

Records of the calibration checks inspections of automatic, mechanical or electronic equipment, including computers or related systems are not maintained.

These systems are used for your stability chambers, ultraviolet (UV) and infrared (IR) spectrophotometer, and for thin layer chromatography (TLC)."

Example-2
“Your firm failed to exercise appropriate controls over computer or related systems to assure that only authorized personnel institute changes in master production and control records, or other records (21 CFR 211.68(b)).”

“Our investigator found that you have not validated 12 computerized systems in your quality control laboratory.

“Your stand-alone computer systems lacked controls, such as routine audit trail review and full data retention, to prevent analysts from deleting data. Although you implemented a procedure to begin reviewing audit trails of your high performance liquid chromatography (HPLC) Empower system on January 11, 2016, you had not performed any reviews prior to our inspection.”