How Compliant and Efficient is Your Spectroscopy Workflow?

Focus on your science and meet tough regulatory demands

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Cary UV-Vis and Fluorescence Product Manager,
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Components of a compliant and streamlined workflow

Compliance Requirements:
21 CFR Part 11 & EU Annex 11

Cleaning validation

System Qualification

Method
validation

Workflow improvement

Audits/
assessments

Process
validation

Metrology

A comprehensive
enterprise content
management system

Training/
education

Pharmacopeia
Requirements

Custom procedure writing
(IQOQPQ, SOPs, etc.)

Computer system
validation (CSV)

Regulatory
submissions
Components of a compliant and streamlined workflow

Compliance Requirements:
- 21 CFR Part 11 & EU Annex 11

Workflow improvement

- Method validation
- Audits/assessments
- Process validation
- System Qualification
- Metrology
- Training/education
- Pharmacopeia Requirements
- Regulatory submissions

A comprehensive enterprise content management system

Custom procedure writing (IQOQPQ, SOPs, etc.)

Computer system validation (CSV)
The Solution…

Is not just a box (or a number of boxes!)
The Solution…

A complete workflow solution will:

• Optimize productivity
• Stay current with industry standards/best practices
• Expand lab throughput with the resources you have now
• Promote global consistency/standardization
• Minimize regulatory risk
• Manage workload spikes
Components of a compliant and streamlined workflow

✓ Using molecular spectroscopy to improve workflow

✓ Hardware Qualification

✓ Computer system validation (CSV)

✓ Pharmacopeia Requirements: e.g. USP <857>


✓ A comprehensive enterprise content management system?

✓ Custom procedure writing (IQOQPQ, SOPs, etc.)

✓ Training/education

✓ Method validation

✓ Cleaning validation

✓ Process validation

✓ Metrology

✓ Regulatory submissions

✓ Audits/assessments
Molecular Spectroscopy

UV-Vis and FTIR

Quickly determine sample identity and purity

Quick, rugged and reliable

Increased uptime
Ideal for multi-user laboratories

Non-destructive

Sample is available for further analysis
Ideal screening step before LC or MS

Low cost and easy to use

No expensive reagents or consumables
Spectroscopy Applications

Drug component or impurity identification

Stability studies and drug binding assays

Raw material QA/QC

Protein analysis

Improve productivity and reliability for all spectroscopy applications
Rapid and Reliable Full Spectrum Analysis to Improve your Drug Stability Workflows

- proteins absorb in UV (280 nm)
- but with the full UV spectrum you don’t miss anything!

Advantages of the Cary 8454:
• Quick and easy full spectrum analysis
• Robust instrument with no moving parts
• Powerful calculation capabilities within the software
• UV-Vis is non-destructive so samples are recoverable

aggregation index (AI): $\frac{OD_{350}}{OD_{280} - OD_{350}} \times 100$

Application example: UV-Vis screening prior to HPLC

doi:10.1016/j.ejps.2009.06.001
Eliminate sample dilution for fast and accurate answers

- Save time and sample
- Improve workflow
- Reduce user errors

Typical samples:
- DNA/RNA (dsDNA, oligonucleotides)
- proteins

Reliably measure:
- Component concentration
- Sample purity

Measurements made using 4 µL BSA protein and the 1 mm path length cap option.
Application example: Protein Stability testing

Experiment: compare innovator monoclonal antibody and its Biosimilar

Method: increasing concentrations of a chemical denaturant (guanidine hydrochloride)

Protocol: changes in spectra show global conformational changes in the protein structure

Cary 60 benefit: ease of use, reliability and rapid results
Fast and confident QA/QC testing of packaging: Increased confidence in API safety

**Experiment:** Improper packaging can cause API degradation. Quick measurements to identify polymers by comparison to standards, and confirm the identity of packaging materials

**Method:** USP 661.1

**Cary 630 benefit:** Robust design based on out-of-lab instrumentation with user-friendly software for error-proof operation

**Protocol:** Lets see…
Streamline your analysis in QA/QC with four steps to certainty

1. Open the software
Streamline your analysis in QA/QC with four steps to certainty

2

• Software automatically recognizes the correct sampling interface and guides the user through the measurement
Streamline your analysis in QA/QC with four steps to certainty

- Easy-to-understand display of the data.
Streamline your analysis in QA/QC with four steps to certainty

- Automatically converts “data” to an actionable result
- Programmed for critical action levels with color coded cues (red, green, yellow)
- Quickly assess results for increased productivity
Streamline your USP<661.1> measurements
Pharmaceutical package testing made easy

- Improper packaging can cause API degradation
- Use transmission or ATR to identify polymers by comparison to standards
- Using the Cary 630 this test can be easily and rapidly implemented

Certainty via a library search result;
The unknown blister polymer, which was searched against the library of known USP 661.1 polymers. The top hit is a nearly perfect match to the correct library material, PVC + SBR copolymer (blue spectrum).
Components of a compliant and streamlined workflow

✓ A workflow improvement
✓ Hardware Qualification
✓ Computer system validation (CSV)
✓ Pharmacopeia Requirements: e.g. USP <857>
✓ A comprehensive enterprise content management system?

✓ Custom procedure writing (IQOQPQ, SOPs, etc.)
✓ Training/education
✓ Method validation
✓ Cleaning validation
✓ Process validation
✓ Metrology
✓ Regulatory submissions
✓ Audits/assessments
## Instrument Performance Testing

<table>
<thead>
<tr>
<th>During installation</th>
<th>Routine performance check</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Tests included in Equipment Qualification Plan</td>
<td>• Instrument test suites included in software</td>
</tr>
<tr>
<td>• Pharmacopeia compliant</td>
<td>• Tests are carried out by user</td>
</tr>
</tbody>
</table>

**Equipment qualification plans for UV-Vis and FTIR systems**

![Cary WinUV Scan Application](image1.png)

![MicroLab FTIR Software](image2.png)

![UV-visible ChemStation Software](image3.png)
USP <857> Ultraviolet-Visible Spectroscopy
Pharmacopeia-prescribed instrument performance tests

Control of Wavelengths:
Six replicate measurements: Hg or D\textsubscript{2} Emission Lines, REE Oxide Solution (e.g. HoO\textsubscript{2}) REE Glass OR a single measurement using a Diode Array. Mean values & certified value

Control of Absorbance:
Six replicate measurements. Two or more Absorbance levels
e.g. Acidic Potassium Dichromate / Neutral Density Filter

Limit of Stray Light
Measurements at 190-205nm, 210-259nm, 250-320nm, 300-385nm.
• Aqueous potassium chloride, aqueous sodium or potassium iodide, acetone, aqueous sodium nitrite (50g/L)

Resolution
Measure ratio of Absorbance (Toluene in Hexane) at ~ 269 and 266nm
• Acceptance Criteria NLT 1.3 (2nm spectral bandwidth)
USP <857> Ultraviolet-Visible Spectroscopy
Automated assurance via the software

Six overlaid wavelength scans of holmium perchlorate using an Agilent Cary 60 UV-Vis spectrophotometer and Agilent Cary WinUV software

PASSED! Automated applications report the %T measured for each stray light analytical sample, and reports a Pass or Fail against the tolerance for the Agilent Cary 60 UV-Vis.
Certified Reference Materials for UV Instrument Qualification

ISO 9001, GLP, GMP and international regulatory standards require evidence that a UV instrument is working to specification and is “fit for purpose”.

- Certified Reference Materials (CRMs) are used to qualify instrument performance
- The CRMs required are dependent on the regulatory standards the user is working to

Agilent’s standard kits include solutions for:
- Photometric accuracy and precision
- Wavelength Accuracy and precision
- Stray Light
- Resolution

<table>
<thead>
<tr>
<th>Parameter Tested</th>
<th>Wavelength Region</th>
<th>EP</th>
<th>DAB</th>
<th>USP</th>
<th>ASTM</th>
<th>TGA</th>
<th>BP</th>
<th>Material</th>
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<tbody>
<tr>
<td>Photometric Accuracy</td>
<td>UV</td>
<td>●</td>
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<td>●</td>
<td>●</td>
<td>Potassium Dichromate solution</td>
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<tr>
<td></td>
<td>Visible</td>
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<td></td>
<td></td>
<td>●</td>
<td></td>
<td>●</td>
<td>Potassium Dichromate solution</td>
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<tr>
<td></td>
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<td>●</td>
<td>●</td>
<td>●</td>
<td>Neutral Density Glass filters</td>
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<tr>
<td>Wavelength Calibration</td>
<td>UV/Visible</td>
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<td>●</td>
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<td>Holmium Oxide solution</td>
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<tr>
<td></td>
<td>UV/Visible</td>
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<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>Holmium Oxide glass filter</td>
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<tr>
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<td>Visible</td>
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<td>●</td>
<td>●</td>
<td>●</td>
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<td>●</td>
<td>Didymium Glass filter</td>
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<td>Visible</td>
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<td>Far UV</td>
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<td>●</td>
<td>●</td>
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<td>●</td>
<td>Rare Earth Oxide solution</td>
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<tr>
<td></td>
<td>UV/Visible</td>
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<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>Samarium Oxide solution</td>
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<tr>
<td>Stray Light</td>
<td>UV/Visible</td>
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<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>Stray Light Cut-off filters</td>
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<tr>
<td>Resolution/ Bandwidth</td>
<td>UV/Visible</td>
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<td>●</td>
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<td>Toluene in Hexane</td>
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<tr>
<td></td>
<td>UV</td>
<td>●</td>
<td></td>
<td></td>
<td>●</td>
<td></td>
<td>●</td>
<td>Benzene Vapour</td>
</tr>
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</table>
Equipment Qualification: IQ/OQ
Analytical Instrument Qualification – On Demand

Installation Qualification – Hardware and Software checking:

1. Verify purchase order documentation
   • ensure that instrument or software matches requirements
2. Preparation and Installation documents
   • gather and record all necessary items
3. System and Installation documentation
   • including reference and user manuals
4. Product Quality Assurance documents
   • evidence the vendor has built and developed the product according to internal standards
5. Start Up Test
   • verify everything starts properly
6. Instrument check
   • demonstrate everything has been installed and connected
Compliance in the laboratory

Computer system validation

All systems (software + hardware) must be fully validated to support data generated for submission to regulatory agencies.

Validation establishes that a system can consistently and accurately produce results that meet a pre-determined specification.

Systems must be validated for their intended use and environment.
Guidelines and regulations for Computer System Validation (CSV). Both must be demonstrably met. And consistently so…

**GAMP5**
Risk-based approach/ V model documentation

**US FDA 21 CFR Part 11 & EU Annex 11**
Electronic records/signatures
CSV requirements: GAMP5

**GAMP5 (Good Automated Manufacturing Practice):** Conducting verifications is to demonstrate that the system functions as intended. This is accomplished by using the requirements and specifications as an objective standard to which the system is tested.

- ✓ Validation plan (VP)
- ✓ Risk assessment (RA)
- ✓ User requirement specification (URS)
- ✓ Functional requirement specification (FRS)
- ✓ Design/configuration specification (DS/CS)
- ✓ Installation qualification (IQ)
- ✓ Operational qualification (OQ)
- ✓ Performance qualification (PQ)
- ✓ Requirements trace matrix (RTM)
- ✓ Validation summary report (VSR)
GAMP5 V Model

- **RA**: Risk assessment
- **URS**: User requirement specification
- **FRS**: Functional requirement specification
- **DS/CS**: Design/configuration specification
- **IQ**: Installation qualification
- **OQ**: Operational qualification
- **PQ**: Performance qualification
- **RTM**: Report
- **Summary Report**

Validation plan → validate → Summary Report
RA → validate → URS
URS → validate → FRS
FRS → validate → DS/CS
DS/CS → validate → IQ
IQ → validate → OQ
OQ → validate → PQ
PQ → validate → RTM
RTM → validate → Summary Report
GAMP5 V Model

Risk assessment

User requirement specification

Functional requirement specification

Design/configuration specification

Validation plan

RA

URS

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DS/CS

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Installation qualification
Guidelines and regulations for Computer System Validation (CSV). Both must be demonstrably met. And consistently so…

**GAMP5**
Risk-based approach/
V model documentation

**US FDA 21 CFR Part 11 & EU Annex 11**
Electronic records/signatures
CSV Requirements
21 CFR part 11

Compliance with 21 CFR part 11 centers on five key (Data Integrity) questions:

• Is electronic data available?
• Is electronic data reviewed?
• Is meta data (audit trails) reviewed regularly?
• Are there clear segregation of duties?
• Has the system been validated for its intended use?
Compliance Requirements
US FDA 21 CFR Part 11 and EU Annex 11

So how do we help prove compliance with 21 CFR part 11?

✓ Electronic records security
✓ Audit trails
✓ Backup
✓ Disaster recovery
✓ Login/password security
✓ Electronic signatures
✓ Data integrity
A modular and upgradable software platform

- **General Purpose (base) software**
  - Standard software for the *routine* or *QA/QC laboratory*

- **Advanced module**
  - Upgrade for the *research and/or method development laboratory*
    - For method development, macro programming, advanced calculations etc

- **Biochemical Analysis module**
  - Upgrade for the *biochemical laboratory*

- **Dissolution Testing module**
  - Upgrade for the *product formulation and/or QA/QC laboratory*
Compliance Requirements
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- **Compliance Pack (G5182AA)**
  - Upgrade for (OpenLab ECM) server-based *FDA 21 CFR Part 11 compliance*
Compliance Requirements

Essential compliance features

• Configurable individual user names and passwords.

• Log of user name, instrument name, serial number and time stamp stored with all data files and included in all reports.

• All data must have its own audit trail.

• All actions **must be** recorded in audit trail:
  • Configuration changes
  • File/folder changes and administration
  • User privilege changes
  • Logon, logoff, system locks
Compliance Requirements
Dynamic user privileges

- A single Administrator account is used to:
  - Disable accounts
  - Remove or add privileges
  - Lock files to read only

- Give users as little or as much access as their roles merit
- Use preloaded roles or create your own
- Dynamic groups and privileges makes conforming to CFR21 Part 11 easier
Compliance Requirements
Automated file indexing and storage

- A comprehensive enterprise content management system makes organising projects and experiments easy and intuitive
- Allows the centralised storage of all data types including PDF and Microsoft Office documents
- All experimental and auxiliary data can be kept in one secure location
Compliance Requirements
Secure, centralised content management

- A comprehensive enterprise content management system provides the ability to allow or deny individual access to data in the secure, central location
- Automate scheduled back-ups or archiving to specific folders, draws, cabinet or locations
- Make files “Read Only” to prevent any revision or changes being made
Compliance Requirements
Easy access to file revisions

• Full traceability of all data.
• Data is never over-written but appended and you can access any version of the file from the original to the latest revision
• Easy-to-follow visible display of the number of revisions within the content manager
• Every revision can be easily loaded and checked or amended (if you have the authority)
Well-designed software and hardware enables an auditor to recreate the sequence of events that occurred at the time the result (or record) was generated using the electronic (meta) data:

• WHO performed the analysis?
• WHAT equipment was used to perform the analysis?
• WHEN was the analysis performed?
• WHY was the analysis performed?
• WHERE is the electronic (meta) data is stored?
Audits/assessments

A complete compliance solution will offer experts to help …

Perform the audit

✓ Review current processes, SOPs, and systems
✓ Benchmark against industry standards/best practices
✓ Perform risk/gap analysis

Develop an audit report

✓ Record findings/observations
✓ Make recommendations
✓ Suggest next steps
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For more information

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• Applications, brochures, flyers
• Product details
• Technology videos
• Compliance tools and services

Thank you