Technical Overview

Recommendations for Hemp Testing: Laboratory Compliance

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Abstract

Designed as a follow-up to the *Agilent United States Hemp Testing* white paper,[1] this technical overview presents recommendations to the industry on laboratory compliance. These recommendations are based on current Good Manufacturing Practices (cGMP) and industry experience in data quality. All manufacturers of edible hemp products require the safeguarding of testing data and accuracy of laboratory equipment. Paired with Agilent products and services, these recommendations will help your laboratory remain compliant with federal regulations.

Agilent compliance products and services are designed with current and future cannabis requirements in mind. Partnering with Agilent will help future proof your laboratory and reduce your risk from regulatory action.

Introduction

With the growing popularity and number of hemp products, the federal government has been struggling to ensure the quality and safety of these products. Due to the sheer number and variety of product types, a broad range of regulatory oversight exists. To add to the complexity, regulatory requirements are changing constantly due to the young age of the legislation. For a hemp testing/manufacturing facility, navigating this regulatory landscape can be difficult, and preparing for the future can seem daunting. In the Agilent white paper *United States Hemp Testing: Laboratory Compliance*[1], these requirements are broken down into three fundamental compliance topics:

1. Qualification/calibration of laboratory equipment
2. Data retention and availability
3. Data integrity controls

All three topics are of critical importance for hemp testing/manufacturing facilities as compliance in these fields are required for many hemp products.[1] As the industry continues to mature, it is expected that laboratory regulations will become increasingly stringent.

This technical overview will provide recommendations from Agilent for the industry concerning these topics. These recommendations are based on thorough research of current Good Manufacturing Practices (cGMP) and industry experience in data quality. Paired with Agilent products and services, these recommendations will help your laboratory remain compliant with current and future federal requirements.

Agilent: a leader in cannabis testing

With 30+ application notes and publications covering the entire operation of a standard cannabis testing facility, Agilent is at the forefront of cannabis analysis. All Agilent solutions and equipment are robust and maximize throughput to meet your individual laboratory needs.

As regulations continue to evolve, Agilent is ready to help you navigate increasing compliance requirements. With over 25 years of compliance delivery, Agilent was voted number one for instrument and software qualification and computer system validation services from an independent survey conducted in 2019.[2] When considering different vendors, align your laboratory with a company that will harmonize and future proof your organization.

Agilent recommendations for hemp testing laboratory compliance

The following sections describe Agilent recommendations for hemp testing/manufacturing facilities. These recommendations have been designed to assist laboratories in complying with cGMP.

Qualify/calibrate laboratory equipment

Follow a risk-based approach to evaluating the performance of laboratory equipment. Computerized equipment, such as chromatography instrumentation, capable of affecting laboratory conclusions should be controlled via a qualification life cycle. Plans should include regular maintenance and verification of equipment's individual parameters at periodic time points. High-risk parameters need to be measured for the equipment's entire range of use with calibrated tools. This should be followed by a periodic holistic chemical check demonstrating the instrument's functionality. These activities are normally broken into four events: Design Qualification (DQ), Installation Qualification (IQ), Operational Qualification (OQ), and Performance Qualification (PQ).[3] Regulatory guidance on instrument qualification/calibration can be found in United States Pharmacopeia's (USP) General Chapter <1058>.

When selecting laboratory equipment and designing a qualification plan, ensure that the manufacturer's specifications and the qualification range meet user requirements. This can be easily documented and achieved by following the format of Bob McDowall and Paul Smith's example in Table 1.[4] In this example, the laboratory has documented its method parameters range under the "Setting" column for each analytical method. Once this is done, the maximum and minimum values are used as the equipment's user requirements. If the instrument specification fails to meet these user requirements, the instrument is not fit for its intended use. Finally, laboratories must ensure that the equipment's reoccurring OQ will physically qualify the entire user requirements range. More information on this chapter can be found in Bob McDowall and Paul Smith's four USP <1058> white papers.[4]

If resources and instrument expertise are lacking, consider outsourcing these services. Agilent can deliver regular preventative maintenance and qualification services as directed by your instrument life cycle. Agilent engineers will clean/replace commonly contaminated/spent parts to ensure that your instruments deliver peak performance while minimizing unplanned downtime. This can be followed by an OQ, a metrology and holistic based testing suite that confirms critical system functions. OQs can be customized to align with your laboratory's user requirements. With the Agilent Automated Compliance Engine (ACE), qualifications can be done quickly, electronically, and securely. For more information, see the *Agilent Equipment Qualification Solution* brochure.[5]

Data retention and availability

The retention and availability of records is a requirement for all cGMP facilities. This applies not only to batch or manufacture reports but to all the documents or data files that were used to support batch analysis. Laboratories can archive their static data (paper records) in their designated records retention room, but dynamic data (e.g., chromatograms) cannot be properly stored in this fashion. The difference between static and dynamic data is discussed in the Agilent white paper *United States Hemp Testing: Laboratory Compliance*.[1] To ensure data retention, first captured electronic and processed data should be handled by a content management system to safeguard the originality and availability of your laboratory's analytical data.

Table 1. Example of user requirements, associated instrument specifications, and OQ protocol tests (McDowall and Smith).[4]

Use	Module	Setting	User Requirements	Instrument Specification	OQ Protocols Criteria to Verify Intended Use
Method	Pump	Flow	Range (mL/min)	0.001 to 10 Accuracy	Accuracy
A		0.5	0.5 to 2.1	≤1%	≤5.00%
B		2.1		Precision RSD	Precision RSD
C		1.8		≤0.07%	≤0.50%
Method	Pump	Gradient Formation	Range (%B)	0 to 100, in 0.1 increments	Steps 20, 40, 60, and 80%
A		35 to 75	25 to 75	<0.2 %RSD	Accuracy ≤2.00%
B		NA (Isocratic)			Linear gradient 100 to 0% (R^2 ≥0.999)
C		25 to 45			
Method	Autosampler	Temperature	Range (°C)	4 to 40 °C	Accuracy
A		NA (Ambient)	4	4 to 5 °C below ambient	Difference from setpoint ≥−2.0 °C and ≤5.0 °C
B		4			
C		4			

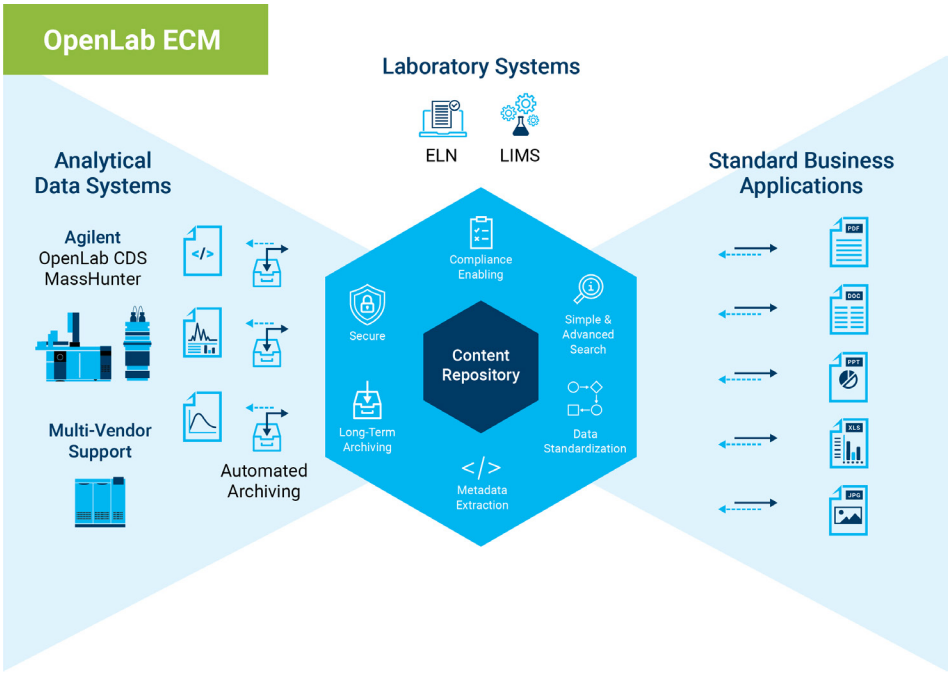

Figure 1. OpenLab ECM gives you a single repository for all your laboratory and non-laboratory data, content, and processes. The platform seamlessly integrates with common chromatography data systems, as well as other laboratory systems.

Your management system should be designed to harmonize, centralize, and protect your laboratory's data. This can easily be achieved using Agilent OpenLab ECM, an Enterprise Content Management system. ECM can store and secure all your data, from any technology or vendor that your lab produces including documents your lab may use to support its activities. It silently monitors your operation and secures data in a central location while ensuring timely completion of approvals, customized tasks, and lab-wide reports.

- Multiformatted data sweeping capability
- Single location for laboratory data
- Data event logger with search features for easy periodic review of all ECM data
- Data version capturing
- Electronic review
- Customizable user roles and privileges

For more information, see the *Agilent OpenLab Data Management Solutions* brochure.[6]

Data integrity controls

In the Agilent white paper, *United States Hemp Testing: Laboratory Compliance*, the advantages of technical controls for safeguarding data are explained.[1] Despite the benefits of technical controls, many laboratories are still heavily reliant on procedures alone to enforce quality policies. This can lead to exorbitant amounts of wasted time, transcription errors, deviations from working instructions, and even fraudulent cases. Invest in your laboratory's data security and automation by utilizing compliant capable acquisition software. The two largest Agilent chromatography software platforms, Agilent OpenLab CDS and Agilent MassHunter allow for easy customized control over your system. Avoid the use of Microsoft Excel and Adobe PDF programs for data processing, as their technical controls are limited.

Protect your laboratories source data with OpenLab CDS and MassHunter

Safeguarding acquisition data is crucial to maintaining the integrity of your laboratory's conclusions. With the advanced controls in OpenLab CDS and MassHunter, protecting your source data could not be easier.

- System security policies (screen timeout, password length, password frequency, etc.)
- Ability to create unique user accounts and roles (User, Manager, IT, etc.) to prevent the unauthorized deletion and alteration of data
  - Software and project logon access
  - Personalized user controls over instrument, project, method, sequence, data, and report access from within the acquisition software
- Ability to customize automated electronic analysis reports to meet internal SOPs
- Detailed audit trails with search features for easy periodic review

Regardless of the software you choose, data integrity controls are not enabled out of the box and will require strategic setup and validation to meet the requirements outlined in 21 CFR Part 11. Certificates of Software Validation or Quality from any vendor provide limited value as the U.S. Food and Drug Administration (FDA) requires laboratories to perform their own validation for intended use.[7] Computerized System Validation (CSV) is necessary to demonstrate that your setup is without critical errors and secure from data manipulation. Validation is not just a single event (like a qualification), but a controlled process that ensures your computerized

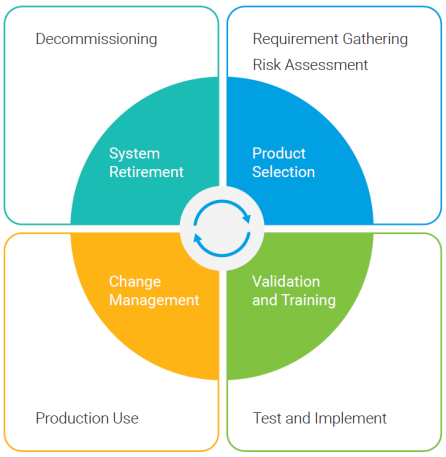

Figure 2. Life cycle of Computer System Validation.

systems are compliant throughout their entire operational lifetime. Take the time to document your computer's user and regulatory requirements and how those requirements are met by software controls. Controls that cannot be addressed by your software should be mitigated through procedures. Validate the system by testing these customized controls.

- Document user, regulatory, and manufacturer requirements
- Document how the system setup will meet the above requirements
  - Determine system vulnerabilities and create procedural controls to mitigate them
- Set up the system as documented
- Challenge the system to ensure data security and proper setup
  - Test custom user roles and privileges
  - Test custom calculations
  - Test the function of audit trails for high-risk actions
  - Test backup and archival procedures
- Create a user training plan
- Create a change control process to maintain the system's validated state during planned changes

If the software is unfamiliar, resources are restricted, or you lack a validation expert, consider leveraging the knowledge of your software manufacturer to assist you. Agilent has a team of compliance experts that can assist you in the validation of your computer system and make recommendations based on your needs. These services have been designed to reduce the time and money necessary to validate your laboratory's computerized system. For more information, see the *Agilent Computer System Validation Services* brochure.[8]

Conclusion

Federal and state regulations overseeing the quality of hemp and hemp-derived products will only become more stringent as the industry matures. As discussed in the Agilent white paper *United States Hemp Laboratory Compliance*, manufacturers who generate hemp-derived dietary supplements or drugs are already mandated to meet compliance requirements.[1] Laboratories that manufacture edible Cannabidiol (CBD) products should anticipate possible FDA oversight similar to dietary supplements. Agilent's products and solutions can help laboratories comply with current and future regulations, but the onus still falls on the manufacturer (or product owner). Ensure that your laboratory is audit-ready by being proactive with your laboratory compliance.

Further reading on Agilent software data integrity controls can be found in the following white papers:

- Support for Title 21 CFR Part 11 and Annex 11 Compliance: Agilent OpenLab CDS[9]
- Support for Title 21 CFR Part 11 and Annex 11 Compliance: Agilent MassHunter for LC/MS[10]
- Support for Title 21 CFR Part 11 Compliance: Agilent MassHunter for GC/MS[11]

References

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9. Support for Title 21 CFR Part 11 and Annex 11 compliance: Agilent OpenLab CDS, *Agilent Technologies white paper*, publication number 5994-2223EN, **2020**.
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11. Support for Title 21 CFR Part 11 Compliance: Agilent MassHunter for GC/MS, *Agilent Technologies white paper*, publication number 5991-6909EN, **2016**.

Have confidence in your data integrity program with Agilent CrossLab, the industry leader in instrument and software qualification and computer system validation services.

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Agilent products and solutions are intended to be used for cannabis quality control and safety testing in laboratories where such use is permitted under state/country law.

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