CANNABIS POTENCY II:

AN EXAMPLE OF APPLYING ISO 17025 PRINCIPLES TO A TEST METHOD

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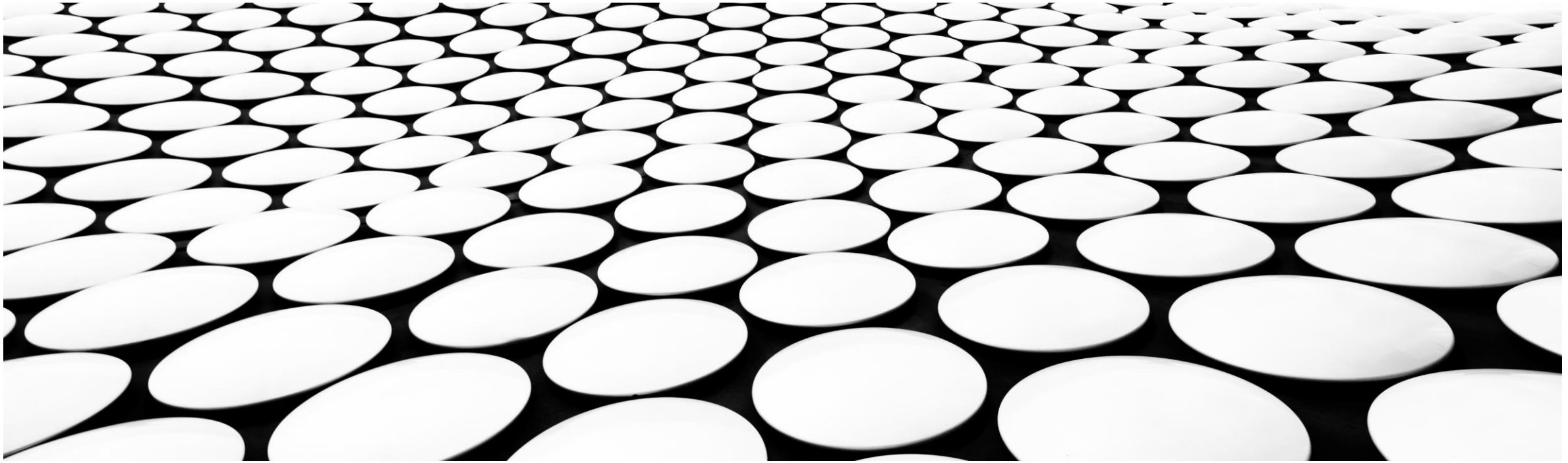
ON BEHALF OF PJLA, INC. - APRIL 13, 2020



PRESENTER: JEFF RAYMOND

- PhD University of Michigan, Engineering; Additional graduate degrees in chemistry and public policy
- ISO 17025 Lead Assessor, Technical Assessor, and Internal Auditor
- Owner; OligoMacro Consulting Services; Board of Directors (three vertically integrated cannabis groups)
- Statistical Process Control/Statistical Quality Control and Statistics SME
- Priors: Paragon Laboratories (VP Operations); Texas A&M (Founding managing director of the Laboratory for Synthetic-Biologic Interactions); AFRL (Sr. Research Fellow); Dow Corning (Development Chemist); US Army
- Highlight: 80+ Publications and patents in the general area of biomaterials and nanomaterials analysis
- Highlight: 100+ Public presentations including seminars, invited lectures, expert testimony, and lawmaker support

GOALS OF SERIES

- Probe a medium complexity process in the lab
- Alignment with ISO 17025 standard
- Clean up of documentation
- Design of processes
- Determination of authorization mechanisms
- Execution of method with appropriate controls
- Execution of method with appropriate staff authority levels
- Roll out from this method to other methods - Start small with a minimal PDCA cycle

LAST TIME….

- Verification of Method
  - General recommendation: Establish set-in-stone, statistically meaningful process with known triggers
- Method Uncertainty
  - General recommendation: Use the foundational standard of the organization from which you draw your method
- Calibration
  - General recommendation: Traceable standards with known uncertainty - zero-deviation policy for calibration and ongoing calibration
- Response to Deviations
  - Without ongoing verification, statistical confidence in calibration, and knowledge of method variation (MU), your response to deviations are just “thundering at the sky”

QUALIFICATION I

- Typical Timeline
- **Pre-installation qualification - Identification of key requirements and confirmation that requirements are met by the system/purchase**
- Installation - Installation of all hardware and software, preparation of space, acquisition of consumables
- **Post-install qualification - Confirmation of key requirements being met for the entire system as installed (Stats!)**
- Method development - Documentation and workflow definitions developed and generated in a version 1 state
- Validation - Initial execution of method over multiple days assessing multiple knowns in order to confirm capability of method (Stats!)
- Initial verification - Initial execution of method over multiple days assessing multiple knowns spanning all matrices verifying the validation based with sample-like materials (Stats!)
- Ongoing verification - Policy and procedures to continually monitor the performance of the system and process (Stats!)

QUALIFICATION II

- Initial (Pre-Installation) Qualification - Hardware
- Identification of Hardware Requirements:

  Must be able to discriminate between THCA, THC, CBD, CBDA - to the exclusion of all other molecules
  Must be able to maintain calibration for a 24-hour period
  Must be able to detect via UV absorption measurements on a Beer's Law basis
  Must be able to use multiple solvents and provide solvent gradients during an analysis
  Must be able to assess a minimum of one sample every 30 minutes
  Must have an auto-sampling mechanism that is capable of 24-hour runs (overnight)
  Must have a modern PC system capable of automated security and OS updates

QUALIFICATION III

- Initial (Pre-Installation) Qualification - Software
- Identification of Software Requirements:

  Must have software that does not conflict with automated security and OS updates
  Must have software that has programmable auto-analysis (integration) of calibration, quality control, and samples
  Must have software that is programmable to auto-flag data based on set conditions (triggers)
  Must have software that allows for automated data transfer to laboratory LIMS software

QUALIFICATION IV

- Initial (Pre-Installation) Qualification - Service/Vendor
- Identification of Service/Vendor requirements:

  Vendor must be willing and able to supply all materials for the system for a minimum of 5 years
  Vendor must be willing and able to supply a service contract for a minimum of 10 years
  Vendor must be willing and able to provide priority (2 day minimum) onsite response
  Vendor must be willing and able to provide thorough training and training materials for the technology
  Vendor must be willing and able to identify a vendor with IUPAC traceable certified standards for qualification of the instrument post-install
  Vendor must be willing and able to perform qualification runs utilizing certified standards at the bottom, middle, and top of the intended range of analysis for each analyte using a set requirement for accuracy, bias, and precision

QUALIFICATION V

- Internal Policy
- Example of Internal Policy for the Qualification of Cannabis Potency

  “The laboratory will determine and document the requirements for onboarding a Cannabis Potency test technology by identifying the system requirements prior to going to market. The laboratory will establish a quantitative basis for evaluating vendors - and will also establish a quantitative requirement for qualification of the system.”

  “Post-installation (final) qualification of the system will include the assessment of certified single-analyte standards to confirm throughput, accuracy, precision, and bias for each analyte. The statistical basis for the quantitation of the system shall be three runs under separate calibrations for a top-of-range, bottom-of-range, and middle-of-range set of standards…”

QUALIFICATION VI

- Internal Policy
- Example of Internal Policy for the Qualification of Cannabis Potency

  “Qualification Performance shall be assessed as follows:
  Between-run data sets must be statistically equivalent.
  All data shall be assessed for normality and normality must not be rejected.
  All data shall be assessed for skewness and the median for each run shall be no more than 5% (relative) from the mean.
  No two data point shall be more than +/- 20 RPD from each other
  No two consecutive data points shall be more than +/- 10 RPD from each other
  The bands for the standard error of the mean for each run must have some overlap with each of the other runs
  Summary statistics for each run and the total data set must be generated and evaluated
  The in-run standard deviation (expressed as a percent) shall be no larger than 10% of the known value
  The total standard deviation of the data set shall be no larger than 5% of the known value
  The average of the total data set shall be no further than 3% from the known value”

  Qualification should be the easiest/tightest study - single analyte, neat samples. This will be tighter than your validation/verification studies.

QUALIFICATION VII

- The standard:
- “4.1.1 Laboratory activities shall be undertaken impartially and structured and managed so as to safeguard impartiality.”
- “5.6 The laboratory shall have personnel who, irrespective of other responsibilities, have the authority and resources needed to carry out their duties, including: …e) ensuring the effectiveness of laboratory activities.”
- “6.2.6 The laboratory shall authorize personnel to perform specific laboratory activities, including but not limited to, the following: …a) development, modification, verification and validation of methods;”
- “6.4.4 The laboratory shall verify that equipment conforms to specified requirements before being placed or returned into service.”
- “6.4.5 The equipment used for measurement shall be capable of achieving the measurement accuracy and/or measurement uncertainty required to provide a valid result.”

QUALIFICATION VIII

- REVIEW
- Give it a name - Call out the policy
- Record - Document decision making
- Lean into the requirements - Use clear language, make it quantitative whenever possible
- Make it repeatable - Could another group in the organization perform the qualification process?

QUALIFICATION OF STAFF/DEMONSTRATION OF COMPETENCY I

- This can be the EASIEST process to structure:
- “A staff member shall be considered initially qualified if the following evidence exists:
  - Readily verifiable training, experience, and education sufficient to allow them to reproduce a multi-day validation study that is as robust as the study performed to generate the initial measurement uncertainty, accuracy, bias, and precision statements of the method.
  - This initial demonstration study shall generate results that are statistically indistinguishable from the foundational study.
  - This study shall be duplicated twice: [a] the first shall be done under the supervision of a qualified individual to the satisfaction of the trainer and [b] the second shall be performed without input or observation by the trainer and shall be reviewed and approved by an authorized person prior to qualification of the individual.
  - The individual will be considered qualified when all objective evidence of the completion of the above has been assembled in a permanent training document and final approval of qualification is both documented and communicated.”
- Sufficiently robust DOC/IDOC (demonstration of competency, initial) section in the SOP.
- Sufficiently robust Job Description.

QUALIFICATION OF STAFF/DEMONSTRATION OF COMPETENCY II

- Important to not vary requirements for demonstration, even if combinations of education, training, and experience exist.
- Does the evidence of competency for the analyst, cluster of qualified individuals, and the process as a whole show competency at a sufficient level for in-court scrutiny?
- Does the qualification process meet the needs of the process, the customers, the regulatory bodies, and the organization?
- Was our qualification process developed based on our own expertise?
- Have we checked our reality through benchmarking, internal audits, and participation in industry work groups or interlaboratory studies?
- Are we reviewing the continued fitness of our process for qualification?

QUALIFICATION OF STAFF/DEMONSTRATION OF COMPETENCY III

- The standard
- “6.2.2 The laboratory shall document the competence requirements for each function influencing the results of laboratory activities, including requirements for education, qualification, training, technical knowledge, skills and experience.
- “6.2.3 The laboratory shall ensure that the personnel have the competence to perform laboratory activities for which they are responsible and to evaluate the significance of deviations.”
- “6.2.5 The laboratory shall have procedure(s) and retain records for: …a) determining the competence requirements; …c) training of personnel; …e) authorization of personnel; …f) monitoring competence of personnel.”
- “6.6.3 The laboratory shall communicate its requirements to external providers for: …c) competence, including any required qualification of personnel;”

HYGIENE I

- The Standard
- 6.3.1 The facilities and environmental conditions shall be suitable for the laboratory activities and shall not adversely affect the validity of results.
- 6.3.2 The requirements for facilities and environmental conditions necessary for the performance of the laboratory activities shall be documented.
- 6.3.3 The laboratory shall monitor, control and record environmental conditions in accordance with relevant specifications, methods or procedures or where they influence the validity of the results.
- 6.3.4 Measures to control facilities shall be implemented, monitored and periodically reviewed and shall include, but not be limited to: a) access to and use of areas affecting laboratory activities; b) prevention of contamination, interference or adverse influences on laboratory activities; c) effective separation between areas with incompatible laboratory activities.

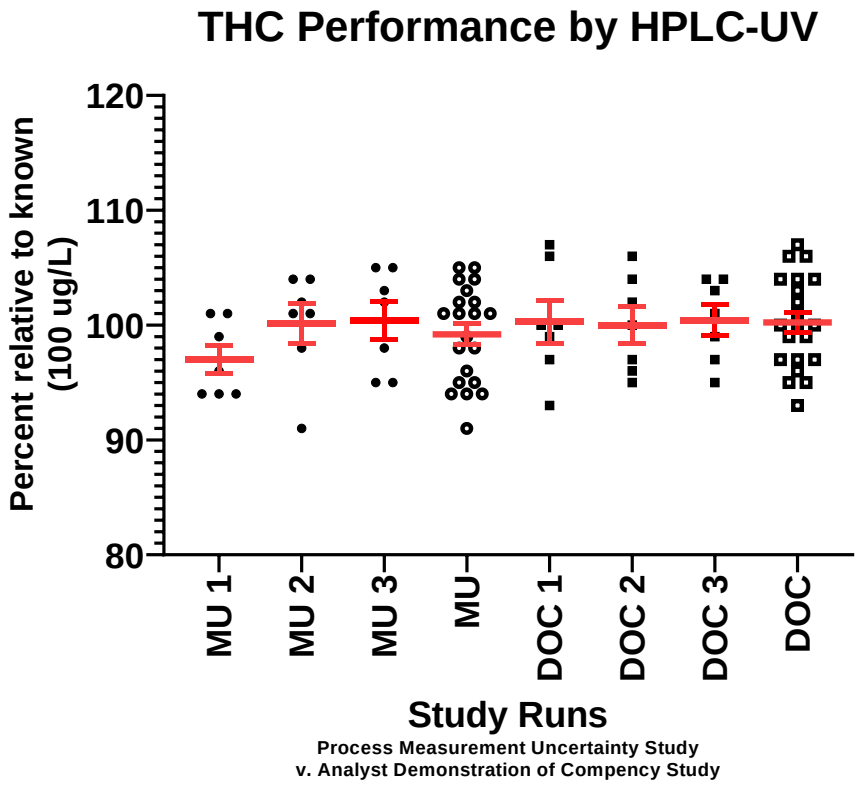
HYGIENE II

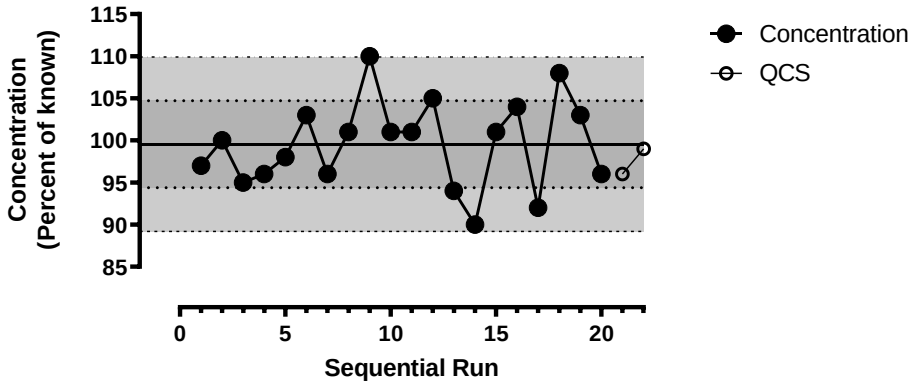
- Clean Space - Dirty Space
- Phones
- Drinks
- Food
- Storage of Materials
- Active process space practices - work flow, in-process sample handling, labelling, etc.
- In-use practices
- Storage of Standards

HYGIENE III

- Solvents
- Standards
- Surfaces
- Hardware
- Computer systems
- ‘Hygiene’ PM vs. Daily
- End of workday
- Start of workday
- Giving people ‘a space’

DOC AND MU AS CUSTOMER RESPONSE





- We report that the MU and DOC study are normally distributed and statistically indistinguishable from each other.
- We report no deviations in QCS results for run and re-run.
- We report the accuracy of this test as the 95% confidence interval for a single measurement:
  +/- 8.0% of the reported value.
- We report the standard error for this test to be <1% relative to the known value.
- We report this test as unbiased based on the bias for this test being less than the standard error for the test.

J. Raymond 07MAY2020

QUESTION AND ANSWER

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