ORELAP Accreditation in the Cannabis Industry

The Ins and Outs
The How-To's
The FAQs

10/5/2015

Oregon Health Authority

Things to Keep in Mind About this Training

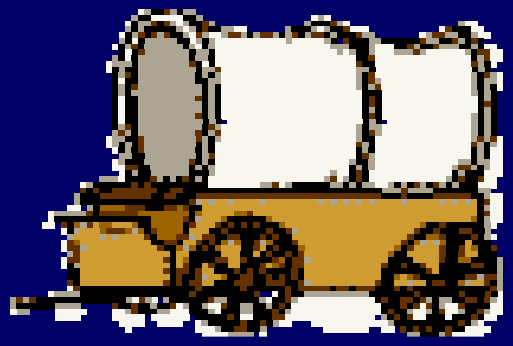
- Let's try to have some fun!
  - Questions, stories, interpretations etc. move this material along.
- The 2009 TNI Standard isn't necessarily in the right order for you (and this training probably isn't either)
  - A bench chemist understands a lab's process differently than a QA officer and very differently from an auditor.
  - Try to find the topic we are discussing in your copy of the TNI standard as we go through them. The practice of finding things in the Standard might be the best thing you get out of today.
- No one is perfect and no one is 100% ready
  - This is an open-forum training with a positive atmosphere towards continual improvement.
- I love questions!
  - This is a myopic view into a very big picture so if you do not know something, please ask!

Cannabis Lab Requirements

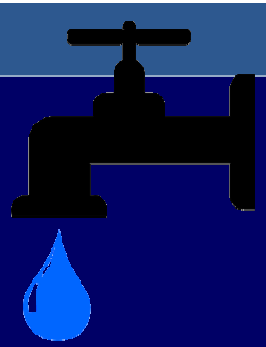
- HB 3400 requires a lab to be accredited by the ORELAP program to the TNI Standard in order to be licensed
  - This is in addition to any regulatory requirements set in rule pertaining to testing.
  - Sampling will be included in ORELAP's assessment
    - How?
  - There will be additional licensing requirements that must be met other than ORELAP accreditation

ORELAP Background

- Oregon was one of the first participating states in NELAC as early as 1995 and accrediting to the first standard in 2002.
- Our program gives primary accreditation to labs in the Water Quality, Environmental, Air Toxics, and Industrial Waste industries in over 12 states and 3 countries. We accredit Organic, Inorganic, Microbiology, Radiochemistry and Whole Effluent Toxicity technologies.



ORELAP Background



- The SDWA (1974) gave the authority to the states to regulate drinking water.
- This was difficult for states to implement on their own so many got together in a national program to promote consistency and share the burden of this dynamic field.
- The NELAC Institute (TNI) has evolved into a non-profit organization of 14 Accrediting states and 39 participating states. The latest revision of the Standard (2009 TNI) is based in ISO 17025 with more prescriptive requirements added by a consensus based process.

ORELAP Vision

- Our main goal of accreditation is ensuring that data of KNOWN quality is reported to clients which is backed up by technically competent laboratory personnel and those committed to a strong quality system.
- We encourage good practice to maintain legal defensibility for labs and their clients.
- ORELAP strives to create a cooperative (not punitive) atmosphere in a regulatory setting.
  - Encourages our lab network to cooperate and share their expertise with each other.
  - Provides Trainings
  - Provides Technical Assistance

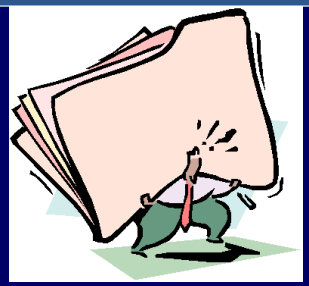
The 2009 TNI Standard

- Buying Volume 1 of the Standard is the first part of becoming accredited.
  - http://www.nelac-institute.org/content/CSDP/standards.php
- TNI
  - http://www.nelac-institute.org/index.php
- Consider becoming a TNI member!
  - The discount to the Standard with membership makes the increase in cost negligible.
  - You can participate in committee meetings and vote or comment on the the next revision of the standard as they are written.
  - TNI conferences are a great source of training and networking opportunties.

The 2009 TNI Standard

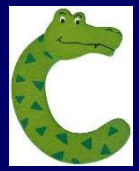
- Module 1 of the TNI standard is for labs becoming accredited.
- Relevant Volumes to Cannabis Labs
  - Volume 1- Proficiency Testing
  - Volume 2- Quality Systems
  - Volume 4- Chemistry
  - Volume 5- Microbiology
- All of the requirements in these volumes must be met in order to become accredited.
  - Familiarity with the Standard in addition to method requirements are essential.
  - Checklists are helpful when getting started.
- This training is not meant to replace reading the Standard! There are many small requirements that will not be covered in this training. READ THE STANDARD!!

The Accreditation Process



- Apply for existing fields and analytes of testing through the ODIE database on the ORELAP website: https://public.health.oregon.gov/LaboratoryServices/EnvironmentalLaboratoryAccreditation/Pages/Cannabis-accreditation.aspx
- Submit your Quality Manual, SOPs, Method Validation and PT data to ORELAP along with a completed (preferably with document references)
  - Thumb drives preferred
- Work with ORELAP to schedule an initial assessment. For initial accreditation, all of the above documentation must be acceptable before an assessment is scheduled.

The ABC's of Quality Systems V1M2



- **Complaints**
  - Always DEFINE and keep records of complaints
  - Everyone in the office who might receive a complaint should know how to keep these records.
  - This helps to identify recurring problems
- **Confidential**
  - Have procedures on client confidentiality
- **Corrective Action**
  - The purpose of Corrective Actions is to address major or systemic nonconformance to the standard.

The ABC's of Quality Systems V1M2

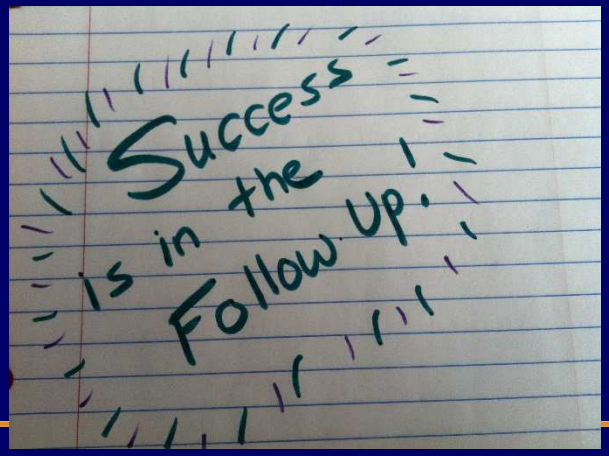
- Corrective Actions
  - Minor nonconformance (such as a QC failure) can be fixed with "correction"
    - These must be defined in your quality documentation and tracked for recurring failures.
  - Major or Systemic Nonconformance need official "Corrective Action"
    - Internal or External Audit Findings
    - Data Recalls
    - Recurring failures
  - What's the difference?
    - Your official corrective action system should include records of:
      - Root Cause Analysis
      - Follow-up for effectiveness

The ABC's of Quality Systems V1M2

- Corrective Action
  - Investigation and Root Cause Analysis
    - "Why did the PT fail?
      - most common response: "analyst error" This is NOT ROOT CAUSE! Let's try again.
    - Why did the PT fail?
      - The back-up analyst ran it.
    - Why did the PT fail for the back-up analyst and not the primary analyst?
      - The back-up analyst made the standards wrong.
    - Why did the back-up analyst make the standards wrong?
      - The back-up analyst was following an old SOP.
    - Why did the back-up analyst have access to an old SOP?
  - Root Cause???
    - Document Control!

The ABC's of Quality Systems V1M2

- Corrective Action
  - Follow-up for effectiveness:
    - Corrective Action should be assigned to the correct person to investigate and follow-up
    - This person should record a goal date for corrective action completion and a date to follow-up!
    - The follow-up date should be appropriate to the magnitude of the problem and there can be more than one follow-up.
    - There must be RECORDS of each follow-up and what was checked to ensure the problem will not recur.



The ABC's of Quality Systems V1M2

- Data Integrity
  - New employees must sign an ethics statement and receive official data integrity training.
  - Data Integrity training must be held annually (with records!) and must include:
    - Time Traveling
    - Manual Integrations
    - Other unethical data processing
    - How to report issues (without repercussion)
  - Mistakes in the laboratory are not always fraud.
    - It's how you HANDLE the mistakes that can lead in the wrong direction.

The ABC's of Quality Systems V1M2

- Demonstration of Capability
  - Two types-Method and Employee
    - Method DOC part of Method Validation
    - Employee DOC is necessary before employee independently performs analysis and reports data
  - Initial DOC includes 4 reps of a spiked sample that is carried through the entire process (including prep)
  - Ongoing DOC (yearly) can be a passing PT, 4 passing blind spikes in runs, or repetitions of blind spikes as in IDOCs.

The ABC's of Quality Systems V1M2

- **Document Control**
  - Must have procedures that control ALL documents in a laboratory system.
    - Forms, SOP's, reference methods, reports etc must all have unique identifiers, revision numbers, and a review schedule.
    - Obsolete documents MUST be removed upon introduction of a new revision.
    - Procedures should include who needs to review and sign a new document with records of those reviews.
    - Document retention schedule must be in quality procedures.

The ABC's of Quality Systems V1M2

- **Facilities**
  - Clean, enough space, care taken to avoid cross-contamination.
- **Internal Audits**
  - The laboratory must audit ALL activities within it's quality system ANNUALLY.
    - This includes SOP review, reference method comparison, analyst technique and following the SOP.
    - The quality officer needs to schedule and be responsible for the internal audit being completed but DOES NOT have to perform the whole thing.
      - Encouraging ownership by having back-ups and supervisors perform the internal audit is good practice.
    - Corrective Action must be performed on findings.
    - The Internal Audit must include an audit of the quality system!

The ABC's of Quality Systems V1M2

- **Management Review**
  - Different Focus than Internal Audit
  - Asks Top Management to look at and report on:
    - Internal Audit Findings
    - Upcoming changes or new work
    - Corrective Actions over the past year
    - Client Feedback
    - Training, resources, staffing etc.

The ABC's of Quality Systems V1M2

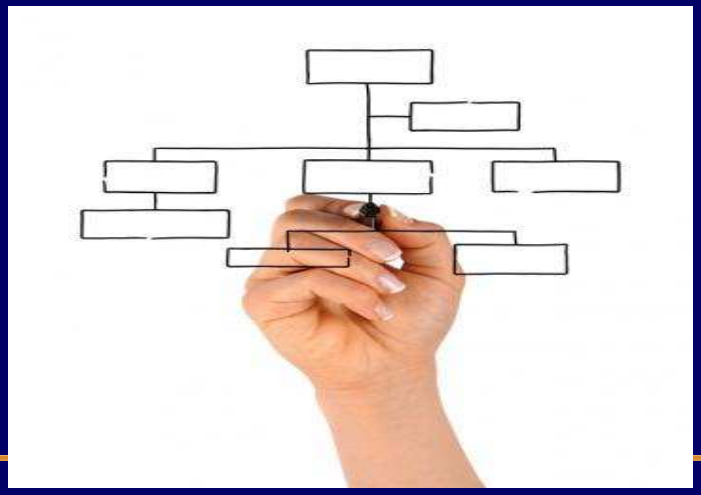
- **Matrix**
  - The five official matrices in the 2009 TNI Standard:
    - Potable Water
    - Non-Potable Water
    - Solid
    - Air
    - Biological Tissue
  - The Matrix challenge in cannabis accreditation
    - At first some Matrix PT's will not be available
      - Round Robins?
    - Often something of the same matrix will need it's own QC to be close to "matrix matched"
  - Sub-Matrices?
    - ORELAP sometimes assesses submatrices separately for QC and PTs.
    - In Cannabis this could mean different blank matrices for food versus extracts etc.
    - Ask ORELAP if you are unsure whether different samples may need different QC or PTs

The ABC's of Quality Systems V1M2

- **Nonconforming Work**
  - Have procedures for when the work does not conform to the standard, the method, the lab's procedures or the client's needs.
    - E.g. What is the procedure for a lab when a refrigerator goes out of temperature control limits?
    - Must decide whether this impacted data quality and client must be informed.
    - Authorization for stopping and resuming work

The ABC's of Quality Systems V1M2

- **Organization**
  - First in your Quality Manual
    - Define lab within higher organization, personnel roles, keeping the work free from undue influence etc.
    - There are a lot of requirements in this section, please read the standard as you are writing this part of your QSM.
- **Personnel**
    - Describe Chain of Authority
    - Each position and responsibilities clearly defined.

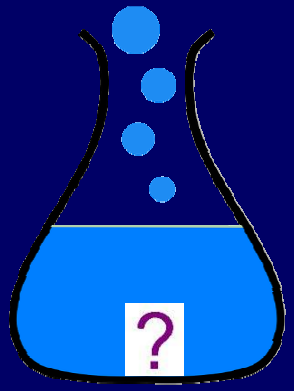


The ABC's of Quality Systems V1M2

- **Personnel**
  - Records of technical background and competency for each person in their position.
  - Procedures for identifying training needs.
- **Preventative Action**
  - The laboratory is often doing preventative action informally. There must be records.
    - Instrument losing sensitivity, training back-ups for leave, etc.

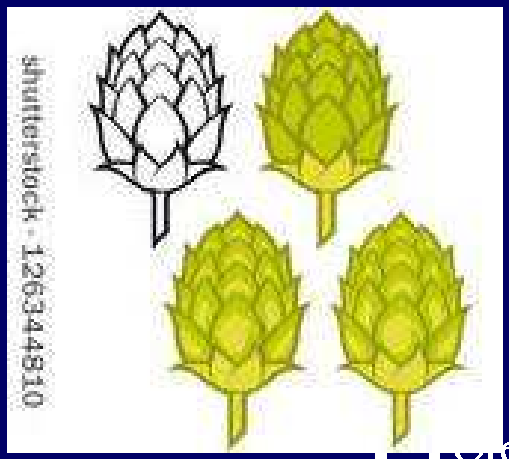
Proficiency Testing 2009 TNI V1M1

- Blind Samples bought from ISO 17043 accredited companies if available.
  - Other options, such as Round Robin, will suffice when not available.
- The lab must pass 2 out of the last 3 every year for every method/matrix/analyte combination. Existing accreditation will be suspended upon a second failure until the above requirement is met.
- Must have two passing samples for initial accreditation of laboratory scope. We need these before scheduling your assessment!



Proficiency Testing 2009 TNI V1M1

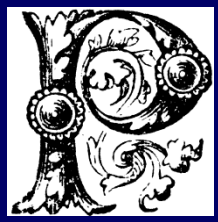
- Currently there is only one ISO 17043 PT for THC and other cannabinoids.
  - It is not a matrix PT but will be accepted for the first round until matrix options are considered.
- PT companies are developing PTs in hops to mimic cannabis for the other analyses. Please watch the ORELAP website for PT study dates.
  - Solvents
  - Pesticides
  - Microbiology
- Study dates probable by November



Proficiency Testing 2009 TNI V1M1

- These samples must be treated the same as any other sample in your system. They must be run by the same method, with the same QC criteria, and in the same manner as an unknown sample.
- You cannot:
  - Calibrate or do maintenance specifically for a PT
  - Run a PT multiple times or by multiple methods for confirmation
  - Try to obtain the PT result from another lab or subcontracting the PT to another lab
  - Run extra QC samples with the PT (this especially applies to the “QCS samples” sold in pairs by the PT company unless you are going to analyze this QC with every batch.

The ABC's of Quality Systems V1M2



- **Purchasing**
  - Must have procedures for vetting vendors, keep a list of approved vendors and keep that list current.
  - Must inspect all supplies and standards upon arrival for acceptability.
  - Apply an expiration date and received by date with initials on supplies.
  - Lot Testing – Is it required? Is it good practice?
    - Containers
    - Reagents
    - Preservation
    - What does the Certificate of Analysis say?
      - If some analytes that you test are over your LOQ, the bottles must be certified by the laboratory

The ABC's of Quality Systems V1M2

- **QC**
  - The standard requires positive and negative controls to assess precision, accuracy, contamination. Etc.
  - All QC measures must be assessed and evaluated on an on-going basis.
    - Checked against control limits (must be set if not in method)
    - The resulting data shall be recorded in such a way that trends are detectable and, where practicable, statistical techniques shall be applied to the reviewing of the results.
      - Control Charts

The ABC's of Quality Systems V1M2

- **QC**
  - Blanks
    - Field Blanks, Trip Blanks, Method blanks, Instrument Blanks
      - Which do you need to ensure a contamination free process?
  - Calibration and Calibration checks
    - Calibration checked against procedural measures such as R^2 value or Average Response Factor
    - Second source check (ICV)
    - Ongoing checks (CCV)
  - Duplicates
  - Laboratory Control Sample
  - Matrix Spikes
  - If references are contradictory, always follow the most stringent control limits!

The ABC's of Quality Systems V1M2

- **Quality Manger**
  - "Irrespective of other duties and responsibilities is appointed to have defined responsibility and authority for ensuring the quality system is implemented and followed at all times and have direct access to the highest level of management at which decisions on laboratory policy are made."
- **Quality Manual**
  - Should contain or reference *all* procedures pertaining to the lab's activities. See the standard for specific requirements.
- **Quality Policy**
  - Must define the objectives of the quality system

The ABC's of Quality Systems V1M2

- RECORDS!!!!
  - "If it is not written down, it did not happen."
  - Records must be:
    - Identifiable with dates and initials of those doing the work.
    - Readily retrievable and protected from loss, theft, flood, fire etc.
      - Electronic Back-ups, LIMS audit trail, and locked Excel sheets for electronic records.
    - Retention Schedule
    - Legible and non-alterable.
      - Changes made by a single line cross out and initialed by staff member making change. Reason for change must be noted.

The ABC's of Quality Systems V1M2

- **RECORDS!!!**
  - Recorded at time of observation
    - No sticky notes or "remembering to write down later"
  - Enough information for the historical reconstruction of the data.
    - Traceability of standards, reagents, glassware, instrument position etc.
    - Enough information to identify the uncertainty of a data result.
  - Lack of sufficient records is one of the most common findings at an assessment. Please read records sections of the standard carefully.

The ABC's of Quality Systems V1M2

- **Reports**
  - The quality of all data reported must be documented
    - Qualifiers, narratives, and estimates are all used to inform the client of non-conformance
  - "Results of each test reported accurately, clearly, unambiguously and objectively"
  - "Include all of the information necessary for the interpretation of the result."

The ABC's of Quality Systems V1M2

- Reports must include:
  - Analyte
  - Method
  - Units
  - LOQ's
  - LOD's (where appropriate)
  - Analysis Date/Time
  - Sampling and Sample Receipt information
  - Many more-Read the Standard!

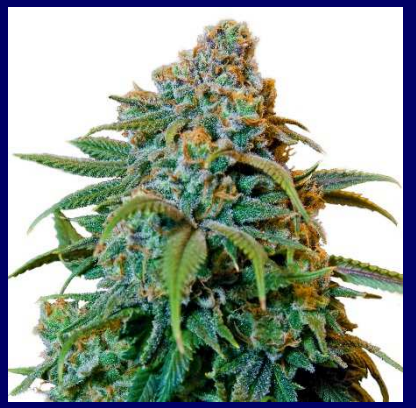
The ABC's of Quality Systems V1M2

- **Requests, Tenders & Contracts**
  - Document all review of contracts and client requirements.
  - Inform the client and keep records of conversations about ANY changes in the contract.
    - Subcontracting

      -Authorized by client in contract or before sending the samples out, if possible
    - Nonconformance
      - They might choose not to analyze the sample depending on the severity of non-conformance
    - Re-Sample

The ABC's of Quality Systems V1M2

- **Sample Receiving**
  - Chain of Custody
  - Uniquely identified from field
    - Site, Name, Number, any linked data on COC
    - Date/Time sampling
  - Assigns unique laboratory identifier.
  - Checks for sample suitability
    - Container, Sufficient Sample size, Homogeneity, Handling, etc.
  - Contacts client and has records of discussions of any nonconformance or difference from the samples to the COC.
  - Many requirements. See Standard



The ABC's of Quality Systems V1M2

- **Standard Operating Procedures**
  - Must contain all of the information necessary to perform the method. This includes but absolutely not limited to:
    - Scope and Applicability
    - Equipment and support equipment
    - Standards and Reagents
    - Quality Control
    - Procedures
    - Calculations
    - Reference Methods and deviations (if applicable)
    - Corrections for Non-Conformances
    - Maintenance

  - Approved and reviewed periodically by appropriate personnel
    - Quality Officer
    - Anyone with a DOC in the method or prep method

The ABC's of Quality Systems V1M2

- **Subcontracting**
  - ORELAP laboratories can only subcontract analyses to laboratories accredited by ORELAP for the scope of analyses being subcontracted.
  - The subcontractor must be approved ahead of time by the client (if possible) and the subcontracted work must be identified in the test report.
  - The subcontractor's report should be included *in full* in the lab report.
  - The Chain of Custody must be carried throughout the subcontracting process.

The ABC's of Quality Systems V1M2

- **Support Equipment**
  - Is covered in the technical standards but tracing support equipment performance often falls to Quality Systems
  - Support Equipment used for any part of the analysis must be calibrated and verified according to the Standard's schedule
    - This includes but not limited to:
      - Sample Refrigerators and Freezers
      - Water Baths, Hot Blocks, Autoclaves, AutoVaps
      - Thermometers, Balances, Weights, Pipettes
- **Reference Standards and Calibration**
  - Verifications are done against Traceable and Calibrated Reference Standards
  - These standards are not to be used for any laboratory analysis.

The ABC's of Quality Systems V1M2

- **Technical Director**
  - Must meet educational and experience requirements of the standard for chemistry or microbiology.
  - Must have a qualified back-up
- **Traceability**
  - Lab must trace all measurements to SI units by using certified ISO Guide 34 standard suppliers when available.
    - What does this even mean?

The ABC's of Quality Systems (V1M2)

- **Training**
  - Procedures must exist for a training program appropriate to the lab personnel's duties and for identifying training needs
  - A Training Record must be kept for each employee
  - These files often include:
    - Initial Training metrics
    - Ethics Policy and Data Integrity training records
    - DOC summaries
  - Additional training records
    - Manual Integrations
    - Equipment training
    - Vendor Training
    - TNI or Quality Training

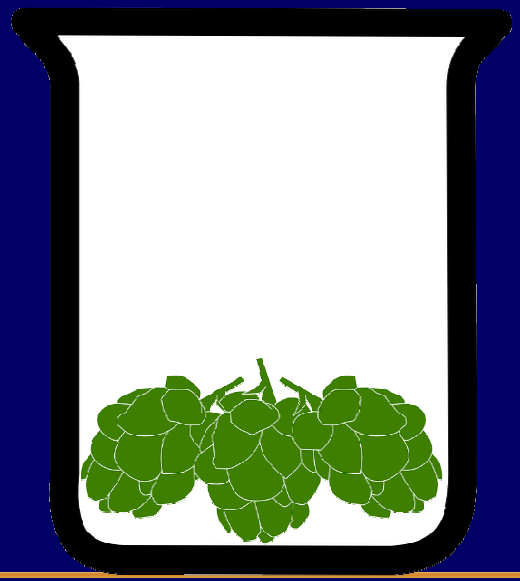
Questions??

Onto the Technical Sections!

Oregon Health Authority

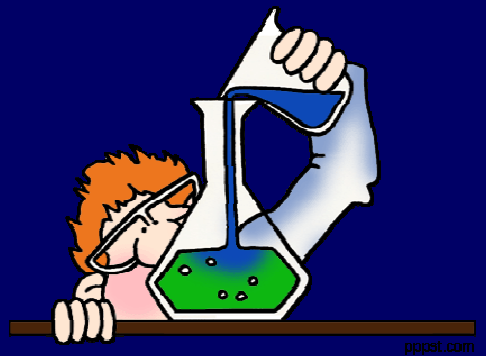
Chemistry V1M4

- **Blanks**
  - Should be a clean matrix matched with matrix of samples
  - Method blank
    - Processed through all prep and analysis steps with sample.
    - Must be processed one for every prep batch of 20 samples.
    - Assessed for contamination down to lowest reporting level. If contamination exists at this level, the associated samples must be reprocessed, if possible.
  - Other types of Blanks
    - Field Blanks
    - Trip Blanks
    - Fridge Blanks
    - Instrument blanks
    - Calibration Blanks



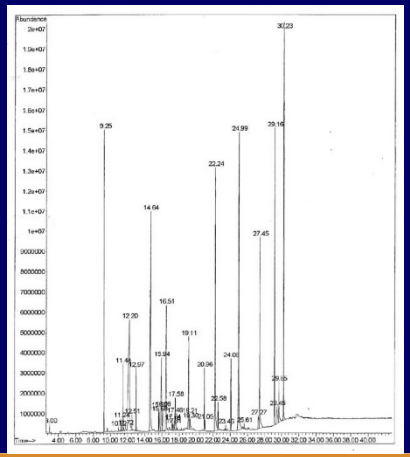
Chemistry V1M4

- **Confirmation**
  - Required on any two-column or single column/dual detector method.
  - MS preferred way of confirming hits
  - All confirmations must be documented
- **Continuing Calibration Verification (CCV)**
  - Performed at the beginning and end of every analytical batch unless internal standards are used.
    - Good practice to have one bracketing batches even with internal standards.
  - Performed more often in Inorganic Methods



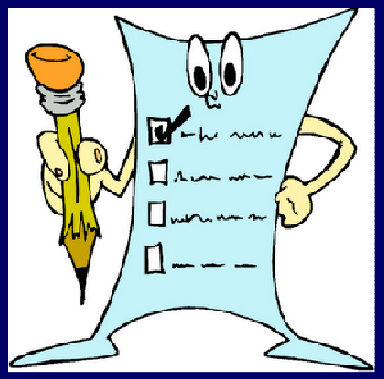
Chemistry V1M4

- Data Analysis
  - Calculations and checks performed in a systematic manner. All Calculations should be included in SOPs
  - Manual Integrations
    - Must have procedures and records (Before and After with a Reason) of manual integrations performed
  - Data reduction by equipment software or LIMS
    - Validation depends on type of calculations.
    - All LIMS systems should have a validation and review process



Chemistry V1M4

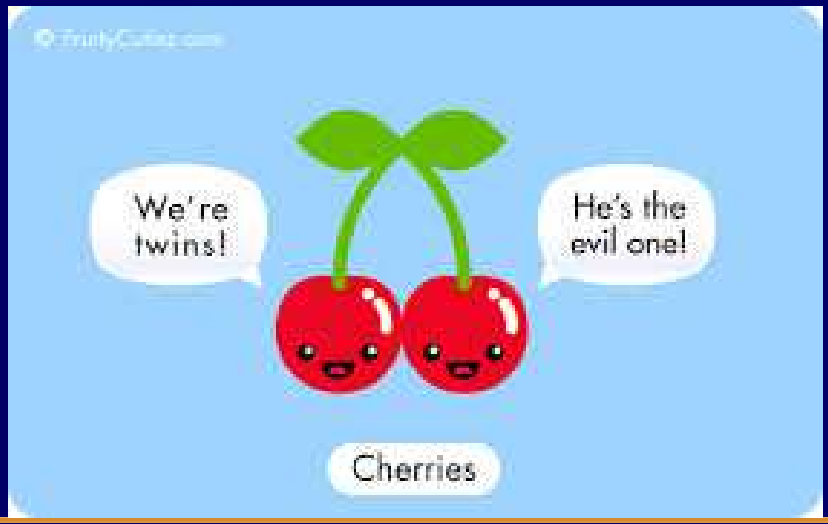
- **Data Review**
  - At least one level of review besides the analyst if at all possible. Often multiple levels.
    - Data transcription
    - QC criteria checks
    - Method Requirement checks
    - Raw Data review



- **Demonstration of Capability**
  - Described in Standard and covered in Quality Systems

Chemistry V1M4

- **Duplicates**
  - The laboratory must have a program for assessing precision in the prep batches.
    - Field Duplicates
    - LCS Duplicates
    - Sample Duplicates
    - Matrix Spike Duplicates
  - Generally assessed to Relative Percent Difference Control limits.



Chemistry V1M4

- **Equipment**
  - Equipment must be uniquely ID'ed and linked to results in records.
  - Capable of achieving the sensitivity and accuracy required by the method.
  - Procedures on Equipment maintenance and a maintenance manual are required.
  - Checked and/or Calibrated before use
  - Standards about sending equipment out for service, equipment leaving control of laboratory etc.

Chemistry V1M4

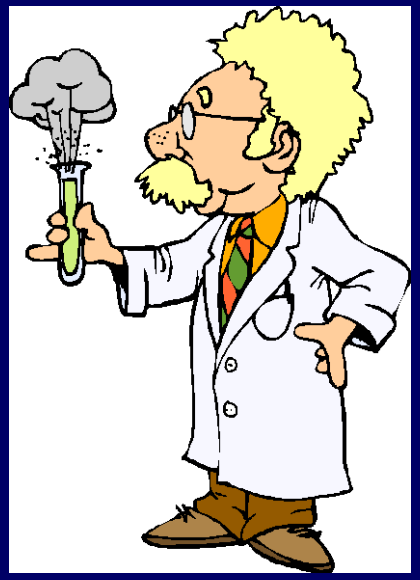
- **Initial Calibration**
  - Calibration must be linked in records to all associated results and calibration models, reductions, and calculations must be outlined in each SOP
  - Things to consider:
    - Enough points for model fit?
    - Low point at LOQ?
    - Cannot report above highest standard
    - Passes criteria (e.g. R^2 >/= 0.995 or Average Response Factor <15% RPD)

Chemistry V1M4

- **Initial Calibration**
  - Verified with a Second Source Standard (ICV)
    - Second source is preferred as second vendor and lot but in the absence of a second vendor, a second lot number is acceptable.
    - Recovery Acceptance limits similar to CCV

Chemistry V1M4

- **Laboratory Control Standard (LCS)**
  - A blank spike of a similar matrix that is carried throughout the entire process, including preparation
  - Required 1 in every prep batch of 20
  - Should contain all reported analytes
  - Control limits sometimes defined by method and sometimes determined statistically with control charts.

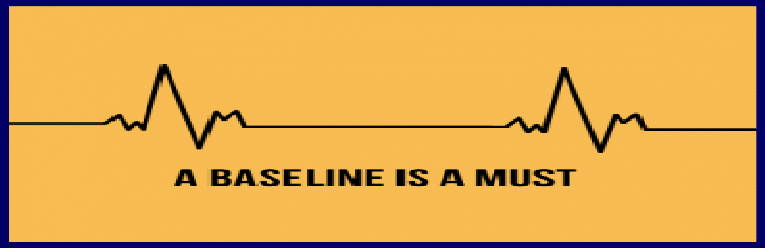


Chemistry V1M4

- **LOD/LOQ**
  - Determining your LOD (V1M2 Section 1.5.2.1)
    - Determined initially and any time there is a major change.
    - All sample processing and analysis steps of the analytical method shall be included in the determination or validation of the LOD.
    - Determined by spikes in the quality system matrix.
      - These spikes are low level (not more than 3-4x the suspected LOD).
      - Challenges of finding blank matrices to spike.
        - » Pesticide and solvent blank matrix is possible
        - » THC matrix possibly hops?
    - Some methods also use a series of method blanks to help determine the LOD

Chemistry V1M4

- **LOD/LOQ**
  - The LOQ should have a direct relationship to the LOD.
  - The LOQ should be the low point of your calibration curve and verified with a low level spike at 50%-150% recovery limits.
    - Recommend this is verified often (every batch) however the requirement is annually.
  - The new revision of the TNI standard will have different requirements for determining the LOD/LOQ. Please refer to the NELAC-Institute website for voting draft standards to see the changes.
  - The LOD does not need to be determined if only reporting to the LOQ.



Chemistry V1M4

- **Matrix Spikes/Matrix Spike Duplicates**
  - Matrix Spikes are required by ORELAP more stringently than the TNI language. If enough sample volume is available, an MS/MSD combination must be included with each prep batch.
  - Exceedences only qualify the sample, not the batch!
    - You do not have to reanalyze or extract the batch due to a matrix spike failure but the report must have the result qualified
  - Matrix Spike Duplicates
    - Preferred over sample duplicates that may be low in concentration for precision measurements.
    - Precision exceedences only need to be qualified on the result.

Chemistry V1M4

- **Method Validation**
  - Precision and Accuracy Studies
  - MDL Studies
  - Two Acceptable PTs
  - Comparison data (to other methods etc.)
  - Appropriate passing QC in sample batches

Chemistry V1M4

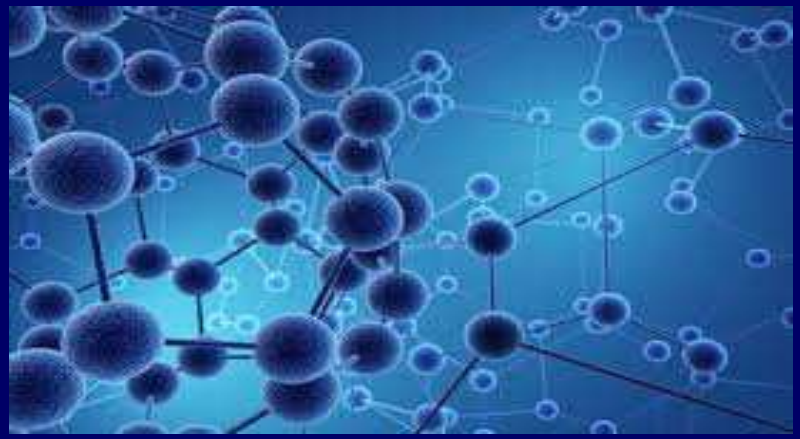
- **Proficiency Testing**
  - Blind sample for each method/matrix/analyte combination
  - Must be treated in the same way as unknown samples from log-in to reporting.
- Sample Receiving (See Quality Systems)
- SOP (See Quality Systems)

Chemistry V1M4

- **Support Equipment**
  - Uniquely ID'ed and linked to sample results
  - Records to document verifications and calibrations
    - Temperature logs (Record thermometer ID)
    - Balance Checks (Record Balance # and Weight Set #)
    - Pipette Checks (Record levels of checks and results)
  - Labeled with expiration date of calibration
    - It is the analyst's responsibility to ensure they are using calibrated and/or verified support equipment

Chemistry V1M4

- **Surrogates**
  - Where appropriate, surrogates should be added to all samples and compared to appropriate control criteria
  - Things to consider
    - Surrogates chosen to reflect chemistry of target compounds?
    - If more than one, are they linked to certain compounds or does one failure fail the list of analytes?



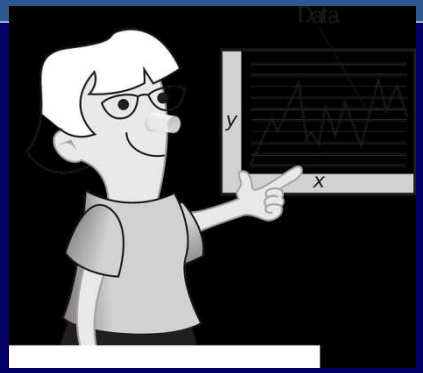
Questions?

Onto Microbiology!!

Microbiology V1M5

- **Method Selection**
  - A reference method is a method issued by an organization recognized as competent to do so.
  - Non-reference methods must be validated against a reference method.
- **Method Validation**
  - "as extensive as necessary to meet the needs of the given application"
  - Validation procedures must be documented
  - Accuracy
    - One known pure reference culture
  - Precision
    - 10 Replicates (if non-reference method used, results must show that the comparison to reference method is not statistically different)
  - Selectivity
    - Verifiy all response in at least 10 samples using mixed cultures that include the target organisms and at varying concentrations. Calculate the number of false positive and false negative results.

Microbiology V1M5



- **Demonstration of Capability**
  - Prior to reporting data, an IDOC (initial) study must be performed and annually a CDOC (continuing) must be recorded for each analyst.
  - See Quality Systems 1.6 for more detail on DOCs
  - Anytime there is a change in instrument, personnel or method a new IDOC must be performed
  - The records must be available for each DOC for:
    - Analysts involved in prep OR analysis
      - Cannabis might possibly need sampler if using real matrix.
      - Matrix
      - Organism
      - Identification of methods performed and SOPs used
      - Analysis date
      - Summary of analysis was in 1.6.2.2c

Microbiology V1M5

- 1.6.2.2 is the possible methods used for IDOC if there is no method or regulation mandated method
  - 4 aliquots of a clean matrix with target organisms
  - Acceptable performance in a PT study that consists of a blank, negative culture and a positive culture for each target organism
- Criteria
  - See 1.6.2.2 for various criteria. If any criteria fails, repeat the DOC.
  - Repeat failures confirms a problem that require corrective action
- 1.6.3.2 is possible methods for ongoing DOC

Microbiology V1M5

- **Calibration**
  - Have documented procedures for calibration, verification and quality control of support equipment.
    - If it is support equipment that is used for an accredited test, it must be used as if the method itself were accredited.
      - Example- P meters should be calibrated every day and checked with a second source
  - Continuous Monitoring
    - Acceptable calibration records once a month
- **Quality Control**
  - All Quality Control checks must be linked to the result
    - Bottles, Media, Equipment checks
      - How do I do that?
  - Equipment must be checked regardless of arriving with a Certificate of Analysis

Microbiology V1M5

- **Quality Control**
  - Method Blanks
    - Demonstrates no equipment, media, or reagents have been contaminated
    - Pour Plate Method Blank
      - Method blanks of the medium shall be made by pouring at a minimum one uninoculated plate for each lot of pre-prepared, ready to use media for each batch of laboratory prepared media
    - Required Sterility Checks
      - Shall be analyzed for each lot of pre-prepared, ready to use medium and for each batch of medium prepared in the laboratory
      - Sterility checks on sample containers shall be performed once per lot of purchased pre-sterilized containers
      - Sterility checks on containers prepared and/or sterilized in the laboratory should be performed one container with nonselective growth media.
        - » Can be done by a contract laboratory
      - Each batch of dilution water

Microbiology V1M5

- **Test Variability/Reproducibility**
  - For tests that specify colony counts, duplicate counts on one positive sample should be performed and shall be within 10% difference
  - If there is only one analyst, they should count the plate twice with a different of less than 5%
- Sample Specific Controls
  - If reference method requires Matrix Spikes or Matrix duplicates, they must be included in the SOP.

Microbiology V1M5

- Standards Reagents and Media
  - Laboratory Prepared Media
    - Tested for performance prior to first use
      - Selectivity, Sensitivity, Sterility, Growth Promotion, and Growth Inhibition
      - Media shall be used within the holding times of the accredited method
  - Purchased and Ready-To-Use Media
    - Must be used by expiration date
  - Reagent Water
    - Monitored for bactericidal and inhibitory substances
    - Monthly monitored for chlorine residual, specific conductance, total organic carbon, ammonia/organic nitrogen, heterotrophic plate count.
    - Annually monitored for analysis of metals and the Bacteriological Water Quality Test (to determine presence of toxic agents or growth promoting substances)
  - Records must include ALL details of preparation of media, buffers, and reagents including lot numbers, final pH, expiration date etc.

Microbiology V1M5

- **Selectivity**
  - All growth and recovery media shall be checked to assure the target organisms respond in an acceptable manner.
  - Target Organisms shall be verified as in the method.
  - Reference Cultures
    - Preferable from ISO Guide 34 providers. LOOK at your C of As!
    - Positive and Negative controls
    - Working Stocks shall not be sequentially cultured more than five times and should not be sub-cultured to replaced reference stocks
  - Negative Controls
    - Demonstrates the medium does not support the growth of non-target organisms and does not show positive results for target organisms
  - Positive Controls
    - Demonstrate that the medium can support growth of target organism
  - Each pre-prepared ready to use lot of medium shall be tested with at least one negative and one positive control.

Microbiology V1M5

- **Facilities**
  - Non-absorbent surfaces, easy to clean and disinfect
  - Sufficient Storage space
  - No dust accumulation
- **Equipment**
  - Temperature Measuring Devices
    - Graduation must be appropriate to meet the requirement accuracy of measurement. Verification must be done annually against a reference thermometer.
  - Autoclaves
    - Pressure cooks can NOT be used as autoclaves
    - Demonstration of sterilization temperatures shall be provided by use of a continuous temperature recording device with every cycle.
    - Biological indicators shall be used to determine effective sterilization
    - Records for every Cycle:
      - Date, contents, max temp reached, pressure, time in sterilization mode, total run time and analyst's initials
    - Autoclave mechanical timing device should be checked quarterly against a stopwatch.

Microbiology V1M5

- **Volumetric Equipment**
  - Automatic dispensers and pipettes to be checked quarterly
  - Non Class-A Glassware and other containers with volumetric markings should be verified once per lot prior to use.
    - Volumetric or Gravimetric
    - Glass-A Plasticware is a misnomer. It does not match the definition of Class A.
  - Sample bottles and disposable pipettes checked once per lot
- UV Instruments
  - If used for sanitation (membrane filter methods), must test quarterly with a UV light meter and replaced if output is 70% less than original.
  - ORELAP recommends non sanitation UV lamps (for reading auto-fluorescence) be changed once a year depending on workload

Microbiology V1M5

- **Incubators, Water Baths, Ovens**
  - Uniformity of temperature shall be established
    - Thermometers on different shelves or in different locations
  - Temperature must be checked twice daily
    - At least 4 hours apart on each day of use
    - Recommend continuous monitoring for when samples are in incubator but personnel is not present. Power outages are common.
- **Labware**
  - Labs shall have a procedure for washing labware with a laboratory detergent
  - Glassware
    - Borosilicate, free of chips and cracks, and have readable measurement marks

Microbiology V1M5

- **Labware**
  - If washed and reused, the lab must perform the Inhibitory Residue Test annually or whenever the lab changes detergents.
  - Shall be tested at least once daily on each day of washing with suitable pH indicated such as bromothymol blue.
- **Sample Handling**
  - If thermal preservation is required, samples must meet the temperature requirement.
  - If thermal preservation is required, samples collected on the same day may not meet temperature requirements but can be accepted if it is noted they are on ice. (Sample receiving must still take temperature)

Accreditation and Assessment What to Expect

- **Application in ODIE**
  - Apply for each method/analyte/matrix combination that you plan for report.
  - If the analyte is not available in the correct combination, please ask ORELAP to add it in the database
    - This can take a few days as most of these combinations will also not be in the National TNI database
  - Submit Application and review Scope

Accreditation and Assessment What to Expect

- **Submit documentation**
  - Preferred in a mailed thumb drive
- **What to submit**
  - Quality Manual
  - SOP's
  - Method Validation
    - MDL studies, other validation
  - PT
    - Add ORELAP as your accrediting body with the PT company and we will receive your scores directly. (Requirement)

Accreditation and Assessment What to Expect

- **Scheduling Your Assessment**
  - Your application will place you in line to be scheduled. ORELAP has an existing schedule of labs within the same expiration timeframe and new labs are scheduled between existing scheduled assessments in order of submittal and readiness.
  - ORELAP will contact you with possible assessment dates and the assessment team.
    - Please divulge any perceived conflicts of interest with the team or ORELAP at this time.

Accreditation and Assessment What to Expect

- Who should be there
  - Schedule permitting, everyone who performs operations pertaining to accreditation should be avalaible for interview.
    - ORELAP understands personal time is necessary and can interview backups
    - This includes positions that perform purchasing, project management, client contracts, etc.
  - ORELAP will have someone mainly assessing the areas of Quality Systems, Inorganic, Organic, and Micro.
    - These people can be shadowed by section leads but interviews will take place at a staff level.
    - We are flexible to production schedules-if you have employees that leave early or come late, please let us know.

Accreditation and Assessment What to Expect

- **The Assessment**
  - Opening conference
    - Introductions, Explanation of process, Confidentiality Agreement, Scheduling
    - Review of Scope
    - Safety procedures and Lab Tour
  - Break-off into individual interviews
    - Usually an assessor will assess Quality Systems with the Quality Officer and one will start in a Technical Section
    - Assessors use checklists for the standard and for reference methods. If no reference method is available, more time will be spent with a generic checklist.

Accreditation and Assessment What to Expect

- **What we will Assess - Quality Systems**
  - Procedures
    - Quality Manual
    - Administrative SOPs
    - Technical SOPs (control charts, LIMS, etc)
  - Records
    - Internal Audits
    - Corrective Actions
    - Training Files
    - All records that document compliance with the V1M2 of the standard.

Accreditation and Assessment What to Expect

- **What we will Assess - Chemistry**
  - Records
    - Instrument maintenance
    - Support Equipment
    - Traceability of Standards
    - Review checklists
  - Procedures
    - Do you perform your SOP as written.
      - "Do what you say and say what you do"
    - Is the technique and performance adequate to perform the method?

Accreditation and Assessment What to Expect

- **What we will assess-Chemistry**
  - Data
    - Raw data packages
    - Calibrations
    - QC
    - Manual Integrations
    - Data analysis
    - Data Review
    - PT Handling
  - Data Reporting

Accreditation and Assessment What to Expect

- **What we will assess-Chemistry**
  - Personnel
    - Education
    - Competence in methods and matrix
    - Knowledge of Quality System
      - Reporting Nonconformance etc.
    - Ability to follow procedures

Accreditation and Assessment
What to Expect

- **Closing Meeting**
  - Discuss any deficiencies.
    - Immediate deficiencies have a Corrective Action plan due immediately.
    - Follow-up Assessment (announced or unannounced may be scheduled to check deficiencies)
- **Report**
  - The rest of the deficiencies will be reported by ORELAP within 30 days of the last day of the assessment.
  - The laboratory has 30 days to respond with a Corrective Action Plan
    - Some CAPs will take longer than 30 days to complete. Goal Date completion is submitted with documentation of CAP by goal date to ORELAP.
  - ORELAP has 30 days to respond with acceptability of deficiencies and accreditation.

Sampling

- Why is Sampling so important?
  - ISO 17025 and the 2009 TNI requires laboratories to have a procedure to estimate uncertainty taking into account every contributing factor.
    - Depending on the project, sampling has shown to contribute up to 75% of the final result!
- Definitions:
  - Representative Sample
    - Sample obtained according to a sampling procedure designed to ensure that the different parts of a batch or the different properties of a non-uniform material are proportionately represented.
  - Random Sample
    - Sample in which the different fractions of the material have an equal probability of being represented.

Sampling

- Sampling
  - Lab personnel is responsible for sampling.
  - Sampling SOP to be written by ORELAP committee in temporary rule
    - Who will be on this committee?
      - Sign Up to be considered
    - The Executive Board of ORELAP will approve the SOP.
      - Three lab directors of the state labs
  - Sample Design
    - What is the purpose of our sampling?
    - What are our Data Quality Objectives?
      - Example: Do we want to know how much THC is in the brownie or the batch of brownies?
        - » The answer will change your sampling design

Questions?

That was easy!

Exercises-Internal Audit

- You are doing an internal audit of your potency method. You review the SOP from the analyst's bench and notice it is an earlier revision than your controlled copy. You look at the reference method and realize you are using a different extraction solvent than is listed. The analyst has not filled out the records for extraction but insists he always remembers when there are dilutions. You ask your analyst how he identifies hits. He says he knows what the THC peak looks like. A reported result is missing a dilution calculation.
- Write your findings:
  - How to write a finding?
    - Reference the 2009 TNI Standard or Method
    - Have objective evidence
- Write your Corrective Actions

Exercises-Tracking Corrective Actions

J2

	A	B	C	D	E	F	G	H	I	J
1	CAR #	CAR Title	CAR Type	Section	Created By:	Assigned To:	Followup Date	Goal Completion Date	Actual Completion Date	Status
2	00001	New Corrective Action System	Audit Finding	Microbiology	SMS	HLC	6/6/2014	2/6/2015		
3	00002		Corrective Action							
4	00003		QC Recurrence							
5	00004		PT failure							
6	00005									
7	00006									
8	00007									
9	00008									
10	00009									
11	00010									
12	00011									
13	00012									
14	00013									

Initiated
Root Cause Complete
Corrective Action in Progress
Corrective Action Complete
Follow-up Complete
Closed

Exercises-Document Control

- How would you treat these different in your document control system?
  - Quality Manual
  - SOPs (technical)
  - SOPs (administrative)
  - Forms (technical)
  - Forms (administrative)
  - Reference Methods (paper copies)
  - Reference Methods (electronic)
- Ask these questions for each one
  - WHO needs to review and approve each revision?
  - WHICH personnel needs to read and sign off on this document before doing…
  - WHAT work?
  - WHEN does this need review and revision?
  - HOW will you secure this document?
  - WHERE will the master document be kept?