What to expect during an inspection-from the perspective of a molecular laboratory?

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Accreditation

- Has a mandate to assess the quality of diagnostic services
- Help laboratories achieve the highest standard of laboratory quality
- Deliver accurate results for better patient outcomes
- Ensure confidence of patient diagnosis
- Manage and reduce the risk of inaccurate and unreliable test results

Molecular Diagnostics-Microbiology

- Most accreditation guidelines reference CLSI MM19-A, CAP, ISO 15189
- Different provinces have different accreditation bodies. Their guidelines target the same general issues, but there are differences in whether things are recommended or required and how specific or vague the requirements are.
- Were originally focused on Genetic molecular testing
- Becoming more refined and specific to microbiology.

Snapshot of Activity

- Assessor comes in for a day or two
- Usually also assessing the rest of microbiology
- Reviews SOPs to see that they have specifically addressed requirements.
- Speaks to staff to see if they know how their SOPs address the requirements.
- Observe activity and review documentation to see if staff is addressing the guidelines as they are spelled out in their SOPs

Areas that the guidelines address

- Physical Requirements
- Reagents
- Instruments and equipment
- Validation and verification of a new assay
- Analytical Testing
- On-going quality control
  - Proficiency
  - Competency
- Reports

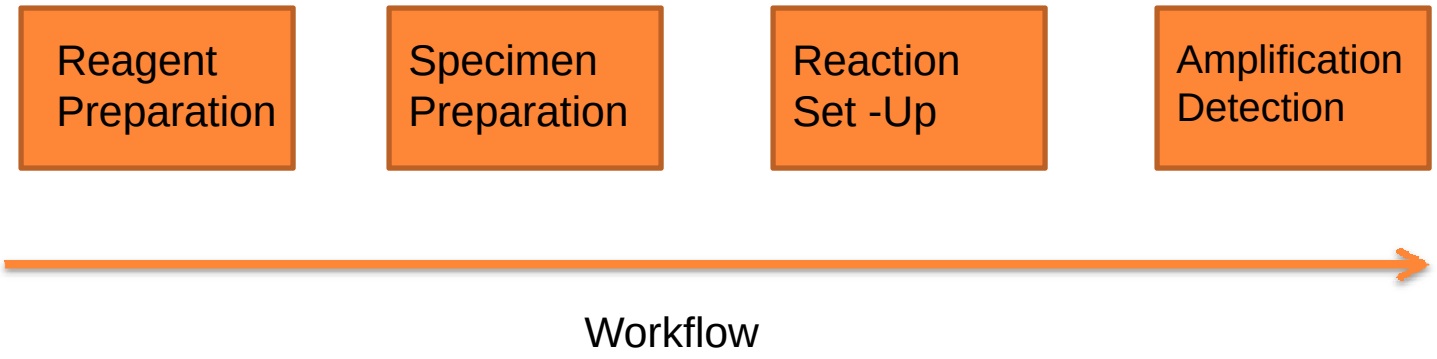
Physical Requirements

- Separate areas for PCR
  - Preparation of amplification reagents
  - Extraction of nucleic acid from samples
  - Assembly of reaction mixes and samples
  - Amplification and detection
- Access is restricted to laboratory personnel
- Unidirectional workflow
- Cleanable countertops and hoods
- Dedicated pipettes and reagents for each area
- Positive displacement pipettes and aerosol barrier tips for set up of PCR
- Dedicated consumables and reagents for each area

Potential Questions from an Assessor

- Can you tell me about the workflow for PCR testing?

- Assessor will observe how samples are processed and inspect the area designated for testing.



Equipment

- Manufacturer's claims for all instrumentation needs to be verified before equipment is placed in service
  - Includes all software
  - Need to run clinical samples through to show that it performs as expected
  - Documentation that it has been validated and approved for use
- Records must be kept for:
  - Maintenance
  - Servicing
  - Trouble-shooting
- If there are more than one instrument being used interchangeably for the same test, need documentation that they perform similarly

Potential Questions

- Can you show me documentation of validation of new instruments?
- What sort of maintenance do you do on this instrument? Can you show me the records for when this maintenance occurred?
- Have any of your instruments needed to be serviced lately? Can you show me the records?
- You have two thermocyclers that you are using for the same test. Do you know that they are performing similarly?

- The assessor will expect to see all records associated with an instrument. Including the initial validation of the instrument prior to use, on-going maintenance, service records and trouble-shooting.

Reagents

- No expired reagents
- All reagents will have an expiry date
- Documentation of when received and the condition it was received in.
- Documentation that new lots perform in a similar manner as previous lots prior to the lot being put into use
- Reagents are kept in an appropriate area
  - Master mixes in the master mix preparation area
  - Specimens stored in a separate area
  - Post-amplification reactions stored in a amplification and detection area

Potential questions

- Do you test new lots of reagents prior to use on clinical specimens? Please show me the documentation.

- The assessor will expect to see documentation that all new lots are tested with appropriate controls prior to use and that the reagents performed adequately and were approved for use on clinical specimens (signed off).
- The assessor will snoop through your fridges and freezers.

Verification of new assays

- Health Canada approved assays:
  - Verify manufacturer's claims for performance of the assay
  - Sensitivity
  - Specificity
  - Precision
  - Reproducibility
  - Accuracy

Validation

- For LDT, RUO assays or Health Canada approved assays with an off-label use (other specimen types, other patient populations, other indications) the laboratory has to determine the performance characteristics and accuracy of the assay
  - LOD
  - Analytical sensitivity and specificity
  - Clinical sensitivity and specificity
  - Reproducibility
  - Precision
  - For all sample types used

Quantitative assays

- There are additional requirements for quantitative assays
  - Linearity
  - Reportable range
  - Uncertainty of measurement
  - Threshold or cut-off value (if applicable)
  - Need to set up on-going monitoring to detect that the assay is performing as expected (mean, SD, CV plotted on Levey-Jennings plots)
  - Tolerance limits for controls must be defined

Potential Questions

- What assays have you recently introduced into your testing platform?
- How did you verify or validate that these assays would perform as per expectations?

- Show documentation of verification and/or validation prior to routine testing.
- Provide documentation that the performance was satisfactory and that the assay was approved prior to its use on clinical samples.

Analytical Testing

- Need SOPs for performing the assays
- Performance and effectiveness of the assay is available
- Staff are adequately trained to perform the assay
- Appropriate controls are used:
  - External positive controls
  - Negative controls (contamination)
  - Extraction controls (internal controls or other mechanism to show extraction was adequate)
  - Levey Jennings plots for quantitative assays

Potential Questions

- What controls do you run with this assay?
- How do you know that the assay worked?
- What do you do when the assay didn't work?
- How do you know that the extraction worked for these samples?
- How do you know there is no inhibition?
- How do you monitor for contamination?

- The assessor will want to see evidence that appropriate controls are used for all assays.
- The assessor will want to see examples of when controls failed and documentation of trouble-shooting actions that followed.

On-going Quality Control

- Proficiency Testing
  - External proficiency testing should be in place for all assays
  - When external proficiency is not available, other methods can be used
    - Swapping of specimens
    - Ungraded challenges (education panels)
    - Blinded testing
  - Needs to be treated as a routine specimen
  - Need to have documentation of actions taken when issues are detected
- Competency
  - All staff needs to be trained appropriately
  - Annual assessment of competency

Potential Questions

- What proficiency testing do you perform on your molecular testing? Are there any assays where you had issues that needed follow-up? How did you trouble-shoot?
- Do you have any recent recruits to molecular or people coming back from a leave? Could you please show me documentation of their training?

- The Assessor will expect to see proficiency testing records for all assays, documentation that they have been reviewed by the laboratory director, and evidence of corrective actions when issues were identified.
- The Assessor will expect to see documentation of training and on-going competency assessment of staff.

Conclusion

- An accreditation visit is a learning opportunity for both the Assessor and the site being inspected,
- Guidelines can still be quite vague and in some cases up for interpretation.
- There is a need to standardize the different requirements from accreditation bodies.
- Ideally, laboratories should work together with accreditation agencies and Health Canada to help standardize our practice

- Questions?

Resources

- College of American Pathologists, Microbiology Checklist 2011
- College of Physicians and Surgeons of Alberta
- College of Physicians and Surgeons of British Columbia Diagnostics Accreditation Program Accreditation Standards 2015
- Diagnostic Quality Assurance Program-College of Physicians and Surgeons of Saskatchewan
- Institute for Quality Management in Healthcare (IQMH) Accreditation Requirements (Version 6.0 December 2013)