Clinical Laboratory Inspections

Know What to Look For

Barbara Randolph, MT(ASCP), MBA, RQAP-GLP

Outline

- Personnel qualifications
- Existing quality systems
- Procedures for technical review
- Analytical assay procedures
- Equipment qualification
- Evidence of controlled operations
- Oversight

Clinical Lab Challenges

- Often overlooked because of automated analyzers
- “Routine”; not much training required
- Frequent use of modified human analytical methods
- Lack of animal QC materials, proficiency testing, and reference ranges
- Data are KEY to the Investigational Veterinary Product (IVP) safety profile

Personnel Qualifications

- Director: DVM Clinical Pathologist
- Supervisor/manager: credentialed specialist
- Lab Technicians
- Animal Technicians
- Science education/experience

Documentation

- CVs
- Credentials
- Training records (including regulatory)
- Job descriptions

DVM Clinical Pathologist

- Director or active consultant
- Additional residency training
- Credentialed by American College of Veterinary Pathologists
- US – DACVP (Clinical Pathology)
- EU - DipECVCP

Laboratory Professionals

- Credentialed by American Society of Clinical Pathologists
- MLT(ASCP)
- MT(ASCP) or MLS(ASCP)
- HT(ASCP) or HTL(ASCP)
- Specialists
- Licensed in some states

Veterinarian Professionals

- Lab training is part of AVMA/CVMA accredited programs (US/Canada)
- Vet Technologist/Technician
- RVT, LVT, CVT according to state laws
- AHT sometimes seen (RAHT, LAHT, CAHT)
- Vet Assistants

Lab Animal Professionals

- ALAT, LAT, LATG
- Animal Husbandry, Health, & Welfare/Facility Admin & Mgt
- No formal clinical laboratory training
- More oversight required
- Review of additional records required

Technical Training

- Science degree
- On-the-job training/lab experience
- Oversight required
- Should review additional records

Existing Quality Systems

- Lab accreditation
- Internal QC sample use and tracking
- Proficiency testing: unknown samples
- Data review procedures
- Species specific assays
- Internal reference ranges

Lab Accreditation

- AAVLD (Accredited Veterinary Medical Diagnostic Lab) – labs administered by a public institution
- A2LA (American Association for Laboratory Accreditation) for Veterinary Labs – available to commercial labs

Lab Accreditation

Human Clinical Lab Standards

- CAP (College of American Pathologists) Lab Accreditation Program
- CLIA – Clinical Laboratory Improvement Act & Amendments
- ISO 15189 – QMS for clinical labs and medical reference labs

QC Sample Analysis

- Commercial samples are used for most instruments; established acceptance criteria
- Monitoring of QC samples run at predetermined intervals is critical to detect shifts and trends
- Nonstatistical QC may include repeat testing criteria, technical data review, reflex testing, correlation with other testing

QC Sample Monitoring

- Request to review QC sample tracking over a period of time
- Look for frequency of QC sample analysis
- Verify that results are review by trained supervisory personnel
- Ensure that any suspect results are investigated and subsequent actions are documented

Proficiency Testing

- Verification of a lab's performance by external assessment
- Programs provide unknown samples for specific assays; results compared with other labs
- Very few veterinary based
- Veterinary Laboratory Association
- Tests all aspects of assay, including technician

Data Review

- Should be timely
- Technical expertise is needed to detect patterns, to correlate results with other tests and, if possible, with clinical signs
- Caution if using human testing lab; study veterinarians need to be aware
- Review must be formalized in an SOP and documented

Species and Ranges

- Species-specific QC samples and reference ranges are poorly defined and have limited availability
- Reference ranges can be determined in-house
- Method (number, description, statistics) should be described generally in an SOP and specifically in the study data

Procedures for Technical Review

Critical SOPs/Documents to review:

- Sample tracking SOP: processing, condition, storage, stability, and retention/disposal
- Proficiency testing/internal QC sample policy/QA oversight
- Repeat sample assay/reporting criteria
- Data review by Supervisor

Technical Review Procedures

Critical SOPs/Documents to review:

- Pathologist review criteria/ “Panic Values”
- Select one or two critical measuring instrument SOPs
- Data handling, transfer to LIMS
- QC monitoring for a time period
- Validation reports for selected instruments

Sample Processing

Blood sample stability

- EDTA: refrigerate; process ASAP
- Sodium citrate: on ice, separate w/in 30 min, keep on ice
- Serum: separate w/in 30 min, refrigerate

Urine sample stability

- Refrigerate; process ASAP

Data Handling

- How are instruments interfaced with the LIMS?
- Are data transcribed or input manually?
- Are QC review procedures adequate?
- Has source-to-archive validation of data transfer been performed?
- Is data transfer adequately described in the SOP?

Analytical Assay Procedures

- Identity of QC material, storage
- Sample handling and storage
- QC sample analysis frequency
- QC sample acceptance criteria
- Procedure for out-of-range values
- Species-specific reference values
- “Panic Values”
- Assay limitations/interferences

Equipment Qualification

- IQ, OQ, PQ translated
- Yes, instruments should have validation reports
- This means more than vendor installation
- Pay particular attention to hematology analyzers

Equipment SOPs Should Address

- Calibration
- QC Tracking
- Maintenance records
- Common flags/error codes
- Back-up instruments or methods

Evidence of Controlled Operations

- Examine data collection form templates and instrument printouts
- Look for sample time tracking
- Review study data, if available
- Confirm traceability of diluted samples
- Verify documented repeat testing
- Ensure reporting is transparent

Oversight

Interview lab management:

- Director & Supervisor available and accessible?
- QA review of routine operations?
- Active review of data, QC monitoring, panic values?
- Hands-on management?
- Ask about any previous information you haven't had time to review

Summary

Look for:

- Quality systems already in place
- Qualified staff
- Applied technical knowledge
- Effective documentation practices
- Controlled operations