Quality assurance for veterinary in-clinic laboratories

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Synopsis

Quality assurance and the implementation of a quality management system are as important for veterinary in-clinic laboratories as for reference laboratories. Elements of a quality management system include the formulation of a quality plan, establishment of quality goals, a health and safety policy, trained personnel, appropriate and well-maintained facilities and equipment, standard operating procedures, and participation in external quality assurance programs. Quality assurance principles should be applied to preanaltyic, analytic, and postanalytic phases of the in-clinic laboratory cycle to ensure that results are accurate and reliable and are released in a timely manner.

Clinics Care Points

- There is minimal regulatory obligation for veterinary in-clinic laboratories to practice quality assurance, but veterinarians should not ignore the necessity for a quality management system.
- The quality assurance approach for an in-clinic laboratory should be outlined in a Quality Policy or Quality Manual.
- Over 85% of laboratory errors occur in the preanalytic and postanalytic phases of laboratory testing (sample acquisition, preparation and requesting, results reporting and interpretation).
- Preanalytic and postanalytic errors can be reduced by using Standard Operating Procedures to standardize processes and by using Key Quality Indicators to define the maximum acceptable error.
- Total allowable error is a benchmark for the degree of analytic error that will affect clinical decision-making.
- Observed analytical error for a method can be quantified from analytical bias and imprecision and should be less than the total allowable error.

Key words: ASVCP, laboratory error, quality assurance, quality control, standard operating procedures, total allowable error, veterinary clinic

Key points

- Quality assurance and the implementation of a quality management system are as important for veterinary in-clinic laboratories as for reference laboratories.
- Elements of a quality management system include the formulation of a quality plan, establishment of quality goals, a health and safety policy, trained personnel,

appropriate and well-maintained facilities and equipment, standard operating procedures, and participation in external quality assurance programs.

- Quality assurance principles should be applied to preanaltyic, analytic, and postanalytic phases of the in-clinic laboratory cycle to ensure that results are accurate and reliable and are released in a timely manner.

1. INTRODUCTION

When a veterinary practice sends patients' samples to a reference laboratory for clinical pathology testing, the expectation is that results will be returned quickly and will reflect the true concentration or activity of tested analytes in the patient with a high degree of certainty. To ensure this, the reference laboratory follows a quality assurance (QA) program that covers elements of sample acquisition, recording, labelling and preparation, equipment maintenance, monitoring analyzer and method performance, accurate reporting of results, and staff training. Laboratory results generated in a veterinary in-clinic laboratory should also be accurate and precise, so in-clinic laboratories should follow similar QA principles. Unfortunately, many veterinary in-clinic laboratories do not follow QA guidelines.[1] As a result, clinically significant errors that can negatively impact diagnosis and patient care have been documented in in-clinic laboratory settings.[2]

This article presents components of laboratory QA and a quality management system (QMS) that can be applied in a veterinary clinic. General concepts of QA will be explained, and essential components of a QMS will be presented. Terms and definitions used in this article are presented in Table 1.

Table 1: Terms and definitions pertinent to laboratory quality assurance (modified from Harr et al, 2013[26])

Abbreviation and term	**Definition**
Bias	Inaccuracy; the difference between a measured value and the true value.
EQA; external quality assessment	Comparison of a clinic's result to a known standard or result from another laboratory
Imprecision	Random error; the lack of repeatability in a test. Represented by the coefficient of variation (CV) of a range of results.
KQI; key quality indicator	Processes and tests that are critical for patients and clinicians and that are monitored as part of a quality management system.
MSDS; material safety data sheet	A document that contains information relating to health and safety for a particular product.
POC; point-of-care	Testing performed outside of the reference laboratory, close to the patient. In-clinic laboratory testing is considered to be POC testing.
QA; quality assurance	The sum of all processes and activities undertaken to ensure that laboratory results are accurate, reliable, and produced in a timely manner.
QC; quality control	Procedures used to monitor analytical performance and detect error.
QCM; quality control material	A specimen which mimics, and is measured like a patient sample. Results are used to monitor analytical performance.
QMS; quality management system	Coordinated activities used to direct and control a laboratory with regards to quality.
SOP; standard operating procedure	A written document providing information and instructions about a laboratory process or procedure.
$TE_{a;}$ total allowable error	An analytical quality goal: maximum combination of bias and inaccuracy tolerable in a single measurement that will still be clinically useful.
TE_{obs}; total observed analytical error	The sum of analytical bias and imprecision (bias + [2 x imprecision]).

Figure 1: Graphical representation of an in-clinic quality management system, using elements described in this article. Initial planning towards the achievement of quality goals necessitates compiling a Quality Manual and including the laboratory in the practice Health and Safety Policy. The resources needed to implement the plan include trained personnel, appropriate facilities, and functioning equipment. Polices and SOPs should document the processes involved in the various phases of the laboratory cycle (Figure 2). Achievement of quality goals like total allowable error and key quality indicators should be monitored using tools such as quality control and external quality assessment. The cycle should drive towards continuous quality improvement, with ongoing adjustment of planning, resources and processes.

1.1 Laboratory Quality Assurance and Quality Management System

In the context of laboratory testing, QA is the sum of all processes and activities to ensure that results are accurate, reliable, and produced in a timely manner.[3] These QA processes and activities form part of a QMS, which is a formal approach to laboratory management, with the goal of attaining predetermined quality goals or standards. Several models for a QMS

have been suggested. For example, the Total Quality Management System loop consists of five elements: quality planning, laboratory processes, quality control, assessment, and improvement, which feeds back into planning.[3,4] At the center of the loop are the quality goals or standards. Another example is the Clinical and Laboratory Standards Institute model, which defines 12 essential components of a QMS, aimed to support the path of workflow through a laboratory.[5] Figure 1 illustrates how the elements of QA most relevant to a veterinary in-clinic laboratory and discussed in this article might fit into a QMS loop.

1.2 The status of QA in veterinary clinical pathology

In human medicine, clinical laboratory testing is usually regulated by national or regional legislation or bodies, such as the Clinical Laboratory Improvement Amendments (CLIA) and Food and Drug Administration (FDA) in the USA. These have oversight over reference laboratories, point-of-care (POC) testing facilities, and diagnostic devices, and ensure that laboratory testing is performed to certain standards.[6,7] In veterinary medicine, accreditation of clinical pathology laboratories is optional, and POC testing devices are not regulated. A survey conducted in 2007 to assess the level of knowledge and practice of QA amongst veterinarians found that most respondents used only very basic QA tools, which often were reactive rather than preventive, and that respondents often lacked knowledge about laboratory quality management.[1] To address the deficit in veterinary clinical pathology laboratory testing and to raise awareness of the importance of laboratory QA in the veterinary profession, several individuals and professional groups have issued guidelines or published articles on veterinary clinical pathology QA in the last two decades.

The American Society for Veterinary Clinical Pathology (ASVCP) Quality Assurance and Laboratory Standards (QALS) Committee published a three-part set of guidelines (Principles

of Quality Assurance and Standards for Veterinary Clinical Pathology) between 2010 and 2012.[8-10] These were intended for use predominantly by laboratory professionals, but many sections were considered applicable for in-clinic laboratories. These guidelines were updated in 2019 as one comprehensive open-access document with sections covering different stages and types of laboratory testing, with checklists at the end of each section.[3] The ASVCP QALS Committee also published a set of guidelines specifically aimed at POC testing (i.e. testing performed outside of a reference laboratory, see definition Table 1). These encompassed recommendations for general QA as well as guidance for quality management of POC clinical chemistry and hematology instruments.[11] In order to further inform veterinarians and veterinary technicians and nurses in practice, several reviews and articles covering practical approaches to quality management in veterinary in-clinic laboratories also have been published. These include topics such as QMS, laboratory facilities and equipment, and recommendations for quality management of hematology and clinical chemistry analyzers.[4,12-18] Additionally, ASVCP recommended that veterinary graduates show competency in basic QA, and that this topic be included in veterinary clinical pathology curricula.[19]

2. DISCUSSION

2.1 QA essentials

2.1.1 The laboratory cycle and laboratory errors

As illustrated in Figure 2, regardless of physical location, the laboratory testing cycle consists of three phases of testing: preanalytic, analytic, and postanalytic.[20,21] The preanalytic phase includes selecting which assays to run based on patient presentation, collecting the appropriate samples, labelling those samples, and transporting them to the laboratory. The analytic phase includes sample preparation and analysis. The postanalytic phase encompasses

verification and reporting of results, interpretation of those results by clinical pathologists and clinicians, and consequent patient management.

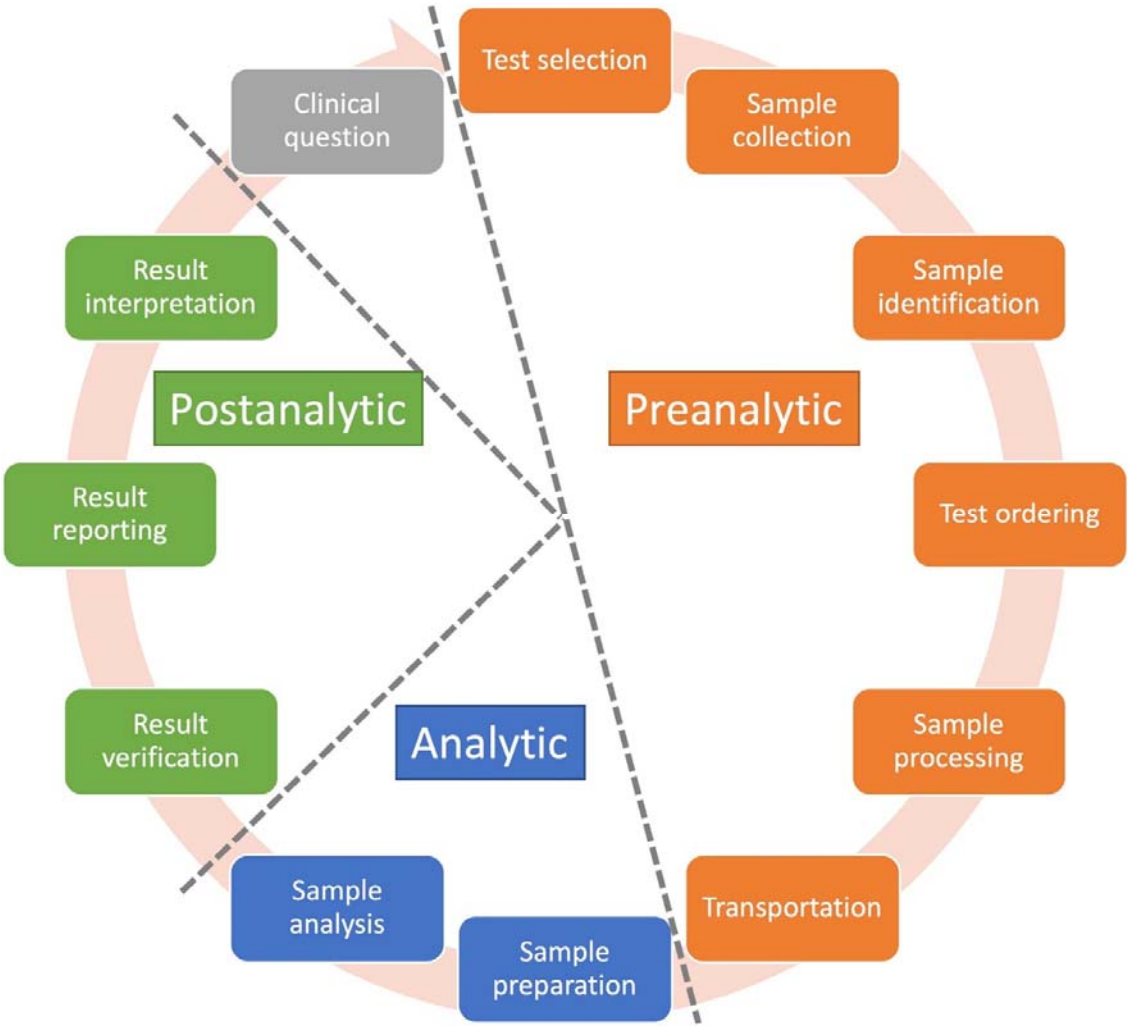

Figure 2: The laboratory cycle, which starts in the preanalytic phase with selection of appropriate tests based on a clinical question and leads through the analytic and postanalytic phases to interpretation of results and a new clinical question.

Laboratory error can occur at any point in this cycle. In both human and veterinary medicine, 60-75% of errors occur in the preanalytic phase, 10-30% in the postanalytic phase, and around 10% in the analytic phase.[22-25] In other words, up to 90% of errors occur outside of the analytic phase, during test selection, sample acquisition and transport, and result reporting and interpretation. As can be seen from Figure 2, most of these steps are under the control of

clinical staff, and do not take place in the laboratory itself. Whether or not sample analysis takes place in the clinic, QA of these error-prone steps is essential to reduce mistakes and limit harm to patients.

No analytical method is error free and completely accurate. The components of analytical error are bias and imprecision. Analytical bias is the difference between the measured result and the true value of an analyte in the patient, and this difference is expressed as a percentage of the true value. Analytical imprecision relates to repeatability of results for samples measured multiple times by the same method. This variability is analytical imprecision, which is expressed as the coefficient of variation (CV), also as a percentage. The total observed analytical error (TE_{obs}) of a test method reflects bias and CV, and is calculated as follows[26]:

$$TEobs = absolute\ analytical\ bias + (2\ x\ CV)$$

Absolute analytical bias: the value of the bias without regard to its sign (+ or -).

Determination of bias and imprecision for an analytical method is discussed in Section 2.1.8

Quantifying errors in the preanalytic and postanalytic phases is determined by defining errors that can occur in these stages, and then expressing the percentage of all samples that were affected by these errors. Examples of specific errors that should be defined and monitored are presented in Box 1 (as Key Quality Indicators, see Section 2.1.2).

Box 1: Key Quality Indicators relevant to a veterinary in-clinic laboratory[4,28]

Preanalytic phase
Number or % of samples misidentified. (This includes samples with the incorrect identification, partial identification, or no identification).
Number or % of samples of incorrect type. (For example, a serum tube collected for hematology).
Number or % of samples with insufficient volume.
Number or % of samples with hemolysis submitted for clinical chemistry testing.
Number or % of samples with lipemia submitted for clinical chemistry testing.
Number or % of samples clotted (in anticoagulant tubes).
Postanalytic phase
Number or % of analyzer results incorrectly transcribed or not transcribed into patient record.
Number or % of results reported to clinician or client outside of specified turnaround times.
Number or % of critical results not reported to clinician immediately.

2.1.2 Quality goals

Quality goals are the standards that must be attained to ensure patient safety and satisfy the needs of clinical staff and owners. Quality goals have different formats in the three different phases of the laboratory cycle.

Ideally, an assay would have minimal bias and low imprecision, so that the result given by the assay is similar to the true value of the analyte in the patient. However, analytical error is inherent to assay systems and is unavoidable. The degree of analytical error in a single test result that is considered acceptable for clinical decision making is the total allowable error, or TE_a. In veterinary medicine, TE_a values have been recommended by expert veterinary clinical pathologists and specialist clinicians for hematology and clinical chemistry analytes.[26,27] TE_a limits for select commonly used hematology and clinical chemistry tests are presented in

Table 2. The use of TE_a to monitor instrument performance is further explained in Section 2.1.8.

Table 2: Total allowable analytical error (TE_a) for hematologic and clinical chemistry analytes.[26,27]

Hematology		**Clinical Chemistry**			
Analyte	**TE_a**	**Analyte**	**TE_a**	**Analyte**	**TE_a**
RBC	10%	**Albumin**	15%	**GGT**	20%
Hemoglobin	10%	**ALP**	25%	**Glucose**	20%
Hematocrit	10%	**ALT**	25%	**Lactate**	40%
MCV	7%	**AST**	30%	**Phosphorus**	15%
MCHC	10%	**Bile acids**	20%	**Potassium**	5%
WBC	20%	**Calcium**	10%	**Sodium**	5%
PLT	25%	**Cholesterol**	20%	**TP**	10%
		Chloride	5%	**Triglyceride**	25%
		Creatinine	20%	**Urea**	12%

MCHC, mean cell hemoglobin concentration; MCV, mean cell volume; PLT, platelet concentration; RBC, red blood cell concentration; TP, total protein; WBC, white blood cell concentration

Quality goals for the preanalytic and postanalytic phases are compiled in the form of Key Quality Indicators, or KQIs.[28] These monitor processes that are critical for producing accurate and timely results. Examples of KQIs most relevant to veterinary in-clinic laboratories are listed in Box 1. Laboratories should set their own limits for the number or percentage of tolerable error for each KQI.

2.1.3 Quality Manual

The QA approach for an in-clinic laboratory should be outlined in a Quality Policy or Quality Manual. This is a written document that includes a statement of intent and outlines the

organization of the laboratory in terms of services offered, laboratory environment and facilities, responsible personnel, operations, and health and safety practices.[3,13] The statement of intent outlines the vision and mission, the laboratory's commitment to provide a high-quality service to users, and the use of a QMS. This is followed by a section describing the laboratory services that are offered by the clinic, the clientele and patients that are serviced by the in-clinic laboratory, and the laboratory environment, including facilities and equipment. Personnel information generally includes an organizational chart, the roles and qualifications of staff working in the laboratory, training requirements, and competency assessment. The operations section should detail that laboratory processes are conducted according to standard operating procedures (SOPs), and state turnaround times (TAT) for various tests and policies for sample and data storage. Lastly, there should be a description of health and safety practices.

2.1.4 Health and Safety

The practice health and safety program should include the laboratory environment. The formulation of a Health and Safety Plan that describes identification and control of hazards and risks, SOPs related to health and safety, and a mechanism for reporting workplace-related injury and illness.[29] Guidelines and instructions for developing a Health and Safety Plan are available from the US Occupational Health and Safety Administration (OSHA).[30]

Chemical hazards relevant to a laboratory environment include reagents, disinfectants, and other chemicals used for sample processing and analysis. A Material Safety Data Sheet (MSDS) produced by manufacturers of each product provides details on health effects of exposure, measures that should be taken to protect workers against exposure, and emergency medical procedures to be followed if exposure does occur.[31] The staff member responsible for

the laboratory or for practice health and safety should ensure that a current MSDS for each chemical is readily accessible in the laboratory.

Biological hazards include zoonotic agents that may be present in blood, body fluids, or tissue samples. Staff working in the laboratory should practice proper hand hygiene and wear protective equipment, like a laboratory coat and gloves. Eye protection and a surgical mask may be necessary in some circumstances.[32] Samples should be stored away from food and drink, in a separate refrigerator. The laboratory space should be cleaned daily, and surfaces disinfected more frequently. All medical waste should be disposed of according to local regulations.

Noise from laboratory equipment can be hazardous if loud, and noise generation should be considered when purchasing equipment. For example, a high speed refrigerated centrifuge may create up to 65 dBA of noise, and normal speech cannot be heard if background noise is greater than 55dBA. The permissible noise exposure limit recommended by OSHA for an 8-hour period is 90 dBA.[33] Long hours of microscope use, repeated pipetting, and computer use can lead to muscle strain, and care should be taken to make these activities as ergonomic as possible.[34]

2.1.5 Personnel

Only designated personnel should work in the laboratory. A veterinary technician or nurse or veterinarian should be assigned overall responsibility for the management of the in-clinic laboratory. Staff working in the laboratory should receive appropriate training that includes QA and the procedures performed in the laboratory.[11] Personnel should also be familiar with the Quality Plan or Quality Manual. Staff can be trained using SOPs and instruction material

provided by equipment manufacturers, and sign-off sheets should be used to record training. Evaluation of competencies can follow formal proficiency testing schemes (see Section 2.5) or be informally assessed by evaluating compliance to SOPs or comparative smear reviews.[12]

2.1.6 Facilities and equipment

The laboratory should be located in a low-traffic area within the clinic with adequate space for sample preparation and reagent storage, and convenient access to electricity and a sink. Most analyzers function within an environmental temperature range of 22–25°C and humidity range of 30–50%. Refrigerators for reagent and sample storage should be monitored daily for accurate temperature.[3]

In-clinic laboratory equipment commonly includes centrifuges, POC hematology and chemistry analyzers, a refractometer, dipsticks, a microscope, and stains. Maintenance of POC analyzers is covered in a separate article in this volume. Centrifuges should be cleaned and disinfected with an alcohol-based product every 1-2 weeks, or immediately after a spill occurs. Centrifuges need to be serviced and calibrated annually by a trained technician. Refractometers should be cleaned after each use with a lint-free wipe moistened with methanol and should be calibrated daily or weekly using distilled water, depending on frequency of use.[3] Urine dipsticks should be not used past their expiry date, and should be stored in their original container with the lid tightly shut to prevent exposure to light and moisture. Regardless of the brand of dipsticks, the leukocyte, nitrate, and specific gravity pads are not reliable in animals, and the urobilinogen test is not considered useful.[3] Microscopes should be dusted weekly. Objective lenses that come into contact with immersion oil should be wiped immediately after use with lens tissue. Immersion oil from non-immersion lenses and other parts of the microscope can be gently removed with lens

tissue moistened with ethanol.[14] Microscopes should undergo annual maintenance and cleaning by trained personnel from the microscope supplier or other services.

Stains used in practice for blood smears and cytology are usually modified Romanowsky quick stains. Individual stain reagents may become contaminated by other stain reagents, water, or bacteria. The former will be noted as poor slide staining, and the latter can be monitored by examining a drop of stain on a slide using the microscope. Before replacing stain reagents, containers should be rinsed and dried, and stain may need be filtered (using a coffee filter) if precipitates are a problem.[14]

There should be a maintenance or performance log for each piece of equipment. This should indicate maintenance procedures, dates for scheduled and completed maintenance, and any other incidents such as breakdowns or replacement of parts.

2.1.7 Standard operating procedures

SOPs are documents that describe how to perform an activity. An SOP provides step-by-step instructions for personnel to follow to ensure consistency and quality of results. SOPs may be administrative or procedural. Examples of administrative SOPs include taking inventory, instructions for reagent storage, and health and safety procedures. Procedural SOPs can be organized according to the three phases of the laboratory cycle. Examples of procedural SOPs relevant for an in-clinic laboratory are shown in Table 3.

Table 3: Examples of Standard Operating Procedures relevant to an in-clinic laboratory, organized according to the phases of the laboratory cycle

Preanalytic	**Analytic**	**Postanalytic**
Laboratory profile for a preanesthetic workup	Preparation and staining of blood and cytology smears	Verification of result reporting
Laboratory profile for a geriatric checkup	Operation of the hematology and chemistry analyzers	Disposal of samples
Laboratory profile for chronic diarrhea	Blood smear evaluation	Reporting of critical results
Collection of blood samples for CBC, clinical chemistry, hemostasis, and hormone testing	Performing a complete urinalysis	Turnaround times
Collection of samples for cytology (masses and organs)	Maintenance and cleaning of the hematology and chemistry analyzers	
Labelling of samples	Quality control for the hematology and chemistry analyzers	

An SOP should have a standard format, and published recommendations for headings and content are summarized in Table 4.[3] SOPs should be available in print or digital format at laboratory workstations so that relevant personnel have easy access. SOPs should be reviewed and updated annually, and new SOPs should be created for any new procedures or methods.

Table 4: Items and content that should be included in a Standard Operating Procedure for a veterinary in-clinic laboratory

Title page or header	Title of the SOP Identification number, date and revision number Names of authors Number of pages; cumulative page number should be repeated on each page (e.g., page 3 of 5)
Purpose/scope	Brief introduction to the procedure Job titles of personnel who will use SOP
Timing	Days of the week that the procedure is performed Expected turnaround time
Health and Safety	List of necessary personal protective equipment Handling and disposal of hazardous materials
Sample requirements	Type and volume of sample Rejection criteria (e.g., hemolysis, lipemia)
Reagents and equipment	Reagents Control material Disposables (e.g., pipette tips, microhematocrit tubes) Equipment (e.g., centrifuge, microscope, hematology analyzer)
Routine quality control	Routine quality control procedure for the procedure described in the SOP (if relevant) Troubleshooting steps to be undertaken if quality control fails
Procedure	Detailed step-by-step instructions
Interpretation criteria	Reference intervals or diagnostic cutoffs Effects of interferents and biological factors (e.g., hemolysis, age, medication) Information about sensitivity and specificity of the test, if relevant Any standardized comments
Reporting and sample disposal	Names of any reporting forms Sample storage and disposal
References	Package inserts Other SOPs Scientific literature

2.1.8 Quality control

Quality control (QC) encompasses procedures used to monitor analytical performance and detect error. For POC instruments this entails internal instrument QC checks and/or the use of quality control material (QCM). It is important to note that internal QC checks only monitor system function (electronic, calibration) and do not assess the entire analytical process.[11] Nevertheless, results of internal QC checks should be recorded and analysis should not proceed if these checks fail.

QCM mimics a patient sample and should be used to monitor instrument performance on a regular basis. The ASVCP POC testing guidelines recommend daily measurement of QCM for non-unit devices (e.g. hematology analyzer) and at least weekly measurement of QCM for unit devices (i.e. using a rotor, cassette, slide, strip or cartridge).[11] QCM contains multiple analytes and is usually available in two or three levels: one "normal" level control in which analytes are within ranges expected for a healthy patient, and "pathological", "low" or "high" controls with analyte concentrations outside of expected healthy ranges. The manufacturer of the QCM provides a target mean and acceptable range for each analyte for each level. The range represents either two ("1-2s rule") or three ("1-3s rule") standard deviations on either side of the mean. The manufacturer's acceptable range may permit more analytical error such as bias and imprecision than is acceptable for clinical decision-making (i.e., analytical error is higher than TE_a). One method of using QCM data to evaluate method performance is to plot measurements over time on a Levey-Jennings chart that also displays the target mean and acceptable limits.[3,15] Levey-Jennings charts may be available within the QC menu of POC analyzer software or can be constructed.[35] An example of a Levey-Jennings chart is given in Figure 3.

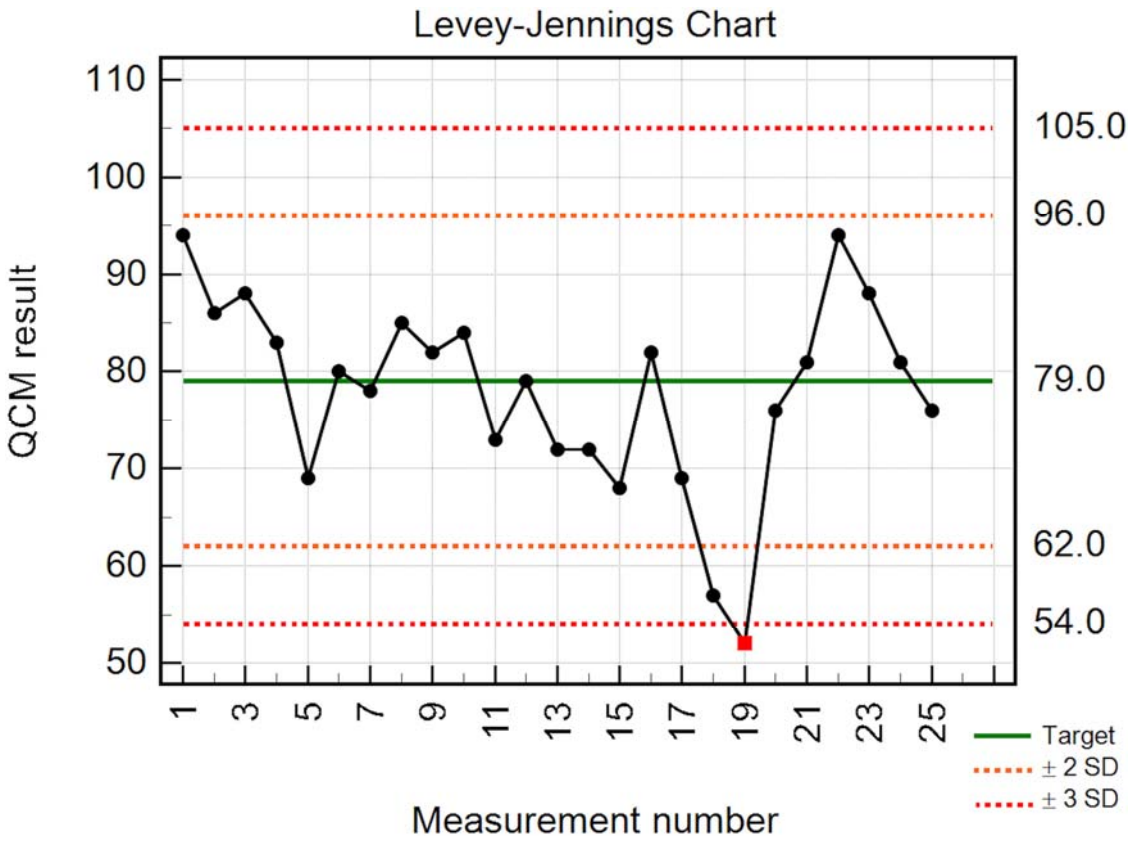

Figure 3: An example Levey-Jennings chart, showing the results of 25 measurements of quality control material (QCM), for a hypothetical analyte (y-axis). The target value provided by the manufacturer or calculated is represented by the central green solid line. The inner set of dashed orange lines represent warning limits that are two standard deviations away from the target and the outer dashed red lines represent control limits that are three standard deviations away from the target value. The black dots represent individual QCM values. One quality control failure occurred at measurement 19. This represents a potentially serious loss of performance of the analytical method. When a QCM result is out of control, troubleshooting to determine the cause for the failure must be carried out, and no patient samples are run until the QCM result is in control again (measurement 20).

A second method is to use QCM results and the target mean to calculate bias and imprecision (CV). This is done with at least 5 QCM results, using the following calculations:[26]

$$Bias(\%) = \frac{(Mean\ of\ QCM\ results - target\ mean)}{Target\ mean}\ x\ 100$$

$$CV(\%) = \frac{SD}{Mean\ of\ QCM\ results}\ x\ 100$$

Bias and CV are then used to calculate TE_{obs} using the formula in Section 2.1.1. If TE_{obs} is greater than the TE_a presented in Table 3, then analytical performance is not acceptable, and analytical error may affect clinical decision-making. The calculated bias and CV can subsequently be used to reset the acceptable QC ranges to ensure that TE_{obs} is less than TE_a. The mathematical handling of QCM results to calculate bias, imprecision, and TE_{obs}; the comparison of these metrics to TE_a; and the subsequent selection of acceptable QC ranges are referred to as statistical QC. The use of a simple 1-3s rule is advised when constructing QC ranges for POC devices, if analytical performance is good enough.[11] Step-by-step instructions and calculation templates for statistical QC approaches for veterinary in-clinic laboratories have been published elsewhere.[11,14,15]

Trouble-shooting QCM failures or high TE_{obs} involves checking various components of the analytical process: expiry, storage, and correct target values for the QCM; results of internal QC checks or calibration; maintenance procedures; storage and expiry of reagents; water quality; waste disposal; and ambient temperature and humidity.[15] If the source of error cannot be identified and corrected, the manufacturer should be contacted. Patient samples should not be run until analyzer performance is once again acceptable.

2.2 Quality Assurance for the preanalytic phase

This is the phase of the laboratory testing cycle in which most errors occur, and poor quality assurance here can result in sample rejection or the need to repeat sample collection,

inaccurate results, and misinterpretation of results.[24,25,36] Monitoring QA in this phase is based on the use of the KQIs listed in Box 1.

This phase begins with the selection of laboratory tests based on clinical presentation, information gained from the history, and results of other diagnostic tests. It may be useful to document which testing profiles should be used in various clinical scenarios, in the form of SOPs (see Table 3). Although the use of testing profiles are convenient and may be more economical than selection of individual tests, the composition of these panels is often not evidence-based, and there is a need for consensus and optimization of this step.[36]

Dogs and cats should generally be fasted overnight before blood collection to avoid postprandial lipemia and hyperglycemia. Lipemia interferes with hematology and clinical chemistry testing, and severely lipemic samples cannot be analyzed.[3] Samples should be collected with minimal stress to avoid laboratory changes associated with catecholamine or cortisol effects.[36] Protocols for patients undergoing dynamic testing, like bile acid stimulation testing or the low dose dexamethasone suppression test, should be described in SOPs and should be adhered to. Correct sample collection techniques, appropriate sample tubes and containers, and optimal sample handling for hematology, clinical chemistry, hemostasis testing, urinalysis, cytology, and endocrinology are well-described in the 2019 ASVCP Principles of Quality Assurance and Standards for Veterinary Clinical Pathology publication, and clinic SOPs for these procedures should be written according to that document.[3]

Samples should be properly identified with unique identifiers such as patient name and surname or patient number. Sample mix-up due to incorrect or incomplete identification is a serious error that can result in potentially fatal decisions being made for the wrong patient.

Samples from dynamic or challenge testing must be clearly marked with sampling times, and cytology samples must be labelled with the site of sampling. Sample ordering can be done manually on a sample submission form or electronically. The animal's name and surname should match those of the sample, and the species, breed, sex and age should be indicated as this assists laboratory staff with interpretation of results.

If samples will not be analyzed immediately, then appropriate storage is important. Whole blood in EDTA for hematology can be stored for up to 24 hours at refrigerator temperature; blood smears and cytology slides must be stored in plastic slide containers at room temperature away from formalin,.[3] Serum or heparin samples for clinical chemistry and hormone analysis preferably should be centrifuged, and for most analytes, the serum or plasma can be stored in the refrigerator for 24-48 hours. Urine can be stored at room temperature for 30 minutes or for 4 hours in the refrigerator.[3,36] If samples are to be transported, they should be triple-packaged (tubes or slide holders wrapped in absorbent packing material, placed into a leak-proof plastic bag or other receptacle, and then placed inside rigid packaging material like a cooler box or stiff cardboard box) and should not be subjected to extreme heat or cold or excessive movement.

2.3 QA for the analytic phase

The use of TE_a (Table 2) and QC to monitor analytic error is the mainstay of QA in this phase. Analyzer and equipment maintenance, correct storage and handling of reagents and tests, personnel training, and ensuring optimal environmental conditions are all critical. Further details on advantages, limitations, maintenance, and QC for in-clinic hematology, clinical chemistry, coagulation, blood-gas and urinalysis analyzers is provided in the Point of Care Testing article, included in this volume.

2.4 QA for the postanalytic phase

As per Figure 2, steps included in the postanalytic phase include result verification, review and interpretation. Results should be reviewed before they are released to identify possible preanalytic and analytic errors, implausible results, typos, and critical values.[3] The latter are test results that need to be reported to a clinician immediately, such as hyperkalemia, hypoglycemia, or bacteria in an effusion or cerebrospinal fluid sample. Ideally, there should be an SOP (Table 4) that lists analytes and cutoffs below or above which results are considered critical values. Repeat testing of any result that seems implausible or may be associated with error is recommended.

Results should be presented in a standard format that includes species- and method-specific reference intervals or decision limits, and the patient's full name and identifying numbers.[3] Interpretation of laboratory results is an important part of postanalytical QA. This requires up-to-date knowledge of the diagnostic utility of the tests being reported, and how results relate to the clinical condition of the patient founded on current evidence-based information.

There should be detailed SOPs (Table 3) for sample storage (retention post-analysis) or disposal including disposal of sharps and biohazards.

QA monitoring in the postanalytic phase is based on the use of the KQIs listed in Box 1. The turnaround time (TAT) is a metric commonly used in referral laboratories and represents the time that it takes for a verified result to be released, after the sample has been received in the laboratory. The TAT will differ for different analyses but provides a good summary of the efficiency of workflow in all three phases.

2.5 External quality assessment

External quality assessment (EQA), also called proficiency testing, is a QA procedure that involves comparison of results between two methods or comparison of in-clinic results with results from other clinics using the same instruments and methods. For in-clinic laboratories, this may mean participation in a formal EQA program, for example the Veterinary Pathology Group EQA Scheme[37] (UK), the IDEXX EQA Scheme[38] (UK) or the Veterinary Laboratory Association QA Program[39] (North America). An alternative is informal comparison of results from POC testing to those from a reference laboratory. It is important to note that results obtained using different analytical methods will differ, so results may need to be compared by calculating whether they show a similar deviation from method-specific reference intervals. The ASVCP released open access guidelines for implementation and interpretation of EQA (ASVCP Quality Assurance Guidelines: External quality assessment and comparative testing for reference and in-clinic laboratories) in 2015, and these provide details of formal EQA programs available in a range of countries, as well as instructions for in-clinic laboratories wanting to take part in informal EQA testing.[40]

3. SUMMARY

Results produced by a veterinary in-clinic laboratory should be accurate, reliable, and produced in a timely manner for optimal diagnostic and therapeutic decision-making and patient care. This can be achieved only through adherence to laboratory QA principles and implementation of a QMS. Elements of a QMS include a quality plan, quality goals, a health and safety policy, trained personnel, appropriate and well-maintained facilities and equipment, SOPs, and participation in EQA programs. QA principles should be applied to preanalytic, analytic, and postanalytic phases of the in-clinic laboratory cycle.. Veterinarians are encouraged to consult ASVCP guidelines and other texts referenced in this article for

more information. Specialist veterinary clinical pathologists and other laboratory professionals also provide QA consulting services.

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