Veterinary
Laboratory Quality
Basic Principles and Selected Topics

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Freeman, Klenner-Gastreich, Korchia, et al.

Westgard QC, Inc.

Veterinary
Laboratory Quality
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A long-needed reference for Laboratory Quality in Veterinary Medicine.

For decades, the Veterinary Laboratory has relied on teachings adapted from the human laboratory. However, the differences between veterinary and human testing, distinct and growing in complexity, have meant the utility of "traditional" reference books has declined. A specialized Veterinary work has been long overdue.

At last, a Veterinary-Specific book on Quality is available. With the support and encouragement of the ECVCP and ASVCP Laboratory Standards Committees and the Veterinary Information Network, editors Drs Kathleen Freeman, Stefanie Klenner-Gastreich and Jérémie Korchia have assembled a comprehensive reference for Veterinary Laboratories. Veterinary Laboratory Quality provides basic principles, in-depth coverage of selected topics and issues specific for veterinary laboratories. It provides a philosophical explanation of the authors' approach to veterinary laboratory quality as well as a practical approach to addressing the unique challenges of the veterinary laboratory. This single comprehensive reference covers in 25 chapters what would require multiple volumes in human laboratory textbooks.

The areas addressed include:

- Basic Quality Concepts
- Business Performance Metrics for the Laboratory
- Instrument, Method, and QC Validation
- In-clinic Laboratory Testing Tips
- A Complete Introduction to Statistics for Veterinary Laboratories
- Special chapters on Biological Variation, Clinical Pathology, Cytology, Endocrinology and LEAN Six Sigma

Together with the editors, the authors of Veterinary Laboratory Quality provide more than a dozen experts with hard-won wisdom and practical insights into the unique field of Veterinary Laboratory Testing.

For Veterinary Laboratories, this is an essential reference.

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Veterinary Laboratory Quality

Basic Principles and Selected Topics

First Edition

Editors

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EBVS® European Specialist in Veterinary Clinical Pathology

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Preface

The idea for this book was originally based on the Laboratory Quality Management Course taught on VIN for a number of years and the experiences of the editors in their own organizations in promoting and implementing veterinary laboratory quality systems. It is not meant to be an exhaustive review of various quality topics; it is meant to cover the basic principles of a veterinary laboratory quality system and address veterinary-specific topics, problems and concepts.

The intended audience for this book includes clinical pathologists wanting to learn more about veterinary laboratory quality, as well as veterinary laboratory technicians, residents in clinical pathology and internal medicine specialties, veterinarians with in-clinic laboratories and veterinary technicians/ nurses involved in in-clinic laboratory testing. The principles of veterinary laboratory quality apply whether the laboratory is a reference laboratory, a university-based laboratory, a commercial laboratory or an in-clinic laboratory.

In order to facilitate learning and provide some structure for the reader, each chapter has a set of learning objectives, a section emphasizing the 'take-home message' and a quiz.

Many chapters also contain 'References' or a 'Further Reading and Resources' section to direct readers to various papers, books, websites or other links that provide information about each chapter topic. We have provided examples of various documents, spreadsheets or forms which can be modified to suit the style and needs of the readers' own laboratories.

We are grateful to the various authors that have provided chapters for this book! They are all experts in the areas of their contributions.

We hope that this book will provide a place for many of you start on your own 'quality journey' in your own veterinary laboratories.

Kathleen Freeman DVM, BS, MS, PhD, DipECVCP, FRCPath, MRCVS

Stefanie Klenner-Gastreich, Dr.med.vet, DipECVCP

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About the Editors

Kathleen P Freeman DVM, BS, MS, PhD, DipECVCP, FRCPath, MRCVS, European Veterinary Specialist in Clinical Pathology, RCVS Specialist in Veterinary Pathology (Clinical Pathology), is an American-trained veterinary clinical pathologist with experience as a laboratory director and senior clinical pathologist in the USA and UK. She is the Founding Chair for the ASVCP Quality Assurance and Laboratory Standards Committee and the ECVCP Laboratory Standards Committee. She received the ASVCP Teaching Award in 2014. Currently, she works as a veterinary clinical pathologist for Veterinary Information Network (VIN), based in Davis, California and works with the VIN-Europe and Beyond branch of VIN. Her special interests include laboratory quality, cytology, equine medicine and pathology, and veterinary medical specialty competency-based education.

Stefanie Klenner-Gastreich Dr.med.vet., DipECVCP, European Specialist in Veterinary Clinical Pathology received her veterinary degree from University of Veterinary Medicine Hannover, Germany and did her doctoral thesis in gastroenterology. After an internship at the Small Animal Clinic of the Justus-Liebig University Gießen she completed her residency at the Central Laboratory. At scil animal care company Dr. Klenner-Gastreich worked with POCT and especially loved method validation, product development and the discussion with colleagues and clients about the various aspects of laboratory diagnostics. Teaching has always been a pleasure during her work as VIN lecturer of the Quality assurance in Veterinary Laboratories online course. She also serves as chair of the European College of Veterinary Clinical Pathology (ECVCP) Laboratory Standards committee and treasurer of the European Society of Veterinary Clinical Pathology (ESVCP).

Jérémie Korchia DVM, MS, DAVCP (Clinical Pathology) graduated from the veterinary college of Alfort (France) and pursued studying with a Master of Pathophysiology and a small animal rotating internship. He worked in academia in small animal internal medicine and then in endocrinology, before moving to the USA for a clinical pathology residency at Michigan State University. After a few positions in the USA as lead scientist and academic instructor, he returned to Michigan State University as an assistant professor, while keeping active in clinical diagnostics and research. Dr Korchia is currently the section editor for clinical pathology of the Journal of Veterinary Diagnostic Investigation, and the Chair of the ASVCP Quality Assurance and Laboratory Standards committee. He chaired the laboratory quality ASVCP premeeting of 2022.

About the Authors

Nándor Balogh DVM, PhD, DipECVCP, is a graduate of the Veterinary School in Budapest, where he also gained a Ph.D. degree a few years later. Dr. Balogh has worked for the Budapest veterinary school small animal and large animal clinics and laboratories for several years, then spent a year in private practice In the Hungarian countryside. After that he worked for Vet-Med Labor Germany (later IDEXX) as a Hungarian representative. He spent nearly a year in the UK working for IDEXX as a clinical pathologist. During that period, he accomplished ECVCP certification. Since 2009, Dr Balogh has run his own private clinical pathology lab, PraxisLab, in Budapest. His special interests include laboratory quality management, lab IT, cytology

and laboratory testing of kidney, liver and vector-borne diseases. He continues as a guest lecturer graduate students at the Budapest veterinary school and works as a member of the Hungarian Veterinary Chamber Educational Committee.

Randolph M Baral BVSc MANZCVS (feline) PhD graduated from the University of Sydney in 1991. After graduating, he worked part-time in Australia and the UK while pursuing a career as a professional triathlete. In 1997, he started Paddington Cat Hospital with his wife, Melissa Catt. Randolph achieved Membership of the Australian College of Veterinary Scientists in Medicine of Cats in 2001, and his clinical pathology PhD in 2015. He has been a VIN consultant since 2001. Dr. Baral has published more than 50 peer-reviewed papers and was a co-editor of the internal medicine section of Susan Little's The Cat: Clinical Medicine and Management, for which he wrote twelve chapters in diverse areas. Randolph administers the vetbiologicalvariation.org website; he became a founding director of CustomClinPath software in 2021.

Amy Browne BSc Veterinary Science is a veterinary scientist with over 10 years' experience working in veterinary diagnostic laboratories in both the UK and Ireland. She worked as a veterinary nurse for a busy referral hospital before moving to the UK and studying with the Royal Veterinary College in London. She continued to work in the UK with Torrance-Diamond Diagnostic Services before moving back to Ireland and continuing in the veterinary laboratory profession. Currently, she works as laboratory manager for VPG Cork. Her special interests are in the continuous improvement of analytical and diagnostic testing for veterinary laboratories including hematology, laboratory quality, technician training and development. Amy also has a keen interest in sigma LEAN and applies this to laboratory systems and principles.

Linn Clarizio DVM, DACVP obtained her DVM from the University of Minnesota in 2019 and completed a clinical pathology residency at Kansas State University in 2022. Her professional interests include hematology, avian and exotic clinical pathology, laboratory methodology, and quality assurance.

Clare Louise Doyle BVSc FRCPath MRCVS, following five years in small animal and equine practice and an internship in large animal internal medicine at University College Dublin, completed a three-year residency in veterinary clinical pathology at the Royal Veterinary College, London in 2009. She became a fellow of the Royal College of Pathologists by examination in 2010 and since then has worked for the Veterinary Pathology Group (UK) as a senior clinical pathologist for 13 years. Clare has a special interest in quality control within the veterinary laboratory, particularly in the application of quality improvement to biochemical testing.

Kendal E. Harr DVM, MS, DACVP received her veterinary degree from Cornell University and completed her residency and Master of Science (immunology, diagnostic validation) at the University of Florida, where she rose to assistant professor. With over 20 years working in diagnostic clinical pathology laboratories focusing on non-domestic species, she recently began using digital and AI tools for diagnosis, which demonstrated the need for QA guidelines for the use of digital samples. Her other professional interests revolve around environmental and pharmacologic toxicology including numerous small investigations and serving as a principal investigator of the forensic avian toxicity study during the Deepwater Horizon Damage Assessment and Restoration Program. She currently works in drug development.

Emma H Hooijberg BVSc, GPCert(SAP), PhD, DipECVCP, European Specialist in Veterinary Clinical Pathology, South African Specialist in Veterinary Clinical Pathology, trained as a specialist veterinary clinical pathologist in Vienna, Austria, and am is currently an Associate Professor and Head of the Clinical Pathology Section at the Faculty of Veterinary Science, University of Pretoria, South Africa. Her current position involves management of the laboratory and diagnostic service provision, undergraduate and postgraduate student teaching and supervision of and involvement in postgraduate and other research projects. Her special interests are non-domestic animal clinical pathology and conservation medicine, and laboratory quality assurance – in particular, method validation and reference interval studies.

Jennifer R. Matlow DVM, MS, DAVCP, is a graduate of Cornell Veterinary School and did my residency in veterinary clinical pathology at Texas A&M University. Dr Matlow has been a board-certified (ACVP) clinical pathologist since 2013, working in veterinary commercial diagnostic laboratories and currently working for IDEXX, Inc. Dr. Matlow has also been a member (and immediate past-chair) of ASVCP's Quality and Laboratory Standards Committee (QALS) since 2015, working on several projects and quality assurance guidelines. Currently, she serves as the lead of IDEXX's avian and exotics clinical pathology reading team, as well as on the Laboratory Analytical Method Advisors committee which assists departments on matters of quality control. Her special interest is in quality assurance education for general practitioner veterinarians, pathology and clinical residents, and laboratory technical staff.

Lucia Sanchini DVM, MSc, DipECVCP, FRCPath, MRCVS, European Veterinary Specialist in Clinical Pathology is a clinical pathologist with diagnostic experience in both glass and digital cytology. She worked in diagnostic commercial laboratories based in the UK since her board certification and has a special interest in cytology. For 3 years, Dr. Sanchini was responsible for laboratory quality at the commercial laboratory Batt Lab. Her enthusiasm for quality in veterinary laboratory medicine started during her previous career as veterinary surgeon, when she learned (often the hard way) that to get a diagnosis one must pay particular attention to the quality of the sample they send out.

Ben Sturgeon Dr BSc, BVM, CertEP, CertESM, BAEDT, MRCVS graduated from Edinburgh University in 1996 before following an internship and residency in Dublin and Edinburgh respectively in large animal medicine and surgery before undertaking a lectureship in Equine Practice at Edinburgh. He then entered private work running his own first opinion and referral practice for several years before moving into animal welfare work where he became a Global Director of humane education, veterinary treatment programs, operational strategy and impact assessment in over 120 projects in 30 countries. He is currently CEO of an NGO delivering animal welfare advocacy. Throughout he developed several organizational and departmental strategies including in them critical pathways, quality assurance, due diligence, and MEAL evaluations. He is widely renowned speaker, published in peer reviewed veterinary literature as well in lay journals and in several book editions.

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Section 3: Laboratory Quality and Quality Control in Specific Fields

1: Quality Systems and Philosophy

Kathleen Freeman and Stefanie Klenner-Gastreich

Quality is everyone's responsibility.

– W. Edwards Deming, Quality Leader

Learning Objectives:

1. Provide multiple definitions for 'quality' with regard to the veterinary laboratory.
2. Discuss the importance of defining quality, quality goals and philosophy.
3. Describe a quality system and its requirements.
4. Describe how your personality can affect your approach to quality planning.
5. Discuss the minimum documentation required for a quality system.

What is the meaning of quality?

Several years ago, I was speaking to a meeting of general practitioners in Finland about in-clinic laboratory quality. In our discussion about the meaning of quality I had a GREAT response from one veterinarian who referred me to the book, *Zen and the Art of Motorcycle Maintenance* by Robert Pirsig (in my opinion a must-read for anyone interested in the philosophy of quality). His response was '*When you define quality you define yourself*!' That is truly a profound statement!

Quality may mean different things to different people. That is why it is important to carefully define our own interpretation as well as that of our clients and other stakeholders (management, shareholders, employees, suppliers) and their needs with regard to

laboratory quality. Clients' expectations for quality will need to be 'translated' into the 'language of the laboratory' in order to accomplish your quality goals. Many veterinarians will not be in a position to judge quality from the viewpoint of a laboratorian, whose focus and training ideally include evaluations of imprecision, accuracy, quality goals (total error, biologic variation, other), observed total error and sigma metrics. The veterinarian's focus will more likely be on factors such as cost, convenience, turnaround time, ability to talk to a pathologist on the telephone and provision of 'useful information' in laboratory comments on various types of results. This makes talking about 'quality' a challenge for all and careful determination of the perceptions of all involved in the discussion is needed to ensure that the conversations are at a level understood by all involved! Sometimes client complaints or misunderstandings can be resolved or minimized with good explanations and discussions of the factors involved, root causes, the expectations of the laboratory about the client and the client's expectations of the laboratory.

What is a quality system and what does it require?

A generic mission statement that I provide for most veterinary laboratories is: *To provide within an agreed upon time frame, accurate and reliable laboratory results that are perceived to be good value for money*. Each laboratory then has to decide how they may differentiate themselves from other veterinary laboratories and to provide this mission in a way that will ensure the continued financial success of the laboratory and the continued ability to conduct business that will provide for the needs of all stakeholders. A **quality system** can be described as *an exercise in documentation*. It can be defined as '*a formalized system that documents processes, procedures, and responsibilities for achieving quality policies and objectives.'* [What is a Quality Management System (QMS)? | ASQ] It requires an organized approach, clear communication, and minimum documentation that shows that the laboratory has a quality system and that it is functioning and resulting in continuous quality improvement over time. This documentation should be able to 'prove' to all stakeholders that the laboratory has an organized approach and quality goals that are being achieved. In addition, it must show that problems are addressed, resulting in continuous quality improvement within the laboratory.

Can you provide a high level of quality without having a 'quality system'?

Yes, it is possible to provide an high-quality laboratory service without having a system. This is more likely to be possible for smaller laboratories with limited numbers of staff who closely collaborate. It is rarely possible to achieve and sustain growth or have a larger organization without instituting a more formal quality system to ensure that working practices are standardized so that quality can be maintained even when 'crucial individuals' are on holiday or sick leave!

How does quality management provide for a personalized approach?

Developing, implementing and/or managing a quality system will be one of the most creative things you will ever do. If you are present as the 'guiding light' for its development and implementation and/or ongoing management, it will truly reflect your personality, preferences and philosophy. Nowhere was that more apparent to me than in my friend, Ernst Leidinger, and his laboratory in Vienna (formerly *In Vitro* Laboratories). One of the first ISO-certified veterinary laboratories in Europe, it truly reflected Ernst's personal philosophy with regard to quality, and his approach to processes and problem-solving. I think you will find that will be the case for each of you as you embark and sail on the every changing water ways of you 'quality journey.'

Some of the personality traits and factors that will play a role in your approach will include:

1. Are you a 'lumper' or a 'splitter' as a pathologist? A 'lumper' is more inclined to have fewer, longer documents and Standardized Operating Procedures (SOPs) that lump items together, whereas a 'splitter' will have more numerous shorter documents and SOPs that address single items. Bench Cards (abbreviated summaries of step-by-step instructions) for both will be similar since these summarize the step-by-step procedures for each item, whether included in a larger SOP or more numerous, smaller SOPs.

2. Are you tolerant of ambiguity or want to know the 'fine print' in detail?

3. Are you comfortable with or have the ability to delegate some things to trusted key individuals or will you have to manage the system all on your own, in addition to other duties and responsibilities? This will play a key role in how much you are able to accomplish and how rapidly you are able to proceed.

4. What areas are most important to the financial stability of your laboratory? These will need to receive a lot of attention since financial success is necessary for any laboratory and quality system to continue to function. The areas of emphasis and importance may vary with the country or area of the country in which you are located and/or the clientele that you already have or would like to attract, as well as the organization you work for (university, research laboratory, commercial laboratory or in-clinic laboratory).

5. What resources do you have or is management willing to provide for you in order to design, develop, implement and manage a quality system? This will depend, in large part, on their OWN philosophy of quality and quality systems. So, it pays to have open discussions about this as part of the process!

6. What is your approach to dealing with client complaints or questions (hopefully you will learn more about this in this book)?

What documentation is required for a quality system?

One of the most common dilemmas for a quality system is determining the documentation associated with it. I always emphasize that one of a leader's jobs is to undertake the struggle of WHAT and HOW MUCH documentation is truly needed to be able to demonstrate to ourselves, our clients, and our management structure that we have a quality system that is working to help achieve continuous quality improvement. Continuous quality improvement should result in saving time and money in the long run and helps ensure a high level of quality service and communication with our clients. Recruiting and retaining loyal laboratory clients in this age of 'commodity laboratory results' is always a challenge!

2: Mission, Vision and Values Statement

Ben Sturgeon and Kathleen Freeman

People don't buy what you do, they buy why you do it.
– Simon Sinek

Learning Objectives:

1. Describe reasons for having a written mission/vision and values statement.
2. Describe why your mission, vision and values are important in guiding your business its development and evolution, prioritization, and ways of working.

Why should I have a written mission/ vision and values statement?

Your mission statement is likely out there already. It exists. It is just not written down, and it is being misinterpreted by those who do not yet know your organization well. In other words, if you don't give your employees (internal clients) and external clients the words or phrases to convey your mission, they will do it in their own words and their own ways. By writing down your mission statement, you:

- Control the message
- Clarify and focus your approach to your business
- Provide a document to help guide your decisions on an ongoing basis
- Help define what quality means to YOU
- Provide insight into your philosophy and values that will be appreciated by others

One of my favorite quotes is from Simon Sinek in the TED talk entitled 'Start with why - how great leaders inspire action': "*People don't buy what you do, they buy why you do it*. He extends the thought that the goal of people is "*to do business with people that believe what they believe*" He further contends that *'What' you do only proves what you believe."* He believes that loyal clients are the result of people who want to be part of what you do! So, carefully considering 'why' you do what you do as the basis for a Mission/ Vision and Values Statement is important!

What is a Mission/ Vision and Values Statement?

A mission statement is a short, meaningful phrase that summarizes the purpose that drives your organisation. Similar to your business' vision (the "what") and values (the "how"), your mission statement answers the question of "why" you do what you do. In addition to helping you convey the purpose of your organization (and serve as a branding tool), your mission statement can be used to attract customers and employees. Importantly, it should be used to inspire yourself and your staff to live its values and consider how to implement them in daily activities and long-term planning.

3: Laboratory Quality Plan

Kathleen Freeman and Ben Sturgeon

> *You've got to know what you want. This is central to acting on your intentions. When you know what you want, you realize that all there is left then is time management. You'll manage your time to achieve your goals because you clearly know what you're trying to achieve in your life.*
>
> – Patch Adams (Founder of the Gesundheit! Institute, WV)

> *Quality is never an accident; it is always the result of high intention, sincere effort, intelligent direction and skillful execution; it represents the wise choice of many alternatives.*
>
> – William A. Foster (US Marine, hero of Battle of Okinawa, World War II)

Learning Objectives:

1. Describe the reasons for having a written Quality Plan.
2. Describe the general categories that need to be addressed in a Quality Plan and give examples of what should be included in each category.

What is a Quality Plan?

A Quality Plan is a statement of intent. It should be no more than several pages long and deal with general statements of intent. For example, job titles can be shown on an organizational chart, but it does not name specific individuals since this may change with time. General characteristics of equipment are included, but specific instruments are not named since this may change with time.

The Mission/ Vision/ Values and Goals statement provided the 'why' of your organization. The Quality Plan defines, in general terms, the 'how' you are going to achieve your mission, vision and goals while adhering to those things you value. The policies, standard operating procedures, reports, and forms define 'what' you do.

Common categories that should be addressed within the Quality Plan are your intentions with regard to the

- Laboratory environment and culture
  - Name, location
  - Clientele
  - Scope/ types of testing
  - Special considerations based on location or activities
  - Laboratory culture that you want to promote
  - Organizational chart
  - May include your Mission/ Vision/ Values and Goals Statement (or this may be separate)
- Facilities and Resources
  - Physical facilities
  - Resources other than physical facilities
- Equipment
  - General categories/types of equipment
  - General approach to equipment
- Personnel
  - General personnel characteristics and specifications
  - Level of expertise
  - Training
- Health and Safety
  - Adherence to local and national health and safety regulations
  - Special considerations for your veterinary laboratory
- Working Practices
  - Policies
  - Standard Operating Procedures

4: Theory of Change and Logistical Frame Model

Ben Sturgeon

> *It is not knowledge, but the act of learning, not possession but the act of getting there, which grants the greatest enjoyment.*
>
> – Leonhard Euler 1808 (Founder of Pure Mathematics)

> *Most of the heuristics (rules of thumb) that humans use lead to bad judgements and biased decisions.*
>
> – Marcus du Sauto (Distinction Professor of Mathematics at the University of Oxford)

Learning Objectives:

1. Know reasons for having a Theory of Change.
2. Understand how a Theory of Change enables you to review your business plan and develop appropriate monitoring and evaluation.

Why should I have a written mission/ vision and values statement?

In considering your Quality Plan and in delivery of your Mission and Values Statement, use of a Theory of Change can outline and define both parts. Importantly this may also indicate areas of weakness, within your overall approach, and identify different means of evaluating performance.

What is a Theory of Change?

A Theory of Change defines a pathway or pathways that guides thinking about how and why a (complex) change happens. Because it hasn't necessarily happened yet, we are using our knowledge, ideas and external evidence to create a theory of how this change happens.

In a laboratory business we may decide that our mission is to provide accurate and reliable results, in a cost effective and timely way, by expert trained professionals, to lead change in animal welfare.

A Theory of Change is a framework that views reaching the mission goal as a purposeful and constructed sequence of events rather than something that could be viewed as chaotic, unmanageable, or happening by chance.

How do I get started on a Theory of Change?

A Theory of Change is a longitudinal (backwards) mapping exercise from a perceived goal/ mission/ objective as in your Mission (and Values) statement.

It should highlight the different steps you take to achieve this end goal by outlining individual, and linked actions; some of these should be or are outlined in your Quality Plan. These include:

- Inputs (i.e. funding to set up the laboratory)
- Activities (actual work done)
- Outputs (result of the work)
- Outcomes (wider tangible benefits or effects of the output)
- Impact or Mission Statement (wider benefit of the outcomes)
- Assumptions (what each step relies upon – i.e. money spent will result in activity, that running a test will provide a useful or diagnostic result)

This can also be described as a "results chain" and be demonstrated:

At each stage we can add the specific expectations:

5: The Laboratory Environment

Emma Hooijberg

Something impractical cannot be beautiful

– Otto Wagner

Learning Objectives:

1. Explain the basic principles that contribute to the design of a laboratory.
2. Explain how maintenance of laboratory equipment should be documented.
3. Describe basic maintenance procedures for core laboratory equipment.
4. Describe factors that should be considered when acquiring instruments and equipment.
5. Give examples of laboratory hazards and explain how to prevent them.

What should a veterinary diagnostic laboratory look like?

A laboratory should be designed to optimize sample flow and provide a suitable environment for laboratory equipment. Personnel comfort within the laboratory space must also be catered for. The laboratory space should be well-lit, well-ventilated, and be temperature-controlled. A first-aid kit and fire-control equipment should be present, in line with local regulations.

Sample flow should physically follow the steps in the testing process, with the sample reception and acquisition space leading to the areas where sample preparation and analysis takes place, which in turn are connected to the area where samples are stored and washing of equipment occurs.

The sample reception area should provide enough space to unpack and label samples and should contain at least one computer terminal and the paperwork necessary for sample acquisition. Where possible, instruments should be placed in a separate room or rooms. Large equipment should be placed on the periphery of a room and should be positioned with enough space for technicians to access all parts of the instrument, if necessary. The use of laboratory benches that form part of a modular system, and can be moved around to reconfigure spaces, is recommended.

All instruments require a stable, grounded supply of electricity. Most instruments are accompanied by a computer terminal, which needs to be taken account when planning the number of electrical points needed. A good rule of thumb is to provide 10 plug points per 160 m of bench space, with 50% of these allocated to computers, printers, and other information technology (IT) equipment. In areas where electricity supply is not always reliable, a back-up generator and uninterruptible power supply (UPS) units may be required.

Some instruments require a water supply. The quality of this water should meet the specifications of the instrument, which generally means it should be purified to a certain standard. Water quality checks should be carried out regularly, as poor-quality water can affect the accuracy of results. Provision should be made for disposal of biological and chemical waste. Waste disposal should be guided by local regulations.

Once analysis has been completed, samples may need to be stored. The sample storage area should be well-organized, and samples should be stored at the optimum storage temperature for each sample type. If paper records are to be kept for a certain amount of time, an area should also be set aside for archiving.

In terms of providing an optimal environment for personnel, there should be easy access to rest rooms, to a space where staff can take breaks and eat and drink, and quiet areas where personnel can perform tasks without background noise and interruption.

6: Documents, Documentation, and Document Control

Kathleen Freeman

> *Documentation is like sex: when it is good, it is very, very good; and when it is bad, it is better than nothing*
>
> –Dick Brandon (Sky Sartorius 2022. MATLAB Style Guide Wiki access and search function (https://www.mathworks.com/matlabcentral/fileexchange/40795-matlab-style-guide-wiki-access-and-search-function), MATLAB Central File Exchange. Retrieved February 27, 2022.)

Learning objectives:

1. Define a document and documentation.
2. Give examples of various documents that apply to the veterinary laboratory.
3. Describe the functions of document control.
4. List advantages of a document control system.
5. Describe key aspects of a document control system.

Introduction

A formal document control system may be daunting when first considered, but can provide many benefits to any veterinary laboratory, regardless of its size and/ or complexity. Like a lot of quality initiatives described in this book, it may require a concerted effort to organize and compile a document control system. But it will provide many benefits, as detailed below. Start with one department or one area of the laboratory. It may be as simple as organizing things in folders and notebooks or on a computer or laboratory information system. Some may prefer to use purpose-designed computerized document control systems. It is up to you to design the document control system that is suitable for your organization.

What is a document and what is documentation?

A *document* is a piece of written, printed, or electronic matter that provides information or evidence or that serves as an official record (Oxford Languages Dictionary – define document – Search (bing.com)).

There are a variety of documents and documentation that should be part of the laboratory quality system and subject to document control as part of the ongoing quality management process.

What are documents of the veterinary laboratory?

In the laboratory documents and documentation include training materials, training records, competency assessment records, ongoing evaluation records, health and safety regulations and records, Standard Operating Procedures, Policies, Laboratory and Instrument Records (Ex: Temperature charts, maintenance records, instrument performance evaluation records, EQA and QC results and records, etc) and forms, improvement opportunity forms, Instrument and reagent package inserts, ordering and inventory records, books and publications and recorded presentations and other things that are used within the laboratory. The laboratory user information brochures, advertising information, newsletters and price lists and laboratory reports are also part of laboratory documents and documentation.

Documentation should follow the 'Goldilocks rule' – it should not be too little or too much; it should be 'just right' for the job! So, it is up to you, as a leader and manager to help determine what is required and what constitutes 'just right' for your organization and your laboratory.

What is document control?

Document control is the set of measures that explain and guide the preparation, approval, release, distribution, access, storage, security, review, alteration, withdrawal and disposal or archiving of documents.

7: Improvement Opportunity Form

Kathleen Freeman

> *Hard work spotlights the character of people: some turn up their sleeves, some turn up their noses, and some don't turn up at all.*
> — Sam Ewing, American writer and humorist

> *It is not good enough for things to be planned – they still have to be done; for the intention to become a reality, energy has to be launched into operation.*
> – Walt Kelly, American animator, cartoonist and satirist

Learning objectives:

1. Describe why an Improvement Opportunity Form (IOF) is a 'good place to start' for a quality system
2. Describe the information that should be documented on the IOF
3. Describe why the follow-up section(s) of an IOF may be the most important part of the form
4. Describe import aspects that help ensure that an IOF is used and useful

Why should I have an Improvement Opportunity Form (IOF)?

Now the hard work starts! You may have found production of your Mission/Vision/Values and Goals statement (the 'why') and your Quality Plan (the 'how') to be difficult but vital parts of your personal and organizational journey in achieving a quality culture, but now the 'what' you do comes into play with design of your documents and documentation! For many laboratories wanting to establish a quality system, the overall project may be daunting. The place I usually tell them to start is with the Improvement Opportunity Form (IOF).

The IOF is used to document and manage response to ANY problem that may arise or to register any idea that may help improve quality. It goes beyond mere recording of 'errors' (reporting wrong

results, near-misses that did not get reported or other problems detected) or 'nonconformities' (we did not do what we said we would do). IOFs can help minimize or eliminate gossiping or complaining within the laboratory – if it is important enough to be talked about or to complain about, then a form should be generated to address it! Like any forms or suggestions, it is important that the submitter gets rapid feedback regarding the submission. Not all ideas may be acted upon, but should be respectfully considered. If the IOF is addressing an error, problem or client complaint, prompt submission (same day as the item is identified) is required in order for these to be addressed in a timely manner.

An improvement opportunity form helps document that the quality system is in place and that it is working and resulting in continuous quality improvement, one of the goals of any quality system! Failure to fill in an Improvement Opportunity Form when a problem occurs or when an idea for improvement is present is a failure for all of us since an opportunity to provide continuous quality improvement is lost and is subject to disciplinary action if a problem is known to be present but not reported.

Documentation of problems may help highlight a need for additional resources or funding to help address recurring problems, increase efficiency and effectiveness, and demonstrate processes or patterns or working that may not be in the best interest of the organization. This may help convince upper management of the need for additional resources or allocate additional funding to address problems, determine risk associated with recurrent problems and demonstrate the effectiveness of actions, projects and processes undertaken to address problems and/or initiate improvements.

What should be included on an IOF?

Elements that should be included on an IOF should help in categorization of the type of problem, its severity, whether or not a 'bad result' was reported and action that was taken as an immediate response, if needed. In addition, sections are needed for root cause analysis, additional preventive and/ or corrective actions based on the underlying cause, and additional follow-up to determine if the additional preventive and/ or correction actions are effective in

8: Instrument Logs and Documentation

Kathleen Freeman and Clare Doyle

> *Without data, you are just another person with an opinion.*
> – J. Edwards Demings

Learning objectives:

1. Describe the benefits of keeping an instrument log.
2. Describe the various aspects of instrument maintenance and documentation logs.

Introduction

Record keeping often is the thing that first falls by the wayside when time is short, fuses are short and frustration is high. This chapter will touch on why keeping logs for each instrument in the laboratory are important.

Why do I need an instrument log?

It is easy to skip over routine maintenance for laboratory instruments on a busy day. However, routine maintenance and cleaning, with calibration, replacement of parts, tubing or other adjustments, or reagent replacement, as indicated, is vital to ensuring that the instruments have a long lifespan and perform well daily and over an extended period of time.

This can be recorded on an instrument log spreadsheet with initials of the technician responsible for the indicated schedule. A paper chart or excel spreadsheet can be prepared at the beginning of each calendar year, with a tab for instructions, including routine calibrations, reagent replacement schedule, and routine maintenance schedule (daily, weekly, monthly, bi-annually, annually, etc) placed in the appropriate month tab and day of the week upon which it should be done. The log should include a space for any additional

actions taken, such as manufacturer's servicing, parts replacement or other adjustments. Use of excel spreadsheets provides a record that can be stored electronically as part of the necessary laboratory documentation and reviewed by management as part of the ongoing laboratory quality system.

These logs can be a valuable resource to determine 'common' things that affect instrument/ method performance. They provide a unique 'history' for each instrument, the instrument 'health' and 'diseases' to which it may be predisposed based on design or individual instrument variation. If experienced personnel are always present in the laboratory, they may already have a feel for what to check when things go wrong. However, if less experienced operators are present, an instrument log may be of benefit to them since they will want to check for 'common things' first. The clinical maxim is 'when you hear hoof beats, initially think of horses, not zebras'… so, you eliminate the common things (horses) first, before concluding that a zebra (less common occurrence) is present!

QC violations can be included in the instrument log or as a separate log. Instrument maintenance and documentation log examples are provided with this chapter. Part of problem-solving with QC includes the ability to determine when there have been actions (such as calibrations, opening new control material, parts replacement, new reagents, etc) that may affect performance of an instrument/ method. Consulting the instrument maintenance and documentation log is an important part of troubleshooting failed QC. There may be a reason for a change in performance recorded there! If not, then other sources for system instability can be investigated!

9: Standard Operating Procedures (SOPs)

Stefanie Klenner Gastreich

> *If you think of standardization as the best that you know today, but which is to be improved tomorrow to you get somewhere.*
> – Henry Ford

Learning objectives:

1. Describe what SOPs are and the circumstances in which they are useful.
2. Discuss who should be the author of an SOP.
3. Describe the structure of an SOP and why a certain structure is needed and is helpful.

How does standardization of processes facilitate laboratory work?

SOPs are written instructions which describe in detail how to perform a task according to the standard of the laboratory in which the task is performed. Although many SOPs across veterinary laboratories will be similar, there may be differences based on the preferred way of doing things within each individual laboratory. SOPs provide a step-by-step instruction on how a job needs to be done and, thereby, are based on general Good Laboratory Practice (GLP) principles, regulatory guidelines (if present), and Health and Safety aspects. The target person to read an SOP are those persons who shall perform the job/task which is described in the SOP.

Every kind of process or procedure in a laboratory can benefit from a written SOP. These can start with sample submission, continue to SOPs for analytical procedures, and include postanalytical evaluations. Here are some examples for such SOPs: *1) SOP for*

sample submission, 2) SOP on how to perform a complete blood count by using hematology machine XYZ, 3) SOP on how to validate and release results of analyzer XYZ.

But SOPs are not restricted to the description of the direct laboratory work; every other aspect of managing a laboratory can benefit from clear structures and outlined performance descriptions. Human resource aspects can be managed by using SOPs and are especially important for onboarding of new personnel and for periodic performance evaluations of all staff in order to establish and maintain the high quality of the laboratory work.

Why do we benefit from SOPs?

Writing SOPs is a lot of work. It is time consuming and labor intensive and removes the author from doing other activities during the time of writing the SOP. To assure that people writing the SOP and staff finally using the SOP are motivated and supportive of SOPs, it is helpful if they understand the SOP's usefulness. Firstly, written procedure instructions help to avoid doubt as to how a respective task needs to be performed as they clearly describe every step in the process. They enable the person undertaking the operation to perform it in a correct, safe, and healthy way. Outlined performance descriptions can also be useful as historical records. The lab can review how a respective task was performed in the past. Such information might be useful in trouble shooting processes, in the evaluation of customer complaints or other observed incidents or activities within the laboratory. Written SOPs provide the basis for consistency if the person who usually performs the task is absent during holidays, on sick-leave or changes job positions. Consistency assures maintenance of high quality of the lab tasks and limits failure and error rates, which can ultimately become very costly for a laboratory. In the case of regulated activities (i.e. GLP), adherence to SOP is required for the laboratory to be in compliance with the regulations. Another important, and very beneficial aspect of SOPs is, that they can be used for training. New staff can easily be informed about how a particular task needs to be performed. And, during ongoing competency assessments, SOPs can serve as checklist for the auditor to evaluate if the member of the staff performs the task correctly.

10: Preanalytic and Postanalytic phases of Laboratory Testing. "The Chain of Quality"

Jennifer Matlow

The weakest link in a chain is the strongest because it can break it.
– Stanislaw Lec, poet

Learning objectives:

1. Discuss the concept of the brain-to-brain loop and how this can inform the roles and responsibilities of the clinician, laboratorians, and clinical pathologists in maximizing the quality of laboratory testing.
2. Described the major phases of laboratory quality, including pre-pre-analytical and post-post-analytical.
3. List the components of the pre-analytic and post-analytic phases. Based on these, describe how to develop monitoring systems for laboratory errors in order to prevent and correct common problems.

Introduction: What is a Brain-to-Brain Loop?

The "brain-to-brain loop" is a concept devised in human laboratory medicine that refers to the interplay of the clinician's, patient's, and laboratorian's thought processes. In this widely accepted conceptual framework, the generation of any laboratory test result consists of ten steps of the *Total Testing Process* (TTP): test order, sample collection, sample identification (at several stages), transportation, sample preparation, analysis, results reporting, interpretation, action, and patient outcome.[See Figure 1]. Those steps prior to analysis (the analytical phase defined as the test modality itself, such as the operation of the biochemistry analyzer or an ELISA)

are collectively termed the *pre-analytical phase* and those after analysis, the collective *post-analytical phase*. The pre-analytical and post-analytical phases are often more difficult to monitor for quality assurance than the analytical phase because there are multiple steps occurring in both the clinic and the laboratory, and thus quality assurance is a shared responsibility across different locations and personnel organizations. Minimization of pre-analytical errors is vital to ensure that appropriate, high-quality biologic samples are submitted for testing (for example, that blood entering the hematology analyzer is not hemolyzed from venipuncture technique, from prolonged storage/ transit under adverse environmental conditions, or from any inappropriate storage media). Several studies have measured the pre-analytical phase as comprising the highest share (up to 70%) of all laboratory error, warranting increased attention to, and documentation of, this phase. On the post-analytical end, it is easy to conceptualize how errors in results verifications, data entry, reporting, and the subsequent clinical actions based on test results can lead to misdiagnosis with potentially grave consequences for the patient.

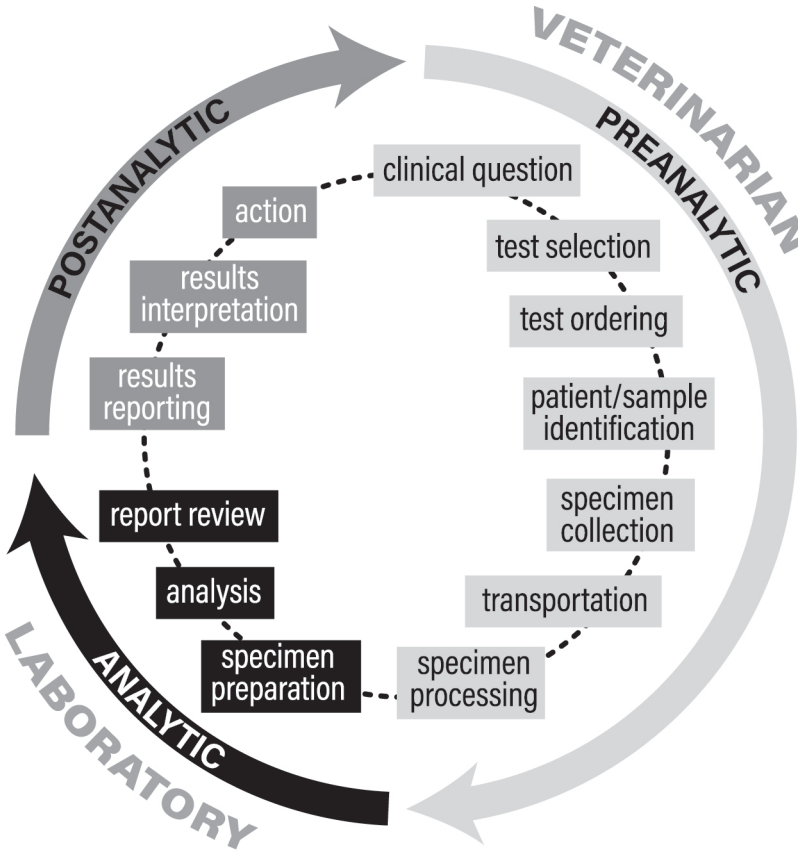


Figure 1. Illustration of the Total Testing Chain and 'brain-to-brain' loop in association with laboratory testing

11: LEAN Inventory Management Systems

Amy Browne

> *The best approach is to dig out and eliminate problems where they are assumed not to exist.*
> – Shigeo Shingo

Learning objectives:

1. Discuss the concept of and focus of LEAN.
2. Describe the principles of operation and implementation of 5S in the workplace.
3. Explain the 5 Steps: Sort, Simplify, Shine, Standardize and Sustain.
4. Define Waste according to LEAN principles.
5. Explain the acronym: TIMWOODS.
6. Describe Kanban Inventory Management Systems.
7. Perform Kanban Calculations.
8. Describe the Step-by-Step Kanban Implementation Process.

Introduction

The concept of LEAN is focused on a culture of continuous improvement of a company's processes. While LEAN thinking can greatly improve the productivity and function of a team or department, LEAN improvements that are implemented across the entire organization have the greatest impact on the customer.

A LEAN organization is one that understands the needs of the customer and focuses its key processes to continuously improve on this. The goal is to provide absolute value to the customer as well as the business becoming as efficient as possible through a process that has limited waste.

What is LEAN manufacturing?

LEAN manufacturing is a production method that focuses on minimizing waste while maximizing productivity. Waste is defined as anything that does not add value to the customer or to the business. This waste can be a process, activity, product, or service that requires an investment of time, money, or skill and that, in turn, does not add value to the overall outcome. LEAN manufacturing is made up of many concepts; two of the most popular of these are 5S and Kanban.

What is 5S?

'A place for everything and everything in its place'

5S methodologies (Seiri, Seiton, Seiso, Seiketsu and Shitsuke), is a LEAN manufacturing concept conceived in Japan and is one of the most suitable methods for cleaning, organizing and standardizing processes and organizations allowing for work to be carried out safely and more efficiently.

5S should be considered a pre-requisite for all LEAN manufacturing. You should not attempt to implement LEAN principles in an organization without first understanding 5S. The initial implementation process requires minimal financial investment, however a successful 5S program requires planning, discipline, organization and, above all, commitment to see the benefits.

12: The Role of the Veterinary Clinical Pathologist

Kathy Freeman

> *We profess to teach the principles and practice of medicine, or, in other words, the science and art of medicine. Science is knowledge reduced to principles; art is knowledge reduced to practice. The knowing and doing, however, are distinct ... Your knowledge, therefore, is useless unless you cultivate the art of healing. Unfortunately, the scientific man very often has the least amount of art, and he is totally unsuccessful in practice; and, on the other hand, there may be much art based on an infinitesimal amount of knowledge, and yet it is sufficient to make its cultivator eminent.*
>
> – Samuel Wilks

> *….Medicine is at once an enormous business and an exquisitely human endeavor; it requires the ruthless efficiency of the modern manufacturing plant and the gentle hand-holding of the parish priest; it is about science, but also about art; it is eminently quantifiable and yet stubbornly not.*
>
> – Robert Wachter

Learning objectives:

1. Reflect on the multiple potential roles of the veterinary clinical pathologist.
2. Reflect on the potential roles and how they may contribute to your ongoing personal and professional growth and job satisfaction.
3. Reflect on the potential roles and how using veterinary clinical pathologists in those areas that appeal to them may help with recruitment and retention.

Introduction

This chapter represents my personal thoughts on and approach to the role of the veterinary clinical pathologist in the laboratory. I believe that recognition of the multiple roles of the veterinary clinical pathologist and the need for participation in multiple roles is important in achieving job satisfaction. Time needs to be allocated for clinical pathologists to be involved in non-fee-for-service activities. Such participation should reap benefits in overall laboratory quality, which should result in cost savings due to increased client/stakeholder satisfaction, ability to recruit and retain veterinary clinical pathology residents and clinical pathologists, as well as give back to the veterinary community and clinical pathology community.

The recruitment and retention of veterinary clinical pathologists has been difficult for most of my professional career and illustrates the need to change the current paradigm in veterinary commercial laboratory practices and some residencies in veterinary clinical pathology for only service activities. Sometimes these service, income-producing activities are extremely restricted (very high emphasis on cytology), resulting in burnout and dissatisfaction. Investigation of the individual interests of veterinary clinical pathologists and the roles with which they may want to engage within the organization may help with recruitment and retention and with providing long-term job satisfaction and avoiding burnout due to excessive pressure associated with unrelenting high service expectation.

Roles of the Veterinary Clinical Pathologist

Clinician pathology in veterinary medicine is a relatively 'young' discipline, but one that has been recognized as a valuable contribution to the practice of veterinary medicine based on knowledge of veterinary laboratory testing, its advantages and disadvantages, selection of tests applicable for a given clinical and financial situation, and interpretation of the findings that may help guide decisions about recognition of health and disease, diagnosis, monitoring and response to treatment.

13: Basic Quality Concepts and Vocabulary

The Language of the Laboratory

Kathleen Freeman and Jérémie Korchia

> *The limits of my language are the limits of my mind. All I know is what I have words for.*
>
> – Ludwig Wittgenstein (Austrian-British philosopher who worked primarily in logic, the philosophy of mathematics, the philosophy of mind, and the philosophy of language)

> *The limits of my language are the limits of my universe.*
>
> – Johann Wolfgang von Goethe

> *A man with a scant vocabulary will almost certainly be a weak thinker. The richer and more copious one's vocabulary and the greater one's awareness of fine distinctions and subtle nuances of meaning, the more fertile and precise is likely to be one's thinking. Knowledge of things and knowledge of the words for them grow together. If you do not know the words, you can hardly know the thing.*
>
> – Henry Hazlitt, Thinking as a Science (American journalist who wrote about business and economics)

Learning objectives:

1. Discuss why 'laboratory error' is an insufficient explanation for unexpected deviations in laboratory results.
2. Discuss the three major categories of laboratory error.
3. Describe the relationship of the categories of laboratory error and the qualitative concepts of error.
4. Describe how the qualitative concepts of error are quantitated in the laboratory.
5. Describe and use the 'language of the laboratory' related to laboratory quality.

Introduction

There are numerous concepts and terms associated with quality in the clinical laboratory. Many of the ASVCP QALS guidelines have glossaries defining the terms used within them. There is a glossary of QC Terms (Glossary of QC Terms - Westgard) and a glossary of ISO Metrological and Related Terms and Definitions Relevant to Clinical Laboratory Sciences (Glossary of ISO Terms - Westgard) available on the Westgard website.

This chapter will present some of the basic vocabulary and quality concepts relevant to the clinical laboratory. Translation of clinical needs and medical significance into the 'language of the laboratory' is often critical in determining when and how errors occur and whether they are of statistical and/or clinical significance.

Laboratory Error

'**Laboratory error**' is often blamed for unexpected deviations in laboratory results from those anticipated based on combinations of clinical signs, laboratory findings, and/or differential diagnoses. Identification of laboratory error is insufficient to explain such deviations and, while error may be involved, further characterization is needed to determine its analytical and clinical significance.

All laboratory measurement systems have some degree of inherent error. Laboratory error is defined as (1) Deviation from the truth or from an accepted, expected true or reference value; between the estimated value of a quantity and its true value. (2) Measurement error: The result of a measurement minus a true value of a measurand. (From the Westgard Glossary of QC Terms).

Two main types of analytical error are **systematic** and **random** error. These contribute to total error associated with a result. Systematic error is that which is inherent within the measurement system (instrument, reagents, operator, environment), is always in one direction and is predictable since it can be quantified by evaluation of instrument performance as part of the instrument validation/ verification process. Random error is error which cannot be predicted and can be either positive or negative. The direction and

exact magnitude cannot be exactly predicted. It is due to random occurrences such as inadequate mixing, bubbles in reagents or other factors that may develop or resolve spontaneously.

Total error associated with a laboratory measurement is the combination of systematic and random error to quantify the magnitude of error that could occur with a result. This is often designated as observed or calculated total error (TE_{obs} or TE_{calc}). The formula is:

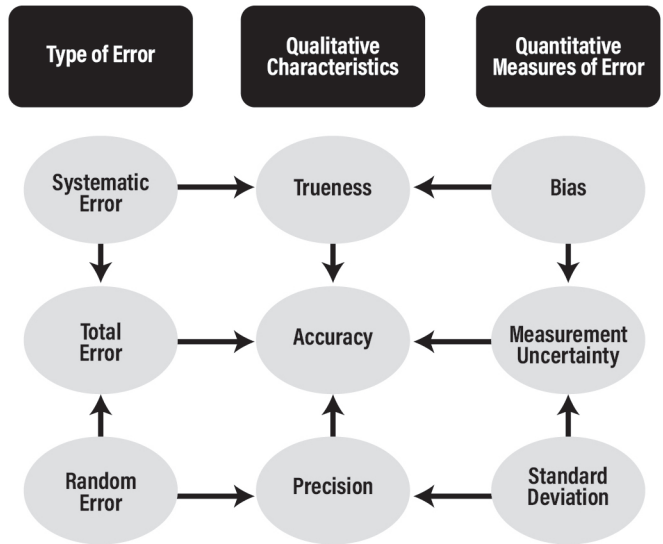
TE_{obs} (units of the test) = Absolute Bias (units of the test) + (K • SD)

or

TE_{obs} (%) = Absolute Bias (%) + (K • CV)

K is a multiplier that may range from 2 to 6, depending on the quantitation of error desired. It corresponds to the number of SD or CV contained within the error budget. The number used for K corresponds to the sigma metric for the test being evaluated (e.g., TE_{obs} (%) = Abs Bias (%) + (2 • CV) corresponds to a 2 sigma test).

FIGURE 1. Relationships of types of analytical error, qualitative characteristics, and quantitative measurements of error



14: Basic Business Performance Metrics for Veterinary Laboratories

Kathleen Freeman and Jérémie Korchia

> *Measure what is important. Don't make important what you can measure.*
>
> —- Robert McNamara.

Learning objectives:

1. Discuss common business metrics used in veterinary laboratories.
2. Describe the importance of common business metrics.
3. Discuss why including employees with summary information about business metrics may help increase the level of trust within the organization and promote employee engagement and satisfaction.

Introduction

Some people think quality management and quality systems are all about mathematical calculations and statistics and boring and dull. In fact, the business metrics that are applied commonly in the veterinary laboratory are fairly simple. These may vary with the laboratory, the type of laboratory clientele, the availability of staff for analysis and/ or problems previously encountered in a particular laboratory. This chapter will introduce some of the metrics that are commonly collected by veterinary laboratories that are separate from those associated with ongoing quality control, external quality assessment and instrument/ method validation or verification. The statistics associated with Method Validation studies and quality control, external quality assessment (EQA) and biologic variation-based goals are presented and discussed in detail in the chapters on these topics.

What is a metric?

A METRIC is defined as a 'standard of measurement', synonymous with a 'benchmark' or 'yardstick' (Metric | Definition of Metric by Merriam-Webster). It is related to the art, science or process of measuring. We use metrics to try to distill information to help us manage laboratory quality, rather than to try to 'prove' quality. Good business management is vital to the continued existence of any laboratory and this is recognized at all levels of stakeholders in the organization (owners, employees, and veterinary clients, owners, and animals).

However, a record of good business metrics and some metrics that can be shared with clients and potential clients can be an excellent marketing tool. These can be a good way to help 'celebrate success' and to show clear commitment to continuous improvement. These may help foster relationships with various practices and individual veterinarians, including key community opinion leaders, that may be vital in word-of-mouth advertising for your laboratory and its philosophy.

The basic business metrics presented here are applicable to virtually ANY type or size of laboratory. Many other business metrics may be applicable, depending on the organization of the laboratory and the emphasis of its management team. The ones presented here are considered by the authors to be the most basic ones and ones of most value in promoting a quality laboratory culture and continuous improvement.

What are common business metrics collected in veterinary laboratories?

There is no set of 'standard' metrics for all laboratories, although commonly the minimum metrics for monthly or quarterly metrics are presented in Table 1. Many organizations have found it help to share this type of summary data with employees to promote employee engagement, job satisfaction and inclusion since they are vital to the success of the organization.

15: Instrument and Method Validation

Kathleen Freeman and Stefanie Klenner-Gastreich

Here's the inner, hidden, deeper, secret meaning of method validation……ERROR ASSESSMENT.

Statistics are just tools for evaluating experimental results.

Comparison of Methods Study. This is NOT a simple study.
—- James O. Westgard.

Regression analysis is like one of those fancy power tools. It is relatively easy to use, but hard to use well – and potentially dangerous when used improperly.
– Charles Wheelan, Author of Naked statistics: stripping the dread from the data

Learning objectives:

1. Describe the types of studies used for instrument/ method validation and considerations for planning validation studies
2. Describe the difference between instrument/ method validation and verification
3. Discuss reasons why validation or partial validation, rather than verification, is more common for veterinary instruments/ methods
4. Discuss the method validation studies that are commonly used and why there is flexibility as to which are chosen for instrument/ method introduction to the laboratory
5. Discuss common problems encountered in veterinary instrument/ method validation publications and how to avoid or address these problems

Introduction

There are many good publications in the human and veterinary literature on instrument/ method validation. The book by James O. Westgard (Basic Method Validation, 4th edition, 2020) provides a good overview of the philosophy, studies needed and statistical evaluations that should be done for instrument method validation for quantitative and qualitative tests.

Because of the lack of regulation of instruments/ methods marketed for the veterinary industry, manufacturers do not have a standard set of required studies to be conducted to provide evidence of the suitability of an instrument/method for veterinary use. Studies are not always conducted with sufficient rigor to allow potential users (either for POC or reference laboratories) to decide about the suitability of the instrument/ method for the intended use.

This chapter provides an overview of recommended instrument/ method validation studies provided by ASVCP and other sources, as well as common problems encountered with veterinary instrument/ method validation studies.

Validation versus Verification

The purpose of **Method Validation** is to determine what error is associated with the method and whether this error can be tolerated for intended use of the test. The purpose of **Method Verification** is to determine whether the manufacturer's claims for performance can be confirmed (in other words, to determine if the method works as advertised). Verification also extends to confirmation that a manufacturer-provided reference interval is appropriate for the laboratory's patient population (See Chapter on Reference Intervals, section on Reference interval transference). In the verification approach, details regarding common interferences (hemolysis, lipemia, hyperbilirubinemia) often are not evaluated and are accepted. This assumes that there is sufficient detail regarding interferences to indicate when specimens should be rejected for analysis and/ or allow interpretation of results.

16: QC Validation

Kathleen Freeman and Stefanie Klenner-Gastreich

> *Valid (adjective): having a sound basis in logic or fact; reasonable and cogent.*
>
> *Validation (noun): the act of checking or proving the validity or accuracy of something.*
>
> – Cambridge English Dictionary

Learning objectives:

1. Define QC Validation and list the parameters used to conduct it.
2. Describe why QC validation should be done.
3. Describe how QC validation is done.
4. Describe when QC validation should be done.
5. Describe the benefits of QC validation compared to the use of manufacturer's acceptable range ('bottle values') for quality control.

What is QC Validation?

QC validation is the process of determining candidate QC rules appropriate for a specified total error goal and based on the observed performance of a particular instrument/ method. It can also be applied in a 'reverse engineering' approach to determine the total error based on specified sigma metric, probability of error detection (P_{ed}), probability of false rejection (P_{fr}) and QC rule choice(s). The working goal of QC validation is to provide a high P_{ed} (usually specified as ≥ 90%) and a low P_{fr} (usually specified as ≤ 5%). The high P_{ed} provides confidence that the QC rule chosen as part of the validation process will determine if unstable performance of the system (instrument, reagents, and operator) is likely. The low P_{fr} is preferred to prevent 'alarm fatigue;' it ensures that when a QC failure occurs there is only

a small risk that it is due to random error and, therefore, without clinical significance.

Why should I do QC Validation?

Manufacturers of QC materials (QCM) often will include acceptable ranges for each measurand for their product. This is often referred to as the QCM 'bottle values.' These may be further broken down according to instrument and/or method used for the analyses. These are typically based on 2 SD ranges across multiple laboratories. Therefore, the acceptable range is often very wide and does not provide a high P_{ed} for QC based on the observed performance for an individual analyzer. Several papers in the veterinary literature have shown that manufacturer's 'bottle values' often have such a wide range that the P_{ed} is extremely low for many measurands, with a few exceptions.

Because of the poor P_{ed} generally associated with QCM 'bottle values', QC customized for the observed performance of each instrument is recommended. Even instruments of the same age and manufacturer and using the same reagents and within the same laboratory may perform differently, necessitating different QC procedures. When instruments are in different laboratories/ locations, further differences in performance may be related to differences in the laboratory environment (temperature, humidity), instrument maintenance, handling and management of reagents and control materials, and/ or operator variability.

How do I do QC Validation?

There are manual worksheets Normalized OPSpecs (westgard.com)- available at https://www.westgard.com/downloads/ and software that can be used for QC Validation. Various quality goals can be chosen to specify the quality goal for QC validation. Consensus-based recommendations for total error goals for veterinary hematology, and biochemistry analytes are available from the American Society for Veterinary Clinical Pathology (ASVCP). Endocrinology total error goals are currently being drafted. If ASVCP recommendations for total error quality goals are not available, internal expert opinion goals

17: In-Clinic Laboratory Testing – Quality for Everybody. How to make QC work in real life.

Lucia Sanchini

> *Quality is the result of a carefully constructed cultural environment. It has to be the fabric of the organization, not part of the fabric.*
>
> – Phil Crosby, Leader in quality management

Learning objectives:

1. Discuss the considerations when planning an in-clinic laboratory
2. Discuss the importance of quality for in-clinic laboratories
3. Reflect upon the practical tips for maintenance and for minimizing pre-analytical errors for selected in-clinic diagnostic methods

Preface

My love story with quality started in the previous chapter of my life, in the long years I spent in general practice. In those days, in-clinic analyzers were already booming, as they were presented as a good way to make a quick diagnosis and lots of money. My partners and I, however, were preoccupied that the results generated internally were not accurate because there was not a dedicated person in charge of the machines and the tests ended up being run when there was time, in between surgical sessions and consults. We were driven by the need for "working well" and we were not willing to accept the possibility of failing a patient due to the poor quality of internal results. At the same time, we were running a 24-hour service and we needed some diagnostic support, so we decided to keep only the minimum tools which are required during emergencies, such

as microhematocrit, glucometer, refractometer, urine dipsticks, microscope and staining kit. This chapter is based on our real-life experience and how we made quality assurance work in our daily activities in practice.

Introduction

According to a survey conducted among members of the Veterinary Information Network (VIN) some years ago most participants had an in-clinic laboratory (92%). However, 3% of these did not perform any maintenance on their instruments, 1% appointed an unspecified "third party" to do instrument maintenance, 4% thought their instruments did not need any maintenance and finally, in 6% of practices the maintenance was carried out by the practice owner.

Fourteen percent of the responding practices equipped with in-clinic laboratories had no idea about the maintenance of their own instruments. This highlights how a quality culture that includes recognition of the importance of instrument maintenance, still has not reached a fair number of veterinarians. In addition, veterinary diagnostic laboratory testing (in any setting) is not subject to government regulation in contrast to human medicine. Therefore, veterinarians and veterinary technicians might volunteer to commit to QA/QC but they are not responsible if they do not. A real commitment to the culture of quality requires time and money, and both seem to be the main concerns for every veterinarian worldwide.

The importance of quality for in-clinic laboratories has been extensively explained elsewhere and the purpose of this contribution is to demonstrate that QUALITY ASSURANCE CAN ACTUALLY BE DONE without excessive struggle in everybody's daily working life and that doing so really pays off. Obviously, doing less is the easiest option. However, if you choose to keep only a few instruments, you still must make sure they perform at their best. This chapter will cover some of the basic financial considerations when considering whether to undertake an in-clinic laboratory, as well as basic laboratory equipment and its maintenance, that are likely to be required for most in-clinic laboratories.

18: Clinical Decision Limits and Reference Interval Transference and Generation

Linn Clarizio and Kendal E. Harr

Normal is an illusion. What is normal for the spider is chaos for the fly.
– Charles Adams

Decision is the spark that ignites action. Until a decision is made nothing happens.
– Wilferd Peterson

Learning objectives:

1. Explain the differences between population-based reference intervals and clinical decision limits.
2. Discuss the interpretation of results using population-based reference intervals and clinical decision limits.
3. Discuss the limitations of population-based reference intervals and clinical decision limits.
4. Explain the process of reference interval transference verification.
5. Be aware of national and international guidelines for reference interval generation and understand how population-based reference intervals are developed.

Introduction

Clinical laboratory testing is an integral part of the medical decision-making process. Results from laboratory tests are useful in detecting deviation from health, diagnosing illness, and monitoring progression of disease or response to therapy. However, a test result is of limited utility without appropriate criteria for interpretation. The concept

of population-based reference intervals was first introduced in peer reviewed literature by Gräsbeck and Saris in 1969 and was used to describe the variation in clinical laboratory values for defined groups of healthy individuals. The concept was then discussed at numerous conferences prior to implementation in hospitals about a decade later. Implementation of reference intervals for veterinary species is reported in the late 1970s and early 1980s. The original Clinical Laboratory Improvements Amendments (CLIA), approved in 1988, codified their establishment and use as a requirement for human diagnostic laboratory function in the USA. Today population-based reference intervals and/ or clinical decision limits frequently serve as the standard for comparison with observed patient values to inform the medical decisions of clinicians.

The most recent update to the Clinical Laboratory and Standards Institute (CLSI) recommendations for reference intervals occurred in 2008 and included clinical decision limits, which were implemented based on national and international consensus in the previous decade, e.g., glycated hemoglobin. Reference interval transference and a verification process using a pre-existing reference interval from another laboratory or instrument manufacturer were also added to better enable diagnostic laboratories to appropriately assess working reference intervals, which previously mandated identification of120 reference individuals for *de novo* generation. Reference interval transference is the process that should be used by all veterinarians with an in-clinic diagnostic laboratory. While population-based reference intervals and clinical decision limits became commonplace in veterinary medicine, many clinicians and laboratorians had limited understanding of how they should be created and potential pitfalls in their use. Guidelines for the generation and transference of reference intervals and clinical decision limit development in veterinary species were published by the Quality Assurance and Laboratory Standards (QALS) committee of the American Society of Veterinary Clinical Pathology (ASVCP) in 2011. Understanding how these values are generated provides further background for identification of interpretation pitfalls which will strengthen the clinician's use of these diagnostic tools.

19: Biological Variation and Laboratory Quality

Kathleen Freeman and Stefanie Klenner-Gastreich

Success is the progressive realization of a worthy goal or ideal

– Earl Nightingale (American radio speaker and author, dealing mostly with the subjects of human character development, motivation, and meaningful existence)

Learning objectives:

1. Describe what biological variation refers to and how it relates to laboratory testing.
2. Describe why biological variation is important in determining laboratory quality goals.
3. Describe individualized reference intervals and how these differ from population-based reference intervals.
4. Describe reference change value and how it is used.
5. Describe dispersion and how it is used.
6. Describe the reasons why and how biological variation can contribute to evidence-based laboratory medicine.

What is biologic variation and how does it relate to laboratory testing?

Biological variation refers to the physiological variation that occurs around a homeostatic setpoint for the various measurands that we test for in the laboratory. A numerical result in an individual patient reflects a range of results centered around the homeostatic setpoint for that individual. There is variation that occurs within individuals (CV_I) and between individuals (CV_G). We can use knowledge about biologic variation in providing quality goals for laboratory testing, interpretation of single and serial results, and in determining individualized reference intervals for our patients.

Studies of biologic variation generate information about physiologic variation described by the within-individual coefficient of variation (CV_I), between individual coefficient of variation (CV_G) and the analytical coefficient of variation (CV_A) derived from the analysis of duplicate measurements based on the instrument/ method and laboratory in which the biologic variation study is done. The laboratory quality goals based on this information seek to minimize the ratio of analytical 'noise' to biologic signal and help ensure that significant changes representing changes in physiologic status can be recognized and are not masked by excessive analytical variation.

The veterinary biological variation website offers a summary of biological variation parameters investigated in veterinary medicine. Papers are reviewed by two members of the Veterinary Biological Variation Committee for compliance with guidelines for biologic variation studies. For those measurands where there are multiple qualifying studies, a separate listing of median values is provided. The website address is: www.vetbiologicalvariation.org

What quality goals for laboratory testing can be derived from biological variation?

Quality goals based on biologic variation are based on consensus recommendations (the so-called 'Milan Hierarchy') for defining analytical performance goals. Biologic variation is the second of 3 levels of goals that can be used.

Quality goals for laboratory testing that can be derived from biological variation information include goals that are labeled as optimal, desirable, and minimally acceptable levels for analytical coefficient of variation, analytical bias, and total analytical error. These reflect increasing variation that may occur in results and our ability to distinguish a true physiological change that should not be obscured by 'analytical noise' associated with an assay.

The following formulas are used to calculate the optimal, desirable, and minimally acceptable biologic-variation-derived quality goals are as follows:

20: Understanding Current Clinical Pathology Paradigms

Randolph Baral

If you want small changes in your life, work on your attitude.

But if you want big and primary changes, work on your paradigm.

– Stephen Covey

Learning objectives:

1. Define and describe the 3 main messages provided by the series of examples presented in this chapter: Bias, reference intervals and dispersion.
2. Reflect on the assumptions made by many veterinarians regarding bias, reference intervals and dispersion associated with laboratory results.
3. Perform calculations for individualized reference interval and dispersion.
4. Interpret laboratory results using individualized reference intervals and dispersion.

Introduction

Using a series of examples, this chapter will explain current clinical pathology paradigms in relation to plasma (or serum) biochemistry testing. Some of these concepts have been present for some time but poorly recognized, others are emerging concepts. The key concepts are:

1. Bias between analyzers.
2. Use of reference intervals (population-based and individualized).
3. Dispersion of results.

Bias

Example 1: Bias between analyzers

Most practitioners are familiar with the International Renal Interest Society (IRIS) staging of chronic kidney disease (CKD) that is intended "to facilitate appropriate treatment and monitoring of the patient" based on the stage of development of CKD. Table 1 shows the standard IRIS staging for cats shown in µmol/L and mg/dL.

Decision Limit	Stage 1	Stage 2	Stage 3	Stage 4
Creatinine µmol/L	< 140	140 - 250	251 - 440	> 440
Creatinine mg/dL	< 1.4	1.4 – 2.8	2.9 – 5.0	> 5.0

Based on this staging, how would you stage a cat with creatinine = 155 µmol/L (1.8 mg/dL), assuming dilute urine? Answer: That's pretty easy, the answer is 'stage 2'.

Along similar lines, what would the staging be for a cat with creatinine = 124 µmol/L (1.4 mg/dL), assuming dilute urine? Answer: Again, that's easy, there are no tricks (yet!) and the answer is 'stage 1'.

Along the same lines, a cat with creatinine = 212 µmol/L (2.4 mg/dL) with dilute urine is also in 'stage 2' but appears to be a little more advanced than the other two examples.

These three examples are all results from, not only the same cat, but the same blood draw and centrifuged in the same lithium

21: Daily Quality Control Practices with Computerized Tools

Nandor Balogh

Before software should be reusable, it should be usable.
– Ralph Johnson, computer scientist, UIUC

Simplicity, carried to the extreme, becomes elegance.
– Jon Franklin, computer scientist

Learning objectives:

1. Describe the evolution and features of the BioRad QC program available for daily QC evaluation and peer group comparison.
2. Discuss the advantages and disadvantages of the use of industry systems for QC

[Please note: the mention of specific software, brand names and companies in the text that follows comes with acknowledgement of their trademarks, registered copyrights, and copyrights, etc.]

Introduction and Historical Information

With the evolution of Quality Control (QC) knowledge and software industry, computerised tools for designing QC rules and the evaluation of daily QC results emerged. Historically the first of these were provided by Westgard QC under the names of EZ Rules (for determining candidate QC rules) and EZ Runs (for the evaluation QC runs). EZ Rules 3 is still available as a standalone application, but EZ Runs was licensed to Bio-Rad and is included in their software package called Bio-Rad Unity Real Time allowing for QC Rules design and results evaluation as well as real time peer group comparison.

This software is available at different content levels and offers both fully web-based, or desktop applications. Meanwhile another global company, Randox has launched their own QC software solution called Acusera 24•7. This is a fully online tool.

In this chapter, I will highlight the most important features of the Bio-Rad system and those we have found useful in our own veterinary commercial laboratory with some outlook on some features of the Randox system for comparison. As I have no real hands-on experience with the Randox system I will only mention a few features that are markedly different from the Bio-Rad System.

The first step is to **configure the system** according to your laboratory environment using dedicated pages to setup instruments, analytes, methods, reagents, and QC materials used. Peer group comparisons will only be available for Bio-Rad's own QC materials, however it is still possible to record third party QC material data. There are comprehensive lists for most globally available analyzers and reagents with their corresponding methods and reagent suppliers. Obviously precise configuration will be key for correct peer group comparisons.

Data entry can be done manually as an option for occasional single results (Figure 1). Bulk data entry is best managed by automation. Both applications will allow for connection to the Laboratory Information System (LIS) to extract QC data and/or offer file-based data transfer depending on actual software version and/or user preference. Both solutions offer the possibility of entering the mean of multiple QC results if this approach is used in a laboratory.

22: Quality in Clinical Pathology Reporting

Kathleen Freeman

> *Tell me the facts and I'll learn. Tell me the truth and I'll believe. But tell me a story and it will live in my heart forever.*
> – Native American proverb

Learning objectives:

1. Discuss the philosophy underlying evaluation of quality in clinical pathology reporting of all types.
2. Reflect on your personal philosophy and approach to clinical pathology reporting.

Introduction

There is some variability in the approach to 'reporting' in clinical pathology globally and pathologists may or may not comment on all, some, or selected laboratory results. However, cytology is reported worldwide by clinical pathologists. In most countries, telephone consultation is encouraged to discuss complex cases or those about which the clinician has questions or wants a clinical pathologist's input. In some countries, internal medicine consultants are employed by large commercial laboratories to discuss, in more depth, the treatment of cases based on the history and laboratory findings. If clinical pathology staffing is stretched the internal medicine consultants may be approached as 'de facto' clinical pathologists but may have limited or no training regarding laboratory instrumentation, quality control or testing artifacts. This chapter will deal with 'general concepts' regarding clinical pathology non-cytologic reporting. See the Chapter on Quality and Cytology for more in-depth discussion of quality issues associated with cytology.

Clinical Pathologists as Detectives and Storytellers

It is my own view that clinical pathologists are those who 'tell the story' and who can help bring meaning to clinical pathology results of all types. There are many internal medicine specialists who can interpret laboratory data, who can interpret cytology specimens and know a lot about the types of laboratory tests that are important in diagnosis of veterinary patients. However, clinical pathologists are those that ALSO know the instrumentation and technology, the validation of the instruments and methods, possible interferences, the performance of and quality control and quality assurance appropriate for the multitude of laboratory tests.

Clinical pathologists are the ones who ensure that technical competence and medical knowledge are considered as part of determining appropriate tests and the ongoing production of accurate and reliable results. They are the 'detectives' who look at the data produced and see the pattern of 'clues' that indicate particular diagnoses or differential diagnoses. They point out the combinations of findings that form typical patterns associated with various conditions, point out results that may indicate deviation from these patterns and may implicate the presence of more than one condition (multiple pathologic conditions) or which may indicate unusual or 'atypical' findings, as well as testing pitfalls or anomalies.

What is the purpose of the clinical pathologist comments?

The purpose of a clinical pathologist's comment is to provide succinct useful information about the results. This may include the likely interpretation/ diagnosis and/ or differential diagnoses, prognoses, need for additional testing or tests useful for monitoring the progression of disease or response to treatment. Therefore, clinical pathologists are highly skilled 'consultant specialists' that are part of the team providing for the best possible care of veterinary patients.

The most rewarding relationships with practices and individual clinicians are those in which the clinical pathologist's and clinician's opinion and expertise are respected and their contributions acknowledged as important in working together to contribute to the diagnosis, treatment, management, and monitoring of veterinary

23: Quality in Endocrinology

Jérémie Korchia

> *The eye sees only what the mind is prepared to comprehend.*
> – Robertson Davies, Tempest-Tost

> *One of the biggest problems with the world today is that we have large groups of people who will accept whatever they hear on the grapevine, just because it suits their worldview — not because it is actually true or because they have evidence to support it. The really striking thing is that it would not take much effort to establish validity in most of these cases… but people prefer reassurance to research.*
> — Neil deGrasse Tyson

Learning objectives:

1. Discuss pre-analytical, analytical and post-analytical factors important for endocrinology testing
2. Describe common limitations of point of care analyzers used for endocrinology testing
3. Discuss the importance of using laboratory-generated protocols for dynamic hormone testing
4. Describe the complexities of endocrine result interpretation

Introduction

Endocrinology testing shares many similarities with other laboratory testing such as hematology or biochemistry, but also differs in important aspects such as the assay type or the testing protocol. Immunoassays typically result in higher imprecision and higher bias, which directly impacts result interpretation. Moreover, testing protocols are more variable among different laboratories, and inquiring ahead of testing to understand the type of test, its requirements and its performance is always recommended. Quality

in endocrinology reporting may be addressed in each of the 3 phases of testing: pre-analytical, analytical, and post-analytical.

Pre-analytical factors

Before sampling to perform an endocrinology test, investigation to determine the sample type, the sample tube, the sampling protocol, and the sample shipping is recommended. It is also the opportunity to obtain the submission form from the laboratory.

Sample type

Submission of the right sample type for hormone testing is critical. Most of the time, the preferred sample is serum. There are few exceptions, such as ACTH or PTH or PTHrP, which are fragile molecules requiring to be submission of EDTA plasma. If the shipping takes > 24h or if the outside temperature is high, shipping frozen EDTA plasma is recommended.

Whole blood is never recommended, as cell lysis may lead to marked hemolysis and potential interference. Serum separator tubes are not recommended until proven otherwise, as their impact on the different hormone measurements has often not been investigated. Heparinized plasma is acceptable for some immunoassays and unacceptable for others, on a case-by-case basis; verification ahead of time with the laboratory is needed.

Sample tube

The sample tube is closely related to the sample type. However, notice that a transfer of tube often occurs following centrifugation to harvest serum or plasma and the final tube may not necessarily reflect the sample type. In the case of EDTA plasma, the blood is collected on a purple top tube, but the plasma is transferred to a plain red top tube (no additive) after centrifugation. The laboratory cannot know that the sample corresponds with EDTA plasma if it is not reported on the tube as well as on the submission form. The same is true for heparinized plasma.

Importantly, the tube needs to be labeled with the following information:

24: Quality in Cytology

Kathy Freeman and Lucia Sanchini

How well you tell your story determines how well your customers tell your story
– Simon Mainwaring, global thought leader

Learning objectives:

1. Describe important aspects of quality assurance and quality control with regard to veterinary cytology
2. Describe some common approaches to quality assurance and quality control for veterinary cytology
3. Describe the meaning and importance of pre-pre analytical and post-post analytical factors for veterinary cytology
4. Describe the importance of various pre-analytical, analytical, post-analytical factors and their effects on cytology quality

Introduction

Quality assurance and quality control for cytology can be challenging. Inclusion of pre-pre-analytical and post-post-analytical factors, which are outwith the laboratory, are particularly important in completion of the brain-to-brain loop (see the Chapter on "Preanalytic and Postanalytic phases of Laboratory Testing: The Chain of Quality") and efforts to include, address, monitor and/ or obtain information about these should be encouraged as part of the continued learning and quality improvement cycle.

Pre-pre-analytical and Pre-analytical factors

The following tables 1 and 2 summarize some of the pre-pre-analytical and pre-analytical factors that influence the quality of cytology

preparations and their interpretation. Some authors suggest that information about pre-pre-analytical factors should be part of the laboratory remit to ensure the quality of the submitted specimens.

Table 1: Pre-pre-analytical factors influencing accurate cytology reporting.

Pre-pre-analytical factors (outwits the laboratory)	Example	Importance	Implications for quality
Selection of lesion(s), organs or systems for cytologic sampling	If mass is present and regional lymph node is enlarged, aspirates from both the mass and lymph node are indicated rather than just one	Helps increase the probability that the relationships between the mass and lymph node and their significance are recognized	Provision of the most information; positive correlation of cytologic features in primary and possible metastatic sites increases confidence in interpretation
	Selection of correct organ or system based on clinical signs, presentation, history and any results of imaging	Should be based on high likelihood of the lesion, organ or system providing information	Helps explain the reason for clinical signs and the clinical presentation
Selection of cytology as sampling method	In some cases, histopathology could be the best option to begin with (i.e. hard masses, bones)	Increases the probability of obtaining diagnostic samples, (especially important when patients are very sick or if general anesthesia is required)	Optimization of resources for best results and best treatment plan
Selection of method for cytology sampling	Fine needle sampling with aspiration, fine needle sampling without aspiration, impression smears, scrapings, washings, brushings, fluid collections	Each method has advantages and disadvantages, depending on the site and type of lesion	Representative specimen suitable for evaluation is more likely to be obtained with the correct method of collection
Anticoagulants as part of collection protocol	Heparinized specimens unsuitable due to poor staining. EDTA helpful in prevention of clots that may entrap cells in samples with blood	Helpful in preventing clotting in bloody specimens that may result in entrapment of cells and/ or obscuring of features	Judicious use of EDTA anticoagulant helps increase probability of a representative sample; helps ensure that nucleated cells are not entrapped in clots
Handling of specimens immediately following collection	Making smears immediately following collection ensures cellular morphology most closely reflects in vivo conditions	Most accurate information obtained from well preserved cells	Delays in preparation of air-dried smears may result in degeneration of cells, cell lysis or distortion
	Refrigeration or fixation of specimens may be helpful if there is a delay prior to cytologic processing	Will depend on the type of specimen, availability of various types of stains	May help reduce artifacts and/ or degeneration associated with a delay prior to cytologic processing
Air-dried smears versus fixed smears, samples in fixative or fixed fluid specimens	Fixation of smears or fixation of fluid specimens may be required for some types of stains (Papanicolaou-like) or contra-indicated for others (Romanowsky stains)	Fixation requires Papanicolaou-type staining rather than Romanowsky staining; recent publication suggests small amount of formalin fixation (1 drop) may not interfere with Romanowsky staining	Appropriate staining based on specimen with presence or absence of fixation is important and helps ensure that cells can be evaluated
Labeling of specimens and slides for the laboratory	Pencil on frosted end slides preferred since less likely to be dissolved with staining and/ or become unreadable	Ensures correct identification of samples and avoids confusion when multiple sites are sampled from the same patient	Correct labeling of specimens ensures that the correct report is generated for a patient and that multiple sites are correctly identified
Requesting appropriate evaluations from the laboratory	Body fluid analysis should be done in addition to cytology for pleural fluid, abdominal fluid, synovial fluid, CSF. May need ancillary testing such as antigen or antibody testing, PCR testing, biochemical evaluation or other tests (TG/ Cholesterol, K+, creatinine), PARR, flow cytometry, immunocyto-chemistry or other tests, depending on clinical considerations and initial cytological findings	Aids in classification of the specimen, recognition of normal versus abnormal specimens, provides support for various differential diagnoses	Correct choice of evaluations that help support cytologic interpretation are helpful in ensuring that the interpretation provides the most complete and useful information

TG = triglycerides, K+ = potassium, PARR = Polymerase chain reaction for antigen receptor rearrangement

25: Basics of Laboratory Statistics

Jérémie Korchia, DVM, MSc, DAVCP (Clinical Pathology)

Statistics is the grammar of Science
– Karl Pearson, of Pearson's Correlation Coefficient

Definition of grammar: The study or use of the rules about how words change their form and combine with other words to express meaning
– Cambridge Dictionary

In God we trust; all others must bring data
– William Edward Deming, quality expert

The business of the statistician is to catalyze the scientific learning process
– George E.P. Box, statistician

Learning objectives:

1. Understand the different types of variables: predictor (X) versus outcome (Y), quantitative versus categorical.
2. Identify whether some statistical results belong to descriptive statistics or inferential (analytical) statistics.
3. Realize that the nature of a statistical test (z-test, t-test, F-test, and χ^2-test) is directly function of the distribution of probabilities the test is using (z-distribution, t-distribution, F-distribution, and χ^2-distribution).
4. Understand the shape of the z-distribution, the t-distribution, and the χ^2-distribution, as well as their relationship (t- and χ^2-distribution tend to the z-distribution when n and k, respectively, increase significantly).
5. Determine the main type of statistical test to use based the nature of the predictor (X) and the outcome (Y) variables.
6. Understand the difference between the null hypothesis H0 and the alternative hypothesis H1, as well as the principle of Null hypothesis significant testing (NHST).

7. Understand the difference between a statistical test and a test statistic (the latter is the result of a statistical test and is also known as test score).
8. Understand the main concepts involved in the generation of a test statistic (or score), and its interpretation compared to a critical value in term of acceptation or rejection of H0.
9. Understand difference between a test statistic and a p-value, correctly define the p-value, and use it for interpretation of statistical tests.
10. List the assumptions for using a parametric test.
11. Compare and contrast parametric and nonparametric statistical tests.
12. List and use the experimental design characteristics to identify an adequate statistical test for hypothesis testing.
13. Use the statistical concepts of the z-distribution for the daily QC monitoring.
14. Use sampling concepts and the parametric/nonparametric concepts for RI determination.
15. Use the all the presented statistical concepts to successfully communicate and collaborate with an expert in statistics.

Generalities in statistics: speaking the same language as statisticians and understanding the principles of statistical tests

- Variables and distributions
  - Variables
  - Distributions
- Descriptive vs analytic (or inferential) statistics
  - Descriptive statistics
  - Analytic or inferential statistics
  - Impact of variables and distribution on inferential statistics
- Generalities about the statistical test
  - Population and population sample
  - Principle of hypothesis testing
  - Generation of the test statistic
  - What is the difference between z-statistics and t-statistics?
  - Interpretation of the test statistic
  - The p-value
- Specifics of statistical tests
  - Use of parametric or nonparametric tests?
  - Advantages and disadvantages of parametric and nonparametric tests
  - Parametric and nonparametric tests in the different types of statistics
  - How to choose which type of statistics to use?
  - Application of concepts: finding the right statistical test

Specifics of statistics in a diagnostic laboratory setting

- Statistics in quality control (QC) monitoring
- Statistics in reference interval (RI) determination
- Statistics in comparison of quantitative methods
- Statistics in research studies

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