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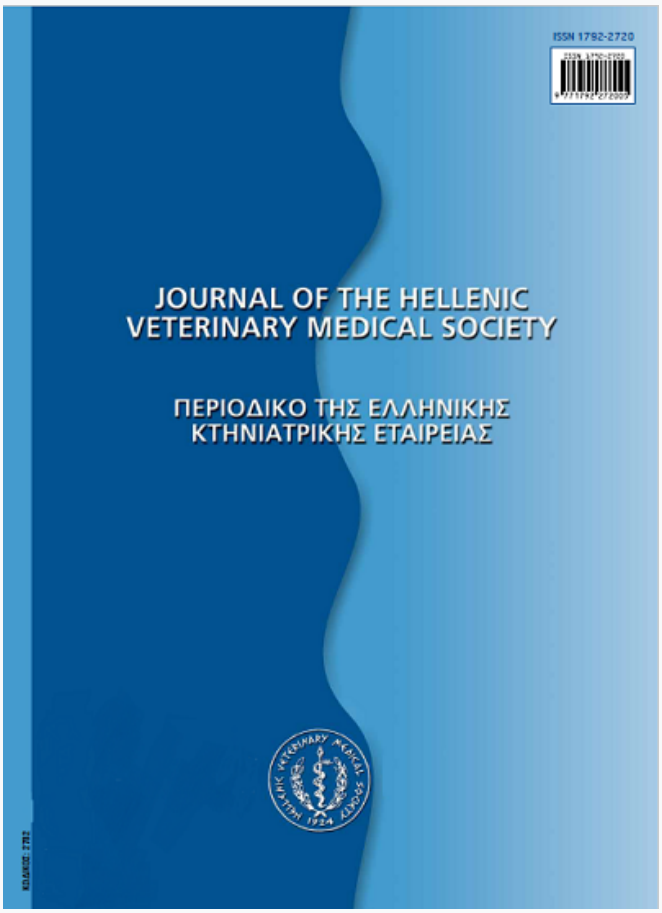

Quality policy in the veterinary diagnostic laboratory; the paradigm of application of Good Laboratory Practice

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Review article
Ανασκόπηση

Quality policy in the veterinary diagnostic laboratory; the paradigm of application of Good Laboratory Practice

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Πολιτική ποιότητας στο κτηνιατρικό διαγνωστικό εργαστήριο. Το παράδειγμα της εφαρμογής της Ορθής Εργαστηριακής Πρακτικής

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ABSTRACT

A quality system such as the Good Laboratory Practice (GLP) in a veterinary diagnostic laboratory is concerned with the organizational process and the conditions under which laboratory work is planned, performed, monitored, recorded, archived and reported. The key persons for applying a quality system are the Management (provides resources), the Director (overall responsibility for the technical conduct of analyses and for the interpretation, analysis and reporting of results) and the Quality Assurance Person (inspects operational phases and audits documents for the purpose of assuring management that the facilities, equipment, personnel, methods, practices, records and controls are in conformance not only with applicable rules and regulations but also with Standard Operating Procedures and Laboratory Protocols). Furthermore, the Standard Operating Procedures (SOPs) that govern all aspects of daily activities at the laboratory are an essential foundation for the production of reliable data as they, by definition, describe how to perform certain routine laboratory tests or activities. The standardization of methods used for a series of critical phases, such as storage and processing of samples is required in order to eliminate systematic errors and to improve the precision, specificity and long-range stability of laboratory performance. The correct identification of all samples needs to be systematically checked. For the validation of methods used, particularly in the absence of chemical standards it is helpful to employ inter- and mainly intra-laboratory controls. Finally, the disposal of chemical substances and the safety of the personnel are also of vital interest. All these principles are applicable to a veterinary diagnostic laboratory in order to promote the quality and validity of the data with ultimate goal the contribution to a reliable diagnosis.

Keywords: quality, standard operating procedure (SOP), veterinary laboratory

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ΠΕΡΙΛΗΨΗ

Η εφαρμογή συστήματος ποιότητας (Αρχές Ορθής Εργαστηριακής Πρακτικής) σε ένα κτηνιατρικό διαγνωστικό εργαστήριο αφορά στην οργάνωση και τις συνθήκες κάτω από τις οποίες προγραμματίζονται, διεξάγονται, ελέγχονται, καταγράφονται, ερμηνεύονται οι διάφορες εργαστηριακές εξετάσεις και αρχειοθετούνται τα αποτελέσματά τους. Για την εφαρμογή ενός συστήματος ποιότητας είναι ιδιαίτερα σημαντικός ο ρόλος του υπεύθυνου της διοίκησης (παρέχει πόρους), του επιστημονικού υπεύθυνου του εργαστηρίου (έχει τη συνολική ευθύνη για την επιστημονική και τεχνική εκτέλεση των εξετάσεων, για την ανάλυση, καταγραφή, ερμηνεία και τη σύνταξη σχετικής αναφοράς των αποτελεσμάτων) και του υπεύθυνου Διασφάλισης Ποιότητας (επιθεωρεί τις κρίσιμες φάσεις της λειτουργίας του εργαστηρίου και τα σχετικά έντυπα με σκοπό τη διασφάλιση ότι οι εγκαταστάσεις, ο εξοπλισμός , το προσωπικό, οι μέθοδοι, οι τεχνικές, τα αρχεία και οι διενεργούμενοι έλεγχοι είναι σε συμμόρφωση με τις τυποποιημένες διαδικασίες λειτουργίας και πρωτόκολλα του εργαστηρίου). Επιπλέον, οι τυποποιημένες διαδικασίες λειτουργίας (Standard Operating Procedures-SOPs) που περιγράφουν λεπτομερώς όλες τις καθημερινές δραστηριότητες στο εργαστήριο είναι θεμελιώδους σημασίας για την παραγωγή αξιόπιστων δεδομένων, αφού περιγράφουν πώς γίνονται οι συνήθεις εργαστηριακές εξετάσεις και οι καθημερινές δραστηριότητες του εργαστηρίου. Η τυποποίηση της μεθοδολογίας σε συγκεκριμένες σημαντικές χρονικές στιγμές, όπως η δειγματοληψία, η αποθήκευση και η συντήρηση των δειγμάτων, είναι ουσιαστική προκειμένου να εξαλειφθούν τα συστηματικά σφάλματα και να βελτιωθεί η ακρίβεια, η ειδικότητα και η διαρκής σταθερότητα της ποιότητας των εργαστηριακών εξετάσεων. Η ορθή σήμανση όλων των δειγμάτων πρέπει να διασφαλίζεται με τακτικούς ελέγχους. Για την επικύρωση των χρησιμοποιούμενων μεθόδων, ιδιαίτερα όταν δεν υπάρχουν πρότυπες ουσίες (standards), πρέπει να γίνονται ενδο- και κυρίως δι-εργαστηριακοί έλεγχοι. Τέλος, η διαχείριση των άχρηστων υπολειμμάτων χημικών αντιδραστηρίων, καθώς και η υγιεινή και η ασφάλεια του προσωπικού είναι επίσης μεγάλης σημασίας. Όλες αυτές οι αρχές εφαρμόζονται στο κτηνιατρικό διαγνωστικό εργαστήριο, προκειμένου να βελτιώσουν την ποιότητα και την εγκυρότητα των αποτελεσμάτων με απώτερο σκοπό την αξιόπιστη διάγνωση.

Λέξεις ευρετηρίασης: κτηνιατρικό εργαστήριο, ποιότητα, τυποποιημένες διαδικασίες λειτουργίας.

INTRODUCTION TO QUALITY SYSTEM AND STANDARDS

The quality of laboratory testing is mandatory for any aspect of health care and health research, including pharmaceutical product development. Although assessment of laboratory quality is a quite recent trend in veterinary medicine compared to human medicine, setting standards in infectious disease testing has been historically essential to provide mutually recognized valid results by public laboratories for cross border animal movements and trade (Caporale et al., 1998). The mission of the World Organization of Animal Health (OIE) is referred as the "safeguard of world trade by publishing health standards for international trade in animals and animal products" through the development of normative documents such as the Terrestrial Animal Health Code, the Manual of Diagnostic Tests and Vaccines for Terrestrial Animals, the Aquatic Animal Health Code and the Manual of Diagnostic Tests for Aquatic Animals (Table 1), while updated scientific information is also disseminated through various works and periodicals published by the OIE, notably the quarterly issue of "Scientific and Technical Review". The OIE standards have been incorporated into the quality standards of the accreditation program for public veterinary diagnostic laboratories implemented by the American Association of Veterinary Laboratory Diagnosticians (Table 1).

The International Organization for Standardization (ISO) provides a standard for systems, including the demonstration of competence and quality in laboratory testing. Among ISO standards the ISO 17025 and ISO 15189 have been mostly used for the accreditation of medical laboratories; the former intended for test and calibration laboratories, emphasizing the

more technical aspects of laboratory analysis and the latter designed specifically for medical laboratories. Since medical and veterinary laboratories share similar ethical and medical aspects of practice, ISO 15189 is applicable to veterinary laboratories to implement a quality system aimed at improving their ability to consistently produce valid results (Wiegers, 2002; Wiegers, 2003; Freeman et al., 2006).

Furthermore, since there has been a paucity of governmental regulation regarding quality policy in veterinary laboratories, the American Society for Veterinary Clinical Pathology (ASVCP) formed a Quality Assurance and Laboratory Standards (QAS) committee in 1996. The guidelines provided by these committees were recently updated and are online available (Flatland et al., 2010; Gunn-Christie et al., 2012; Vap et al., 2012; Flatland et al., 2013; Harr et al., 2013). In Europe, the same need has driven the European College of Veterinary Clinical Pathology (ECVCP) to implement a quality policy system. Accreditation for this system is compulsory prior to assignment of a veterinary laboratory as a training laboratory for the ECVCP board examinations (Sacchini and Freeman, 2008).

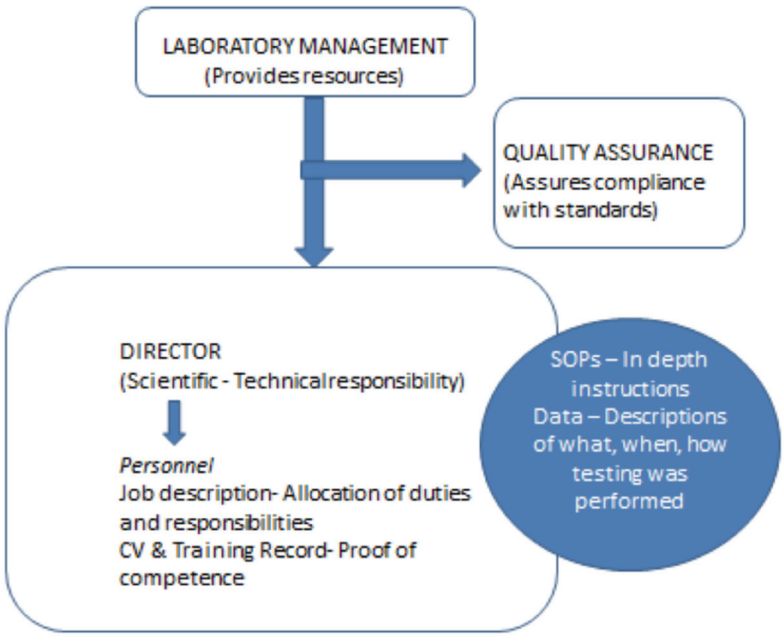

Figure 1.
Basic elements and structure of a GLP compliant laboratory

GOOD LABORATORY PRACTICE IN THE VETERINARY LABORATORY

"Good Laboratory Practice (GLP) is a quality system concerned with the organizational process and the conditions under which non-clinical health and environmental safety studies are planned, performed, monitored, recorded, archived and reported" as defined in the website of the European Medicines Agency (http://www.ema.europa.eu).

GLP as a formal regulation was first created by the Food and Drug Administration (FDA) in USA in 1978. It was the corrective action of FDA to confront a lot of fraudulent activities and cases of poor laboratory practice related with safety testing that had been reported all over U.S.A. such as the probably most known Industrial BioTest Labs scandal (Sneider, 1983). In 1981 the Organization for Economic Co-operation and Development (OECD) produced GLP principles that became international standard. Exhaustive information about GLP can be found on the websites of the OECD while the European Commission Directive 2004/9/EC and 2004/10/ are also applicable. Applicable directives are presented in Table 1.

Similarly to the already mentioned quality standards set by different authorities and scientific committees, the purpose of the development of the Principles of GLP by the OECD was to promote the quality and integrity of test data and ensure reliable standards of testing. In this way, data obtained from studies conducted in compliance with GLP principles and GLP accredited laboratories are acceptable by all OECD member countries facilitating trade among these countries, protecting Public Health and environmental safety.

To maintain quality in a laboratory it is critical that all of the key quality elements irrespectively of a specific quality system are in place and operational (Plebani et al. 2013). These elements include a)

Table 1. Normative reference documents

Nr	Document
1.	Terrestrial Animal Health Code http://www.oie.int/international-standard-setting/terrestrial-code/access-online/
2.	Manual of Diagnostic Tests and Vaccines for Terrestrial Animals http://www.oie.int/international-standard-setting/terrestrial-manual/access-online/
3.	Aquatic Animal Health Code http://www.oie.int/international-standard-setting/aquatic-code/access-online/
4.	Manual of Diagnostic Tests for Aquatic Animals http://www.oie.int/international-standard-setting/aquatic-manual/access-online/
5.	American Association of Veterinary Laboratory Diagnosticians (AAVLD): 2006, Essential requirements for an accredited veterinary medical diagnostic laboratory. Version 4.1. AAVLD, Davis, CA
6.	2006 Revision: Finalized ACVP meeting, Monterey, CA, December 2009 Newly formatted and revised ASVCP Quality Control Guidelines Principles of Quality Assurance and Standards for Veterinary Clinical Pathology http://www.asvcp.org/pubs/qas/index.cfm
7.	OECD Principles on Good Laboratory Practice (revised 1997, ENV/MC/CHEM (98/17)
8.	Directive 87/18/EEC (as amended by Directive 1999/11/EC) of 18 December 1986 on the harmonization of laws, regulations and administrative provisions relating to the application of the principles of good laboratory practice and the verification of their applications for tests on chemical substances.
9.	"Commission Decision of 2002/657/EC implementing Council Directive 96/23/EC concerning the performance of analytical methods and the interpretation of results", Official Journal of the European Communities, 17/08/2002, N° L221/8-36.
10.	"Guidelines on Validation of Analytical Procedures: Methodology" (CVMP/VICH/591/98-Final)
11.	"Guidelines on Validation of Analytical Procedures: Definition and Terminology" (CVMP/VICH/590/98-Final).

organization and personnel, b) method validation, c) standard operating procedures (SOPs), d) recording, reporting and archiving data, e) handling of disposals, environmental and personnel hygiene and safety, and e) quality assurance/quality control program (Ezzelle et al. 2008).

Standards for organisation and personnel

The laboratory has an organizational chart, and the responsibilities of personnel are defined.

Key personnel include i) the Laboratory Manager ii) the Director and iii) the Quality Assurance Person. An example of the organogram of a GLP compli-

ant laboratory is depicted in Figure 1. According to the GLP principles the Laboratory Manager should ensure that the principles of GLP are complied, with sufficient qualified and trained personnel, appropriate facilities, availability of equipment, materials and reagents, as well as that SOPs are established and followed (Hendriks et al. 2008). The study director or the scientific/technical director of the laboratory has overall responsibility for the scientific/technical conduct of the study and/or laboratory testing for the analysis, reporting and interpretation of results.

The director should regularly meet with all personnel involved in the laboratory and effective communication processes among all laboratory personnel should be ensured. The GLP concept includes the notion that personnel should have adequate education, training including training in the principles of GLP applicable to their involvement in the laboratory, and experience relative to the demands of their position to properly perform laboratory testing. To the author's experience scientists first dealing with quality issues often express their doubts for the need of quality assurance practices and their perception of these practices as "bureaucracy, time-consuming increased study documentation". However, after a period of adjustment they find it difficult to work without following well-defined standards. Because of the vital importance of human factor to the success of a testing laboratory, study personnel should be motivated to operate under standard operating procedures (SOPs), analytical methods and protocols, guidelines, principles and regulations (Bennett et al., 1988). Accordingly, each individual involved in laboratory testing has a responsibility for assuring the quality and integrity of the data associated with testing. Laboratory staff are not influenced by external pressures (e.g., commercial, financial), and laboratory activities are ethical. Confidentiality of patient information is maintained. Main personnel responsibilities as per OECD regulations include those directly related to the conduct of the study such as following protocols, SOPs and analytical methods, reporting problems, mistakes and unexpected events, and being involved in corrective actions, recording data promptly, accurately and completely and taking responsibility for of their quality, as well as responsibilities relative to safety and hygiene such as taking health precautions to minimize risk to themselves and ensure the integrity of laboratory testing and generated data and being excluded from laboratory work when presenting a health or medical condition likely to have an adverse effect on the laboratory testing or to other staff members.

Method validation

Measures that should be taken to ensure capability of a laboratory to provide data of adequate quality include employing validated methods, internal and external control procedures such as participating in proficiency testing schemes and finally accreditation (Caporale et al., 1998; Freeman and Gruenwaldt, 1999; Allen, 2013). Method validation is defined as the process by which the reliability and relevance of a procedure are established for a specific purpose. A method validation involves among others determining accuracy, precision, sensitivity, range, limit of detection and limit of quantitation. Definition of parameters usually validated in GLP compliant studies are presented in Table 2. However, although GLP compliance implies existence of validate methods exact guidance is not available. Laboratories usually refer to relevant European Medicines Agency (EMEA) directives (Table 1) or method validation guidelines available in the literature (Wiegers, 2003; Flatland et al., 2010).

Standard operating procedures

The SOP is a working document driving the conduct of a procedure contributing to the consistency, comparability and reproducibility of results (Sacchini and Freeman, 2008). The OECD guidelines are similarly define the function of SOPs as to "describe how to perform certain routine laboratory tests or activities normally not specified in detail in study

plans or test guidelines" and the purpose "to ensure the quality and integrity of data generated in the course of the study".

All SOPs must be adequate in scope to describe the function in sufficient detail such that the study data are reproducible. As methods and procedures are improved, SOP revisions are necessary to maintain SOP adequacy and applicability. The replaced SOP is put into a historical SOP file and all copies of the replaced SOPs are destroyed. SOPs should be technically valid, clear, and concise, with sufficient detail for a trained operator to perform the procedure correctly, immediately available in areas where they are relevant and supplemented by published textbooks, analytical methods, articles and manuals when necessary (Lindgren, 2008; Sacchini and Freeman, 2008).

Regarding the subjects that must be covered according to OECD, GLP subjects that should be covered include but "not limited to" test and reference items, equipment, materials and reagents, record keeping, reporting, storage and retrieval, use, care and housing of animals, quality assurance procedures, health and safety precautions. By the phrase "not limited to" the need for more areas to be covered is implied. Historical copies of all SOPs should be kept in the archive. The fact that the historical collection of SOPs, mandated in OECD's guidelines under management's responsibilities does not mean that their creation is a managerial duty. To the contrary, management should give the opportunity to the laboratory personnel to create SOPs in order scientists who are most likely to perform a certain procedure to assess existing methods and procedures and put better ones in place. Furthermore, since one of the reasons why personnel may resist using an SOP is that the user knows another (better) method, the above suggested way to create an SOP will increase SOPs acceptance and conformity by the personnel. Authorship of SOPs by the personnel usually means fulfillment of this purpose. To overcome these problems in our laboratory, when a new SOP should be written, one member of the laboratory personnel usually writes a draft after consulting the relative manual or information found in the literature and then another one follows, preferably one who is totally unfamiliar with this procedure is asked to perform it so as to any technical shortcomings of the SOP to be identified and corrected.

The information which the SOP should contain irrespectively of the topic to be covered is 1) the title and coding of the SOP which should be easily found in the front page of the document. The title should be descriptive but also short and representative of the contents of the SOP; 2) date and signatures of author/s and the person who authorize the release of the certain SOP; 3) version/edition number and a statement about regarding the previous version/edition that is replaced; 4) the distribution list; 5) the aim of the certain SOP. This is to emphasize that SOPs are not a necessary evil with the exception of very technical SOPs where the aim is very obvious. The way that this information can be organized is illustrated in Figure 2.

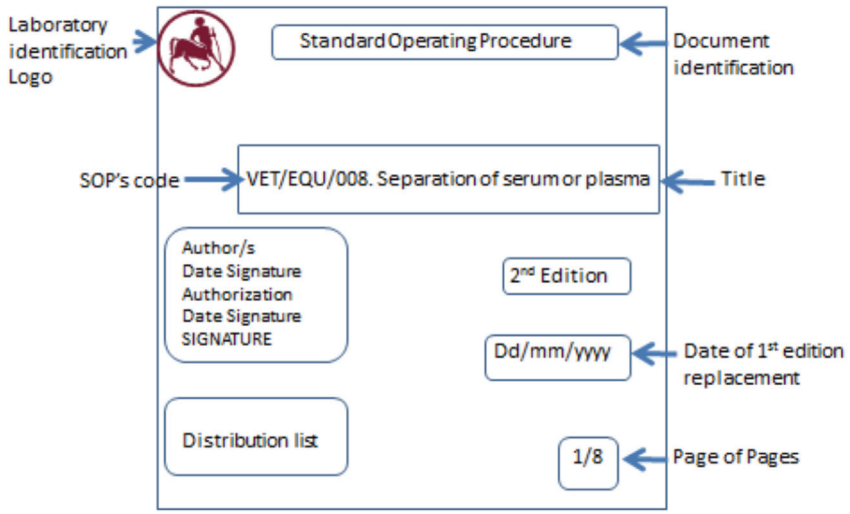

Figure 2. An example of SOP cover page format

Table 2. Definition of indicative validation parametres in GLP compliant studies

Parameter	Definition
n	Number of values taken into consideration
SD	Standard Deviation
CV %	Coefficient of Variation % = (SD/ mean concentration found) x 100
Accuracy %	The closeness of agreement between the true value (in this case the value of a spiked sample) and the mean result of the samples of the specific spiked level found during the analysis. Expressed as recovery= (Mean Concentration found / Spiked Concentration) x 100
Specificity	Specificity is the ability to measure accurately and specifically the analyte of interest in the presence of other components that may be expected to be present in the sample matrix. It is a measure of the degree of interference from such things as other active ingredients, excipients, impurities, and degradation products, ensuring that a peak response is due to a single component only. i.e. that no co-elutions exist.
LOD	The limit of detection (LOD) is defined as the lowest concentration of an analyte in a sample that can be detected, not quantitated. It is a limit test that specifies whether or not an analyte is above or below a certain value. Calculated by the formula: 3.3 σ/ S
LOQ	The limit of quantification corresponds to the smallest measured content of an analyte, above which a determination of the analyte can be made with a specified degree of accuracy (70 – 110 %) and precision (CV< 20%).
Absolute Recovery (%)	(Analyte Concentration calculated from the curve / spiked analyte concentration) x 100%
Within Laboratory reproducibility/ Intermediate precision	The distribution of measurements results obtained under in house reproducibility conditions (same method, different operators, different days)
Repeatability	The closeness of agreement between mutually independent test results obtained under repeatability conditions (the same method on identical test material in the same laboratory by the same operator using the same equipment)

Recording, reporting and archiving data

Raw data are all the original laboratory records and documentation, or their verified copies, which are the result of the original observations and activities in a laboratory. Raw data can also include photographs, computer documents and sheets, dictated observations, recorded data from automated instruments, or any other data storage medium that has been recognized as capable of providing secure storage of information for the required time-period.

According to GLP principles all data recording should be direct, prompt, accurate, permanent and legible, signed/initiated and dated. Data generated as a direct computer input should be identified at the time of input by the individual(s) responsible for direct data entries. Any changes made to raw data should not obscure the original entry. A sensible and clear reason for change should be given and the change should be signed and dated by the person making that change. Changes or additions to data

should be made promptly and it is not acceptable to add missing signatures or values days later. Everyone should ensure that files containing study data are kept in a manner which facilitates easy retrieval of data. Forms used for data capture are identified, approved and controlled. All raw data should be transferred to a suitable archive. Data transfer to archives is prompt in order that the data can be protected against loss, alteration or theft.

Handling of disposals, environmental and staff hygiene and safety

Laboratory facilities and operation should assure safety of both environment and the personnel. General and specific precautions should be taken upon handling of chemicals, chemical waste as well as possible contaminated biological materials depending on the corresponding risk. Appropriate safety and biohazard training of the personnel should be offered and documented in the training records (Gunn-Christie et al. 2012).

Quality assurance (QA)

According to OECD principles the prime function of QA is to monitor the operations of the testing facility to assure management, sponsors and regulatory agencies that studies performed are in accordance with GLP. QA performs three types of audits/inspections: a) study-based inspections/audits b) facility/systems-based inspections/audits c) process-based inspections/audits.QA may also audit contractors and suppliers. Except for the study-based inspections all other inspections/audits are applicable to all kind of veterinary laboratories. Process-based inspections are also performed to monitor procedures or processes of a repetitive nature. The frequency of process-based inspections is determined based on the risk of non-compliance with the pre-determined specifications, the severity and the importance of a procedure, the possibility of a corrective action to be taken (Freeman and Gruenwaldt 1999; Gunn-Christie et al. 2012). The OECD recognizes "that the performance of process-based inspections covering phases which occur with a very high frequency may result in some studies not being inspected on an individual basis during their experimental phases". Other useful process-based inspections are those that focus on cross-organizational processes – for example, the transfer of test samples from the animal facilities to the laboratory. Attention goes to all aspects of quality management in the laboratory organization (Kilinc 2009), including staff training, the maintenance and calibration of all equipment used, the laboratory environment, safety measures, the system of sample identification, record keeping and storage, the use of validated and standardized methods and the documentation of these methods and of all information concerning the followed procedures (SOPs).

CONCLUDING REMARKS

Good quality of laboratory testing is essential if results are to be used to contribute to or to confirm diagnosis. Therefore high standards of laboratory practice should be set and followed so as the outcome of testing to be reliable.

Although, quality policy, standard operating procedures and quality controls might be perceived as purely bureaucratic at first by medical and veterinary doctors they provide a way whereby a laboratory may meet standards and provide assurance to the attending veterinarian that the laboratory is providing high quality results to rely on.

Even if a laboratory cannot afford the cost of external control for accreditation, all laboratories can undertake the low-cost or no cost actions that are elements of all quality standards.

Irrespectively to accreditation programs, the laboratory determinants of high-quality testing are competent management, well trained, motivated personnel, appropriate methodology and method validation, standard operating procedures and adequate quality control. When all these are fulfilled the end result is usually highly accurate and precise testing. As for other quality principles GLP places a great burden of responsibility on everyone. Interaction and commu-

nication in the laboratory remain essential to make sure that all systems that have been set to ensure compliance are really efficient.

CONFLICT OF INTEREST

The author of this article does not have any financial or personal relationship with other people or organizations that could inappropriately influence or bias the content of this paper.

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REFERENCES

Allen LC (2013) Role of a quality management system in improving patient safety - laboratory aspects. Clin Biochem 46:1187-1193.

Bennett G, Evans J, Roadcap N (1988) The human element of quality assurance, Good Laboratory Practices: An Agrochemical Perspective, ACS Symposium Series No 369.

Caporale V, Nannini D, Ricci L (1998) Quality assurance in veterinary diagnostic laboratories. Rev Sci Tech 17: 459-468.

Ezzelle J, Rodriguez-Chavez IR, Darden JM, Stirewalt M, Kunwar N, Hitchcock R, Walter T, D'Souza MP (2008) Guidelines on good clinical laboratory practice: bridging operations between research and clinical research laboratories. J Pharm Biomed Anal 46:18-29.

Flatland B, Freeman KP, Friedrichs KR, Vap LM, Getzy KM, Evans EW, Harr KE (2010) ASVCP quality assurance guidelines: control of general analytical factors in veterinary laboratories. Vet Clin Pathol 39:264-277.

Flatland B (2012) Veterinary laboratory quality management--it takes a village. Vet Clin Pathol 41:171-173.

Flatland B, Freeman KP, Vap LM, Harr KE (2013) ASVCP guidelines: quality assurance for point-of-care testing in veterinary medicine. Vet Clin Pathol 42:405-423.

Freeman KP, Bauer N, Jensen AL, Thoresen S (2006) Introduction to ISO 15189: a blueprint for quality systems in veterinary laboratories. Vet Clin Pathol 35:157-171.

Freeman KP, Gruenwaldt J (1999) Quality control validation in veterinary laboratories. Vet Clin Pathol 28:150-155.

Gunn-Christie RG, Flatland B, Friedrichs, Szladovits B, Harr KE, Ruotsalo K, Knoll JS, Wamsley HL, Freeman KP (2012) ASVCP quality assurance guidelines: control of preanalytical, analytical, and postanalytical factors for urinalysis, cytology, and clinical chemistry in veterinary laboratories. Vet Clin Pathol 41:18-26.

Harr KE, Flatland B, Nabity M, Freeman KP (2013) ASVCP guidelines: allowable total error guidelines for biochemistry. Vet Clin Pathol 42: 424-436.

Hendriks R, Van den Eynde H, Coussement W (2008) Responsibilities of test facility management and sponsor in a GLP environment. Annali dell'Istituto superiore di sanita 44:407-408.

Kilinc C (2009) Laboratory quality management systems: missions, goals and activities in quality assurance. Clin Biochem 42:301-302.

Lindgren V (2008) To err is human; to follow the SOP divine. Int J Cancer 123: 979-980.

Plebani M, Chiozza ML, Sciacovelli L (2013) Towards harmonization of quality indicators in laboratory medicine. Clin Chem Lab Med 51:187-195.

Sacchini F, Freeman KP (2008) Quality documentation challenges for veterinary clinical pathology laboratories. J Vet Diagn Invest 20:266-273.

Schneider, K (1983). Faking it. The case against Industrial Bio-Test Laboratories. Amicus Journal (Natural Resources Defense Council) 14-26.

Vap LM, Harr KE, Arnold JE, Freeman KP, Getzy K, Lester S, Friedrichs KR (2012) ASVCP quality assurance guidelines: control of preanalytical and analytical factors for hematology for mammalian and nonmammalian species, hemostasis, and cross-matching in veterinary laboratories. Vet Clin Pathol 41: 8-17.

Wiegers AL (2002) The age of competence: an update on the international laboratory accreditation scene for veterinary testing laboratories. J Vet Diagn Invest 14: 89-96.

Wiegers AL (2003) Valid methods: the quality assurance of test method development, validation, approval, and transfer for veterinary testing laboratories. J Vet Diagn Invest 15:303-310.


HELLENIC VETERINARY MEDICAL SOCIETY
1924