Guidelines of the Office International des Epizooties for laboratory quality evaluation, for international reference standards for antibody assays and for laboratory proficiency testing

Summary
Three guidelines, adopted by the International Committee of the Office International des Epizooties (OIE), have been combined for publication in a single document.

The Guidelines for evaluating laboratory quality (adopted in 1995) form part of the OIE Guidelines for evaluating Veterinary Services. General requirements for equipment, staffing and management of laboratories are outlined.

The guidelines for international reference standards for antibody assays (adopted in 1998) provide general rules governing the preparation of immune sera by OIE Reference Laboratories. A data sheet should accompany each preparation dispatched from the laboratory, and details are given of the information to be contained in the data sheet. The guidelines are to be used in conjunction with the OIE Manual of standards for diagnostic tests and vaccines.

Guidelines on the proficiency of laboratory testing (adopted in 1996) describe how the operation of a laboratory can be assessed by inter-laboratory testing, and by voluntary participation in an accreditation (quality assurance) audit, operated by an independent authority. Criteria for assessing serological testing are provided.

Keywords

Guidelines for laboratory quality evaluation

Introduction
Purpose
This document provides guidelines for evaluation of laboratory quality and is to supplement the 'Guidelines for the Evaluation of Veterinary Services' of the Office International des Epizooties (OIE) (5).

Scope
These guidelines are intended for use by OIE Member Countries for the evaluation of laboratories that are carrying out tests to qualify animals and animal products for international movement. A Member Country can supplement this guide with more detailed requirements to meet specialised situations. This could include the monitoring of laboratory performance by the use of proficiency testing or inter-laboratory comparisons for specific assays.

This guide is based on the relevant requirements of the International Organisation for Standardisation (ISO) 9000 series of standards (4) and ISO/International Electrotechnical Commission (IEC) Guide 25 (2).

Formal accreditation
Laboratories may seek formal accreditation to standards compliant with the ISO 9000 (4) and ISO/IEC Guide 25 (2). Accreditation to the above standards should provide sufficient reassurance to Member Countries of the competence of a testing laboratory. Nevertheless it is recognised that in many circumstances such a high level of accreditation may be difficult to achieve for a variety of reasons. Accordingly, the present guidelines have been prepared to help facilitate removal of trade barriers by the acceptance of test results between countries. They are also intended to help facilitate co-operation between laboratories by assisting in the
exchange of information and the harmonisation of test procedures.

Laboratory organisation and management
The laboratory should be legally identifiable.

It should have documented procedures to ensure the protection of proprietary rights and confidential information.

A technical manager should have overall responsibility for technical operations within the laboratory.

A quality manager should have overall responsibility for the laboratory quality system and its implementation, and should have direct access to the technical manager and to senior management.

The quality manager and technical manager roles may be carried out by the same person.

Employees should be free from pressure or inducements which might adversely influence their judgement or the results of their work.

Adequate supervision should be provided by staff familiar with calibration, test methods and procedures, the objectives of the procedures and the assessment of the results.

Environment
The laboratory should provide a suitable environment for the proper performance of the test and this environment should not adversely affect or invalidate the outcome of the test.

The laboratory should provide and maintain essential utilities such as power, lighting, heating/ventilation/air conditioning, water and waste disposal.

The laboratory should provide suitable workspace for testing procedures with effective separation of areas in which incompatible activities may adversely influence the outcome of the test.

The laboratory should provide adequate measures to ensure the cleanliness of the work environment.

The laboratory should control authorised access in order to ensure the security of the facility.

The laboratory should comply with national standards of health and safety.

Human resources
The laboratory should have an adequate number of staff for the functions it undertakes. They should have the necessary education, training, technical knowledge, skills and experience for the range of testing carried out.

The training of all laboratory staff should be kept up to date, and records should be maintained of the relevant qualifications, training, skills and experience of the technical personnel.

A member of staff with appropriate skills should be nominated as supervisor of the day-to-day running of the laboratory in the absence of the technical manager.

Unskilled staff must be adequately supervised and should not undertake tasks normally assigned to skilled personnel.

Equipment
The laboratory should possess or have access to all the equipment necessary for the correct performance of calibrations and tests.

All equipment should be properly maintained and calibrated. Maintenance and calibration procedures should be documented in terms both of technical specifications and frequency with which they are carried out. Defective or suspect equipment must be taken out of service until repaired, tested and recalibrated.

Each item of equipment should be labelled in an identifiable manner so that its maintenance and calibration record can be referenced.

Records should be maintained for each item of equipment including its name, manufacturer, model, serial number, date of acquisition, previous history (if not new), operating instructions given by the manufacturer, dates and results of calibrations, details and dates of maintenance, history of malfunction, damage, modification or repair.

Wherever possible and applicable, calibration of equipment should be traceable to national or international standards of measurement.

Where traceability to national standards of measurement is not applicable, the laboratory should provide evidence of satisfactory performance in a programme of inter-laboratory comparisons or proficiency testing.

Sample handling
The laboratory should have a documented system for logging and uniquely identifying test samples on receipt, such that there can be no confusion regarding the identity of the samples at any time.

The condition of samples should be examined on receipt at the laboratory. Any abnormalities or departures from standard condition (as prescribed in the relevant test method) should be recorded. If the condition of the sample is such as to cast doubt on the validity of the test, the person submitting
the sample should be consulted and any test result marked
with an appropriate warning.

Samples should be kept in appropriate containers and
environmental conditions throughout their time at the
laboratory to avoid or minimise deterioration of the analyte(s)
under investigation. The storage conditions, procedures and
maximum duration of storage should be documented where
appropriate for each type of sample and each assay.

All procedures for the receipt, handling, storage and disposal
of samples should provide adequate biological and chemical
protection for personnel. Biological containment procedures
should take into account both human and animal health
hazards.

Guidelines for the transport, handling and storage of samples
are provided in the OIE Manual of Standards for Diagnostic
Tests and Vaccines (hereafter referred to as the OIE Manual)
(6).

Test methods and procedures

The OIE Manual will provide the principal source of standard
methodologies for tests carried out under these guidelines (6).
When standard methodologies have been modified by an
individual laboratory or when tests not appearing in the OIE
Manual are used, they must be fully documented and
validated, and the laboratory should have such information
available if requested.

Each reagent, chemical or biological used in the test shall be
appropriately labelled and its history should be documented.
Documentation should include information with respect to:

a) origin and date of receipt
b) date of preparation for use
c) storage conditions
d) expiry dates where applicable.

A demonstrable internal quality control programme for each
assay should be documented and in use. Documentation
should include:

a) detailed bench protocol
b) work sheets
c) internal quality control and raw sample data
d) quality control charts, where applicable
e) positive and negative cut-off criteria
f) details of internal check sample programme, if performed.

Record keeping and reporting

The laboratory shall maintain a record system for all
laboratory procedures outlined in this guideline which specify
a requirement for documentation (e.g., general laboratory
operation, maintenance and calibration of equipment, staff
qualification, sample tracking, quality assurance, etc.)

Test results should be reported accurately, clearly and
objectively, in accordance with the OIE Manual (6), and must
include all information necessary for sample tracking and the
correct interpretation of the test results.

External recognition

Wherever possible, the laboratory should participate in
national and international programmes which recognise
laboratory diagnostic proficiency. This usually requires
participation in external check sample programmes or other
inter-laboratory comparisons.

Guidelines for international reference standards
for antibody assays

Introduction

Purpose

This section provides guidelines for the preparation,
validation and distribution of international reference
standards for antibody assays for infectious diseases of
animals. Such standard preparations are designated by the
OIE as primary reference standards for use in conjunction
with tests described in the OIE Manual (6).

Definitions

Standard test protocol

‘Standard test protocol’ refers to a validated, internationally
accepted test procedure, often an ‘OIE prescribed test for
international trade’ which is described in the OIE Manual (6).

International reference standard

The term ‘international reference standard’ is synonymous
with ‘primary reference standard’. It represents the standard
by which all others are compared and calibrated.

Secondary and working standards

Secondary standards are prepared by direct comparison with
the international reference standard, and should so far as is
possible mimic the characteristics of the primary standard
when used in the standard test protocol. A ‘secondary
standard’ would typically be prepared by a National Reference
Laboratory and be designated as the national or local
standard.

Working standards may be synonymous with secondary
standards, or they may be tertiary standards calibrated against
the secondary standard. Working standards should be
available in sufficient quantities for use by diagnostic
laboratories to standardise routine daily testing (1, 2, 7).

Scope

International reference standards are necessary to ensure that
given antibody assay is capable of measuring antibody
activity to a specified level of diagnostic sensitivity. Diagnostic sensitivity relates to the risk of a false negative reaction occurring in an antibody assay when in fact an animal is, or has been, infected. International reference standards are normally intended for use by international, national and other reference laboratories in calibrating standard assays and as templates for the production of secondary standards. The secondary or other working standard, and not the international standard, are to be used on a daily basis to standardise testing.

For a limited number of diseases, there has been international agreement on a system of ‘international units’ of antibody activity. In such cases the international reference standards define the scale of these units. In the vast majority of animal diseases no such system exists, and assay systems, working standards and test samples are defined relative to the international reference standards.

**Approach**

For most assays, three primary reference standards should be established: a strong positive, a weak positive and a negative standard. These standards should be selected and characterised by a designated Reference Laboratory using an internationally accepted standard test protocol and internationally accepted reagents.

The weak positive standard is critical for providing assurance of the diagnostic sensitivity of the test. For non-quantitative assays (e.g., immunodiffusion tests) the weak positive reference standard may be the only positive standard required.

For quantitative, non-titration assays, such as indirect enzyme-linked immunosorbent assays (ELISA) (8, 9), the strong positive standard should define an arbitrary level of 100% positivity. The weak positive and negative standards should then be assigned a proportional percentage positivity corresponding to their reactivity when tested in the standard test protocol.

**Selection of materials for use as standards**

**Types of material**

The majority of international reference standards will be prepared from blood serum. This should be free from haemolysis and from excessive lipaemia. Antisera should, where possible, be produced in specific pathogen-free or gnotobiotic animals of a species appropriate to the assay being standardised. Other materials, for example defatted milk or monoclonal antibodies, may be used where appropriate to the assay being standardised.

**Safety**

The starting material for preparation of reference standards should be free from infectious material. Bovine sera should be from a bovine spongiform encephalopathy (BSE)-free source. To facilitate shipment between countries it is recommended that the standards be irradiated at 25 to 30 kiloGrays (2.5 to 3.0 Mrad). Irradiation should be carried out before freeze-drying and final characterisation of the standards.

**Positive reference standards**

Positive reference standards should be selected from animals that exhibit a typical humoral (i.e., antibody) immune response to the organism in question. Hyperimmune animals are not considered to be typical, and should be avoided if possible. The immune response may be elicited by experimental infection or by immunisation with vaccines. The timing after immunisation for collection of the material should be determined by the response of the animal as measured in the standard test protocol. This may vary according to the nature of the disease and the assay. Full details of the immunisation schedule and the nature of the immunogen must be provided so that secondary standards can be prepared by equivalent methods. The standards should be free from antibodies to organisms that might cross-react in the standard assay. The standard may be derived from a single animal or a pool of samples from a number of animals. Exceptionally, naturally infected animals may be used as the source of the standard where controlled immunisation or infection is not feasible.

**Negative reference standards**

Negative reference standards should be selected from animals that have never been exposed to, or vaccinated against, the organism in question. They should be free from antibodies to organisms that might cross-react in the standard assay. The negative standard may be derived from a single serum or a pool of sera.

**Characteristics of international reference standards**

**Strong positive reference standard**

For tests such as complement fixation, virus neutralisation or indirect ELISA, that demonstrate typical sigmoidal dose/response curves, the strong positive reference standard should exhibit an antibody activity that lies on the linear portion of the curve just below the plateau phase (9). In other tests, the strong positive reference standard should contain sufficient antibody to produce consistently the maximum reaction within the selected limits of the test, e.g., a clear-cut line of identity in an immunodiffusion test or 100% inhibition in a competitive/inhibition ELISA.

**Weak positive reference standard**

The weak positive reference standard should exhibit an antibody activity that again lies on the linear portion of the curve just above the positive/negative threshold. The reaction produced should never be equivocal. In other tests, the weak positive reference standard should contain sufficient antibody to produce consistently the minimum detectable reaction, e.g., a weak but unequivocal line of identity in an immunodiffusion test. For competitive/inhibition assays, which frequently show a sharp transition from positive to negative, the selection of the weak positive standard can be
particularly difficult. The same principles apply, in that the standard should give a consistent positive response, just above the positive/negative threshold, in the standard test protocol.

**Negative reference standard**

This standard should always give a reaction below the positive/negative threshold in the standard test protocol. The reaction produced should never be equivocal.

**Preparation of reference standards**

**Constitution of the standards**

Where possible, the positive reference standards should be prepared from materials showing the desired level of reactivity without further dilution. However, in many cases it may be necessary for the Reference Laboratory to make a one-time dilution of a positive serum in negative serum in order to achieve the desired level of reactivity as specified above. In such cases the weak positive reference standard may be derived from the same positive serum stock as the strong positive reference standard.

An international reference standard should not require any special manipulation (e.g., pre-dilution) by the recipient laboratory prior to its use in the assay in question. The standard should be tested as would any field sample under routine diagnostic conditions (including any dilution steps that are a normal part of the assay procedure). This prevents the introduction of error or bias related to special handling or preparation. Therefore the amount of antibody activity in a positive reference standard should be within the accurate detection limits of the diagnostic test.

**Stability and storage**

All materials should be stored frozen or refrigerated pending evaluation. Repeated freeze-thaw cycles will affect the consistency of performance of the reference standards and should be avoided. To ensure stability it is recommended that the final standard be freeze-dried, and it would be advantageous to provide the sterile diluent for reconstitution of the material along with the freeze-dried standard. Sealed glass ampoules, rather than rubber caps, are preferred for long-term storage. Freeze-dried stocks should be stored at 4°C, although short periods at ambient temperature (e.g., during shipment) should not be deleterious.

After freeze-drying, several bottles of the standard should be reconstituted and re-evaluated. There should be no evidence of cross-reacting antibodies or other non-specific factors that interfere with the interpretation of assay results.

**Batch control**

The original reference material must begin as one single stock with enough to last at least five years. This can be kept frozen (preferably at -70°C or below) and a batch can be freeze-dried for a minimum two-year supply (approximately 500 tests). For each batch, whether frozen or freeze-dried, batch references must be allocated and full quality control data maintained.

Each freeze-dried batch must be recalibrated. Each bottle or ampoule should contain from 0.5 ml to 1 ml.

**Labelling**

The label should contain the following minimum information: OIE logo; OIE international reference standard for (disease) (test); specify if strong positive, weak positive or negative; the name of the Reference Laboratory; reconstitution method; and storage conditions. The space available on the label may prevent the inclusion of all these items; abbreviations may be used and some of the items may need to be put on the data sheet instead of on the label.

**Data sheets**

OIE Reference Laboratories issuing international reference standard sera should ensure that all aliquots are accompanied by an appropriate data sheet. It should be made clear to requesting laboratories that international reference standards are intended for use in the calibration of their own assay and for promotion of international harmonisation.

For a diagnostic laboratory to prepare a secondary reference standard for its own use, it will be necessary for the OIE Reference Laboratory to supply specific data on the selection and/or preparation of the primary reference standards. This is especially true when primary reference standards have been prepared by dilution of strong or hyperimmune positives in negative sera.

**Data required**

The data sheet should repeat all the information specified for the label (see above). The following information must also be supplied in order to facilitate the selection and/or preparation of secondary reference standards which, as closely as possible, duplicate the primary reference standard:

a) description of donor animal for positive and negative serum, including species, age, reproductive status and origin (i.e., natural production, specific pathogen-free, gnotobiotic, etc.)

b) nature of antibody response (i.e., to natural infection, experimental infection, immunisation, etc.)

c) details of organism used to elicit the immune response (i.e., source, strain, serotype, etc.)

d) details of experimental infection or immunisation protocols (i.e., route, dose, immunisation schedules, method and time of sample collection, etc.)

e) reference tests used to select positive and negative reference sera candidates and to characterise the antibody response (e.g., ELISA, agar gel immunodiffusion, virus neutralisation, etc.)

f) sample of titration profiles of hyperimmune sera and criteria for selection of appropriate dilutions of defined activity

g) presence of heterologous antibodies, if known, and tests used in detection
h) details of any safety testing carried out on the materials
i) a statement that the standard is for in vitro use only
j) description of sterilisation methods, including type of irradiation and dose and condition of sample at time of sterilisation (i.e., liquid, frozen, freeze-dried, etc.)
k) batch number and date of production
l) recommended reconstitution (type of reconstituting fluid, and volume), handling and storage conditions
m) full contact address, telephone and fax numbers and e-mail address of the Reference Laboratory as a source of further information.

Approval of reference standards by the OIE
An international reference standard may not be issued under the name of the OIE unless it has been endorsed by the OIE Standards Commission acting under authority of the OIE International Committee.

The full technical and statistical data on the evaluation of the candidate reference standards, together with the full data sheet information as specified above, should be submitted to the OIE. The OIE Standards Commission will review the information. If the Standards Commission approves, the reference standard will be added to the list of international reference standards available. This list will be supplied to all OIE Members Countries on request, and may also be accessed on the OIE Web site (http://www.oie.int).

Guidelines for laboratory proficiency testing

Introduction

Purpose
This section provides guidelines for evaluation of laboratory capability to conduct diagnostic tests for infectious diseases and is to supplement the OIE Guidelines for the Evaluation of Veterinary Services (5).

Scope
These guidelines are intended for use by OIE Member Countries as part of the evaluation of laboratories that are carrying out tests to qualify animals and animal products for international movement. These guidelines should be used in conjunction with the OIE Guidelines for Laboratory Quality Evaluation for overall assessment of laboratory quality and capability.

These guidelines are based on the relevant requirements of the ISO 9000 series of standards (4) and ISO/IEC Guides 25 and 43 (2, 3).

Inter-laboratory test comparisons
Inter-laboratory test comparisons may be undertaken for a variety of reasons which may include:

a) determining the capability of a laboratory to conduct specific diagnostic tests
b) checking or certifying the performance of individual operators
c) checking or certifying the calibration of instrumentation
d) harmonising existing test methods
e) evaluating new test methods
f) assigning values and ranges to standard materials
g) resolving inter-laboratory differences.

Proficiency testing
When an inter-laboratory test comparison is conducted for the express purpose of determining the capability of a laboratory to conduct specific diagnostic tests (the first item listed above), it is referred to as proficiency testing. Proficiency testing is an integral part of laboratory accreditation programmes.

Proficiency testing schemes are based on defined sets of highly characterised test materials which are sometimes referred to as check sample panels. These panels are simultaneously sent to participating laboratories for testing. The results are collected and analysed against assigned values in order to determine the capability of a participating laboratory to conduct a diagnostic test and produce correct results.

Accreditation
An accreditation programme is a formal process for recognition of laboratory quality and capability by an independent authority. It requires that laboratories successfully participate in an accreditation programme on an ongoing basis in order to maintain their recognition status. The independent authority awards or denies recognition based on stipulated requirements for quality and capability.

In the initial stage of accreditation, laboratories are required to demonstrate a specified and sustainable level of quality. Ideally this would involve compliance with ISO 9000 (4) and ISO/IEC Guide 25 (2) in order to qualify for entry into the programme. However, it is recognised that in many circumstances such a high level may be difficult to achieve for a variety of reasons. The OIE Guidelines for Laboratory Quality Evaluation were prepared in order to establish a minimum acceptable level of quality.

The second stage of accreditation entails regularly scheduled proficiency testing for the evaluation of the capability of a laboratory to conduct specific diagnostic tests. As proficiency testing schemes are a form of inter-laboratory comparison, they must involve two or more laboratories. There is no agreed standard for proficiency testing in veterinary diagnostics, although several schemes are in operation at
international and national levels. The present guidelines have been prepared to be used in conjunction with the OIE Guidelines for Laboratory Quality Evaluation. Together, these guidelines form an acceptable basis for a quality assurance programme.

**Authority and recognition**

Accreditation programmes and proficiency testing schemes should be operated by an independent authority in order to prevent any bias in the award or denial of recognition.

Participation in an international accreditation programme and proficiency testing scheme should be voluntary. Lack of participation or failure to achieve recognition should not prevent a laboratory from conducting diagnostic tests or a country from entering into trade agreements.

Participation and recognition status should be made available by the independent authority to trading partners only at the request of or with the consent of the participating laboratory or country authority.

Such a programme and scheme may involve a cost to the participating laboratories for this service.

**Organisation and management**

Details of the proficiency testing scheme and its purpose, eligibility of participating laboratories and disposition of the results should be documented by the co-ordinating organisation to ensure the protection of proprietary rights and confidential information.

A programme manager should have overall responsibility for the operation, quality and security of the proficiency testing scheme.

It is also the responsibility of the programme manager to ensure that laboratories involved in the production of test materials are compliant with the relevant requirements of the ISO 9000 series of standards (4) and ISO/IEC Guide 25 (2).

Employees should be free from pressure or inducements that might unduly influence the analysis of proficiency testing results or the recognition status of the participating laboratory.

Adequate supervision and security should be provided by staff involved in either the production and distribution of test materials to be used in the proficiency testing scheme or the receipt and analysis of test results submitted by participating laboratories.

**Standard methods**

For the characterisation of test materials to be used in check sample panels, the standard method should meet or exceed the minimum diagnostic performance characteristics required for eligibility as a prescribed test in the OIE Manual (6).

The standard test should be calibrated against international standard materials, if these are available. Participating laboratories should also be encouraged to calibrate their own assays against the same international standards.

**Selection and composition of check sample panel**

**General principles**

For the purpose of selection of test materials for inclusion in the check sample panel, the initial assessment of the status and/or reactivity of the sample will be determined by the producing laboratory, using the standard method.

Acceptance of test materials into the proficiency panel should be based on repeated testing by more than one analyst conducting multiple runs of the test on different days. Sufficient values should be generated to assure the unequivocal status of the test material.

The number of test samples that constitute a check sample panel is not well defined. This will be dictated by the type of analysis to be performed on the results and the numbers required to ensure statistical validity.

**Serological tests**

Irrespective of the type of test, a minimum of three samples should be included:

a) an unequivocal strong positive
b) an unequivocal weak positive
c) an unequivocal negative.

However, using only three samples of this nature would render the results very predictable after a few rounds of proficiency testing. It would be advisable, therefore, to add at least two more samples to the check sample panel which could be varied from one proficiency test round to the next. This would prevent participating laboratories from anticipating the expected outcome. The additional samples could be different from the above or replicates of the above or a combination.

Additional requirements for serological test materials are that:

a) they are derived from a single animal or pool of animal sera
b) they are undiluted, or diluted in negative serum
c) they are not lipaemic
d) they do not contain secondary clots
e) they are not contaminated
f) they have not been repeatedly frozen and thawed
g) they are free from infectious agents
h) they are of sufficient volume for at least two consecutive proficiency test runs from the same processing batch
i) they are stable under conditions of processing and transport to participating laboratories for at least two years.
Statistical analysis for serological tests

Types of data
The choice of statistical analysis will in part be determined by the type of data generated by the test method in question. Qualitative data such as ‘positive’, ‘negative’ and/or ‘suspicious’ are somewhat limited in the statistical procedures which may be applied to them. Quantitative data such as end-point titres and semi-quantitative data such as percentage inhibition values are more flexible with respect to the types of statistical analysis possible.

Irrespective of the type of data to be analysed, it is important that the data from all of the participating laboratories be compatible. In some cases, this may require that participating laboratories be instructed to use a specific dilution series or to express their data against a common standard.

Assigned values
In the initial selection of test materials for the check sample panel, the producing laboratory will have assigned a preliminary value, range or status to the sample. For qualitative data, the assigned value may be the only acceptable value. If this is to be the case, then the producing laboratory should verify the status on a battery of tests to increase the confidence that the assigned value is in fact correct. However, as a goal, at least 80% of the participating laboratories should obtain the same result in proficiency tests. For quantitative and semi-quantitative data, the assigned value should be recalculated after proficiency testing results are submitted, and it should be taken as the mean value after removal of outliers.

Statistical methods
Many statistical procedures have been applied to inter-laboratory comparisons, some of which are far more sophisticated than others. As a general rule, the statistics being applied should be valid, straightforward and meaningful to the participating laboratories.

Frequency analysis is a simple and meaningful method for participating laboratories to see where their performance lies with respect to the other laboratories in the proficiency testing scheme.

Measures of intra- and inter-laboratory variance through repeatability and reproducibility indices will often provide valuable information on the precision and robustness of the test methods.

Youden analysis is a useful indicator of systematic or random error sources that may be causing problems in individual laboratories.

Pass/fail criteria
Decision criteria with regard to passing or failing a laboratory on a proficiency test should be clearly documented. These criteria must take into consideration factors which may vary from one disease to another and between types of tests. Once established, the criteria must be applied uniformly.

The types of statistical analyses chosen should assist in making pass/fail decisions. Laboratories submitting results that fall outside ranges established by statistical means should be identified. Results of serological tests that would potentially lead to a false negative classification of an infected animal would have to be weighed against results that would potentially lead to a false positive classification of a healthy animal. In most instances, the former type of error should not be tolerated as it indicates that there is a problem with diagnostic sensitivity. However, there may be some latitude in awarding a provisional status to laboratories experiencing problems with diagnostic specificity.

Frequency of proficiency testing
It is recommended that proficiency testing be done on a biannual basis. Depending on the country and disease, some consideration should be given to peak testing periods. Whenever possible, at least one of the proficiency tests should be scheduled to coincide with active testing periods.

Twice-yearly testing provides sufficient time between proficiency tests to undertake any corrective actions which might prevent a participating laboratory from losing its recognition status.

Laboratory recognition
The criteria for awarding, denying or withdrawing recognition should be clearly documented.

Logistics
Eligibility and acceptance
Eligible laboratories should be sent a comprehensive outline of the quality assurance programme and the proficiency testing scheme. This outline should include details pertaining to frequency of testing, commitments and deadlines, methods of data analysis, reporting structure, criteria for recognition, disposition of results and confidentiality. In addition, a form to be signed and returned to the co-ordinating organisation should be included to indicate that the eligible laboratory accepts the terms and conditions of the programme.

Notification and shipment of panels
Participating laboratories should be notified at least one month in advance of a pending proficiency test. Notification should also include the projected date and method of shipment of the check sample panel. Longer notification may be required by those laboratories in countries requiring import permits for the check sample panels.

Test materials in the check samples should be coded so as not to indicate their expected result. The coding may be alphabetic or numeric. Each participating laboratory should receive a panel with a unique set of codes to prevent collusion between laboratories.
All shipments should be by the most expedient and direct method. All shipments should comply with the International Air Transport Association (IATA) regulations concerning the shipment of biological materials.

Upon shipment, the recipient laboratories should be informed of pertinent details (i.e., method of shipment, carrier, air-way bill, etc.) in order to facilitate rapid retrieval and clearance of the shipment upon arrival.

Check sample panels arriving in a damaged or questionable condition should be replaced immediately.

Testing and return of results
Participating laboratories should be given an adequate volume of test material and adequate time to complete the testing of the check sample panel to their satisfaction. The panel may be tested more than once and by more than one person in the participating laboratory. However, only one set of results should be returned to the co-ordinating organisation for analysis. Normally, the person responsible for running the test routinely should be selected to run the check sample panel.

The check sample panel should be accompanied by a complete set of instructions with respect to reconstitution, storage and handling, special testing requirements, data expression and deadline for the submission of results.

Results must be returned in the proper format and on time. Failure to do so could lead to omission from the round of proficiency testing and loss or downgrading of recognition status.

The co-ordinating organisation should acknowledge receipt of the results and their acceptance into the analysis.

Analysis and reporting
Analysis and reporting should be completed in a timely fashion after the deadline for the receipt of results.

A general report summarising the results of all of the analyses should be prepared for distribution to all participating laboratories. Participating laboratories should be randomly assigned a code to ensure anonymity in the general report. Individual laboratories should be informed of their unique code for this run of proficiency tests.

Individual laboratories should also receive a summary of their own performance and their recognition status. This summary should indicate clearly all factors contributing to any change in their status. Where the status has been downgraded, it is especially important to indicate real or potential causes which may have contributed to downgrading. In some instances, it may be pertinent to re-issue a second, identical panel after corrective actions have been taken.

A statement of status may also take the form of an official certificate.

All data, results of analyses and the recognition status of participating laboratories should be kept in confidence at all times.

Disclosure
The primary purpose of these guidelines is to remove trade barriers and not to create them. It would be expected that participating laboratories having achieved full recognition status may request that official verification of their status be made available to trading partners from the independent authority or co-ordinating organisation. This should only be done at the request of or with the consent of the participating laboratory or country authority.

References


