1. Background
One of the main objectives of the Office International des Epizooties (OIE) is to provide guidelines for the regulation of trade in animals and animal products with regard to infectious diseases. Guidelines and standards are published in the *International Animal Health Code* (the *Code*), in which the most important infectious animal diseases are divided into List A and List B diseases and the requirements necessary to minimise the risk for importing countries are defined. The OIE *Manual of Standards for Diagnostic Tests and Vaccines* (the *Manual*) specifically describes the diagnostic techniques and associated tests for each of these diseases and for the relevant vaccines. In the *Manual*, the OIE provides a list of diagnostic tests for List A and B diseases that are designated as prescribed or alternative tests for international trade. Prescribed tests are those that are required by the *Code* for the testing of animals before they are moved internationally. Alternative tests are those that are suitable for the diagnosis of disease within a local setting, and can also be used in the import/export of animals after bilateral agreement. There are often other tests described in the chapters, which may also be of some practical value in local situations or which may still be under development. All the tests described are ‘validated’ tests, i.e. the results that arise from their implementation can be taken with confidence for the prediction of the infection status of the animal to which the tests are applied, e.g. identification of the animal as being positive or negative for the analyte/process the test is measuring.

Validation is the evaluation of a process to determine its fitness for a particular use, e.g. identification of a product or a reaction. It quantifies the performance of the assay, the possible errors and the likelihood of their occurrence. Overall, it should give criteria of reliability (specificity, sensitivity, accuracy, etc.), reproducibility (importance of internal quality control, intra- and inter-laboratory variability, etc.), and relevance (relationship to biological status for decision making). Therefore many variables are to be addressed before an assay can be considered to be validated.

In Chapter I.1.3 of the 2000 edition of the *Manual* ‘The Principles of Validation of Diagnostic Assays for Infectious Diseases’ are given. These are, in fact, a summary of the development of an assay, the feasibility studies, the optimisation and standardisation of the reagents, the characterisation of the assay performance (sensitivity and specificity) and the interpretation of the assay results. Because the *Manual* provides the principles of assay validation but not standards for assay validation, the term ‘validated assay’ elicits various interpretations, e.g. many consider that validation of an assay is a time-limited process and not an on-going assessment of assay performance for as long as it is used as is clearly stated in these principles. Many points therefore need to be clarified for the ‘harmonisation’ of assay validation and use:
- **Identification of the purpose for which the assay will be used**
- **The validation process**
The validation process is meant to determine the usefulness/relevance of an assay to a defined problem by providing performance characteristics. Which samples and which players are involved in that process?

• Assay recognition procedures (certification of a validated assay)

Currently the adoption of an assay as a prescribed or alternative test is obtained from the OIE International Committee during the annual OIE General Session following a recommendation from the OIE Standards Commission. It is unclear what data are needed for this evaluation by the Standards Commission. Normally the data submission and request for an assay classification are made by the Delegates of the Member Countries to the OIE.

The list of prescribed and alternative diagnostic tests in the OIE Manual is limited to their application in international trade and there is no obligation on testing laboratories to adhere to those assays for other purposes.

It has become obvious that it is necessary to improve the current system for the qualification and certification of diagnostic assays for infectious animal diseases. This is why the Animal Production and Health Sub-Programme of the International Atomic Energy Agency (IAEA) and its laboratory, the OIE Collaborating Centre for ELISA¹ and Molecular Techniques in Animal Disease Diagnosis, have convened a consultants meeting on the validation and certification of diagnostic assays for infectious animal diseases. This meeting was meant to elicit discussions on two main areas:

• Validation with respect to ‘fitness for purpose’,
• The process by which the assay (kits/reagents) can be certified by the OIE for a purpose.

The conclusions and recommendations of the meeting will be sent to the Director General of the OIE as proposals for the improvement of animal health management in terms of risk assessment.

2. Conclusions and Recommendations

Animal disease management is carried out for economic, public health, and environmental reasons. Risk assessment is the key component in disease management. An important factor in risk assessment is evaluation of animals and their products. Diagnostic testing is an important activity in this process and is useful only if it is applied within specific contexts. Therefore, testing can be classified as to its fitness for purpose. The purposes can be classified into six broad categories:

---

¹ ELISA: enzyme-linked immunosorbent assay
Fitness for Purpose

**Purposes**

1) Demonstrate population ‘freedom’ from infection (prevalence apparently zero)*

   a) ‘free’ with and/or without vaccination

   b) historical ‘freedom’

   c) re-establishment of ‘freedom’ following outbreaks

   *Note: Apparent freedom – absolute proof of freedom from infection in populations is not possible

2) Demonstrate freedom from infection or agent in individual animals or products for trade purposes

3) Eradication of infection from defined populations

4) Confirmatory diagnosis of clinical cases

5) Estimate prevalence of infection to facilitate risk analysis
    (surveys, classification of herd health status, implementation of disease control measures)

6) Determine immune status in individual animals or populations (post-vaccination)

The importance of analytical sensitivity and analytical specificity will vary depending on the purpose of use of the assay, but repeatability and reproducibility are always important factors to be considered. In addition to these performance characteristics some other factors need to be taken into account, such as sampling strategy, estimated disease prevalence, population characteristics, clinical evaluation, feasibility (including cost), efficacy of veterinary services, and host response to organisms and their variants.

**Recommendation:**

Recognising that the OIE has made considerable progress in the application of prescribed tests for purposes of international trade, it is recommended that in the future the OIE considers the adoption of the following more broad-based approach to the application of tests.

- It is recommended that the OIE gives top priority to adopting a process for the evaluation of diagnostic tests for specific purposes. The six purposes identified above should be the basis for test classification and validation. For each disease described in the Manual tests should be classified according to their fitness for purpose.

- Currently, there is no guideline for submission of an assay following initial validation. It is recommended to develop a standard template. Its purpose is to standardise validation methods, provide guidance through the validation process, promote quality in diagnostic assays, support the incremental process of validation, and aid in the establishment of a registration process. For that, a registry of test methods would be created and managed by the OIE with the support of other organisations (FAO, IAEA, WHO) and possibly independent
experts. This registry would have different levels of validation to be followed successively by the developers. These will be defined in the template (to be written and proposed by a group of experts).

- It is recommended that serum/sample collections be established by the OIE Reference Laboratories to provide analytical references, evaluation panels, and proficiency panels. Funding is a serious constraint to progress in this area, and it is recommended that the OIE should emphasise to international and national funders the importance of providing adequate resources on an ongoing basis.

- It is recommended that the OIE review the procedure for test validation and data submission. This should be based on the template and the fitness for purpose:
  1) Assay developer applies standard template requirements towards validation of new test.
  2) Total validation package is evaluated by other laboratories (they should not have been involved in the original validation).
  3) Evaluating laboratories must have established records in working with assays for the disease in question (at least one OIE Reference Laboratory if possible).
  4) The template with supporting documents are submitted to the OIE for evaluation.
  5) The OIE will accept the assay after a positive and independent peer review of results. The OIE provides an independent opinion on the purpose(s) for which the assay is deemed to be fit at the time of the OIE evaluation. Any subsequent changes need re-evaluation and demonstration of equivalency or improvement.

It is also recommended that OIE and the Collaborating Centre at the FAO/IAEA hold a meeting in 2003 with stakeholders (users, assays developers, private firms, donors, etc.) with the objective of providing the standard template and addressing the problems linked to references materials.