1. Background

In the Manual of Standards for Diagnostic Tests and Vaccines, the OIE provides a list of diagnostics tests that are labelled as prescribed or alternatives tests for the lists A and B diseases. Prescribed tests are those that are required by the International Animal Health Code for the international trade purpose. The alternative tests are those that can be used for the import/export of animals provided there is an agreement between parties involved in the trade. In the chapter devoted to each disease described in the Manual, are indicated some other tests along with the prescribed and alternative tests. All the tests described in the Manual 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 provides, in a quantifiable way, the performances of the assay, the possible errors and the likelihood of their occurrence. Overall, it should give criteria of reliability (specificity, sensibility, accuracy, etc), reproducibility (importance of IQC, intra and inter laboratories variability, etc), and relevance (relationship to a biological status for decision making). Therefore many variables are to be addressed before an assay can be considered as validated.

In the OIE Diagnostic Manual are given “The Principles of Validation of Diagnostic Assay for Infectious Diseases.” They 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 is giving principles of assay validation but not standards for assay validation to be referred to, 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 need to be clarified for the “harmonisation” of assay validation and use:
- **Identification of purpose for which the assay will be used.** Is a “prescribed test” fit for all purposes or for a specific purpose e.g. for sero-monitoring (measuring the efficacy of vaccination), for detecting disease, for verifying freedom from disease (disease eradication process), for differentiation of vaccinated animals from naturally infected animals? It is clear that the assay performances characteristics needed for each of the purposes are likely to differ.

- **The validation process.** This will usually involve both the research scientist and the diagnostian. The initial development and optimisation of an assay is frequently undertaken by the researcher but further characterisation of the performance of the assay is carried out by diagnostic laboratories. What are the criteria for designating the laboratories that will be involved in that stage of validation? How many laboratories should be involved: 1, 2, 4, 6, 10 or 20? Is it mandatory or not to include at least one OIE/FAO reference laboratory in that step?

- **Samples to be used in the validation assay.** A test which has been validated in European animal sera might not give the same results in African zebu or short horn cattle. This indicates the need for geographical validation but who should undertake this? Commercial concerns are rarely interested in validation in multiple countries. The current OIE reference sera are usually available based on animals from one location and breed of animal. Reference sera should ideally represent known infected and uninfected animals from all populations that eventually will become the target of the validated assay.

- **Multiple species infections.** Limited reference sera might be acceptable for a disease that affects only one animal species. In the case where many species are involved as for rinderpest, what will be the value of an indirect ELISA used to detect RPV antibodies in wildlife sera while it has been on cattle sera? In case of there must be a need for reference standards from each target species but this exacerbates the problems of who will pay for the collection and maintenance of these standards?

- **Level of continual quality assurance monitoring.** The OIE Manual states that the reproducibility of test data between laboratories should be assessed at least twice a year (EQA). Who should undertake this? Who should provide an audit of the results and who should cover the considerable costs involved?

- **Assay recognition procedures.** Currently the acceptance of an assay as a prescribed or alternative test is given during the OIE Annual General Assembly following a recommendation by the OIE Standard Commission. It is unclear what data is needed for this evaluation by the Standards Commission or even who should be making the submission of such data.

The overview given above highlights many gaps in the procedures through from the development of an assay to its adoption by OIE as a prescribed/alternative test. The AP&H Sub-programme and particularly the OIE Collaborating Centre for ELISA and Molecular Techniques receives a significant number of requests for clarification and a detailed account of how to go about “validating” assays for the OIE. In the current atmosphere of international trade agreements, the SPS agreement and all the implications therewith regarding animal products and animal movements, the sanitary status should be proved by validated assays. Although laboratory accreditation is now proven mechanism for addressing laboratory
activities, there is uncertainty on what assays should or could be used for international trade purposes and what criteria are used to assess this.

2. **Objectives of Meeting**

2.1. Overall

To provide an acceptable system for prescribing assays that should be used for diagnostic or surveillance purposes for infectious animal diseases within the context of international trade in livestock or livestock products.

2.2. Specifically

- to clarify issues relating to assay development and validation
- to clarify issues relating to validation of assays in different animal populations and species
- to clarify issues relating to assay quality assurance
- to clarify issues relating to the development and use of reference sera for assay development and use
- to clarify issues relating to the recognition by the OIE of assays for trade purposes
- to identify financing mechanisms to ensure a “level playing field” for all countries in this process

3. **Outputs and Outcomes**

A transparent and workable system for the use of validated assays for trade purposes that will provide assured data for effective risk analysis between trading partners of livestock and livestock products in terms of infectious animal diseases. This should result in improved trade opportunities and the further globalisation of livestock and livestock product trade.