OIE Procedure for Validation and Certification of Diagnostic Assays

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Summary of the presentation

- OIE principles and methods of diagnostic test validation
- OIE Procedure for the validation and certification of diagnostic assays
- Conclusions

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OIE Principles and Methods of Diagnostic Test Validation

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The relevant OIE Publications

- Manual of diagnostic tests and vaccines for terrestrial animals (chapter 1.1.4. and 1.1.5. in the paper version and combined chapter 1.1.4./1.1.5. on “Principles and Methods of Validation of Diagnostic Assays for Infectious Diseases” available on the OIE website)
- Manual of diagnostic tests for aquatic animals (chapter 1.1.2. identical to the combined chapter 1.1.4/5 of the *Terrestrial Manual*)
- OIE Quality Standard and Guidelines for Veterinary Laboratories: Infectious Diseases (4 Guides)

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Content of the Principles and Methods of Diagnostic Test Validation

- Definition of the validation:

  The validation of a diagnostic test method is a **process** that determines the **fitness of the test method**, which has been properly developed, optimised and standardised, for an **intended purpose**.

  It is an ongoing process.

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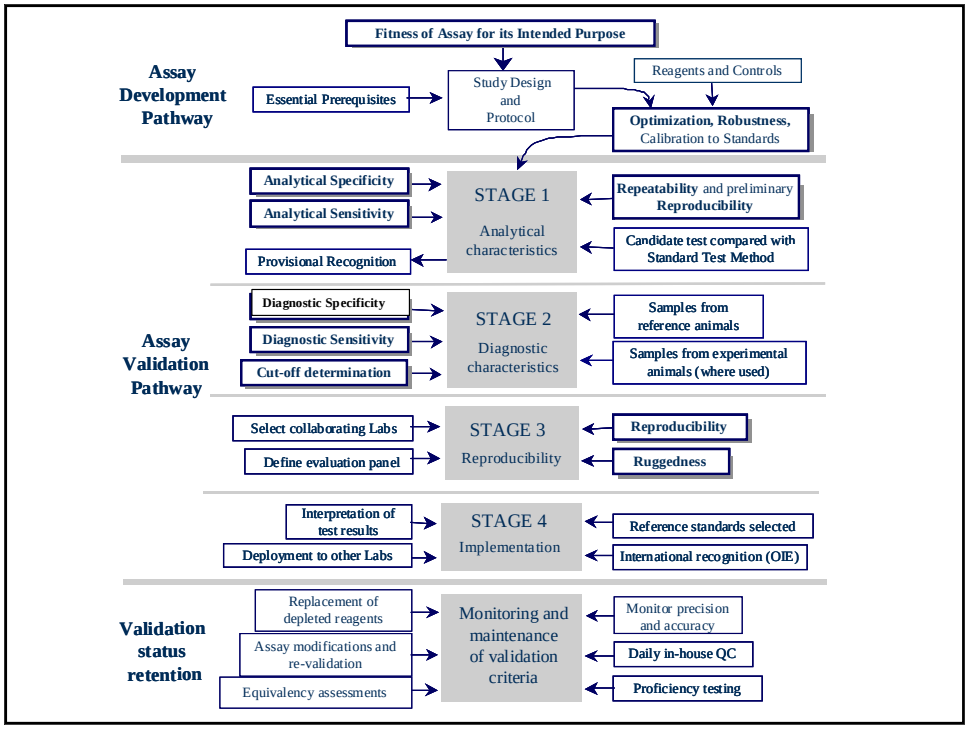

Content of the Principles and Methods of Diagnostic Test Validation

1. **Development of the diagnostic test**:

   Definition of the intended purpose(s),
   Design of the test method,
   Selection of the reference materials,
   Calibration, optimisation and standardisation,
   Robustness,
   Etc.

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Content of the Principles and Methods of Diagnostic Test Validation

- The most common purposes are to:
  - Demonstrate freedom from infection in a defined population (country/zone/compartment/herd)
  - Certify freedom from infection or presence of the agent in individual animals or products for trade/movement
  - Eradication of diseases or elimination of infection from defined populations
  - Confirmatory diagnosis of suspect or clinical cases
  - Estimate prevalence of infection or exposure to facilitate risk analysis
  - Determine immune status of individual animals or populations

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Content of the Principles and Methods of Diagnostic Test Validation

2. OIE validation pathway: 4 stages defined

- The OIE has defined the following chronological validation pathway:
- Stage 1: Analytical performance characteristics
- Stage 2: Diagnostic performance of the assay
- Stage 3: Reproducibility
- Stage 4: Programme implementation

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Content of the Principles and Methods of Diagnostic Test Validation

➢ Stage 1: Analytical performance characteristics

- Analytical sensitivity: smallest detectable amount of analyte that can be measured with a defined certainty
- Analytical specificity: Degree to which the assay distinguishes between the target analyte and other components in the sample matrix
- Repeatability: Level of agreement between replicates of a sample both within and between runs of the same test method in a given laboratory

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Content of the Principles and Methods of Diagnostic Test Validation

➢ Stage 1: Possible acceptance of a diagnostic test as validated at this stage

- Provisional recognition:
  Example: Assays developed and used in emergency or outbreak situations. To be assessed: ASe, ASp, repeatability and an estimate for reproducibility
- Adjunct tests or procedures:
  Example: VNT to type an isolated virus or molecular sequencing to confirm a real time PCR result.
  To be assessed: ASe and Asp

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Content of the Principles and Methods of Diagnostic Test Validation

➢ Stage 2: Diagnostic performance of the assay

- Selection of reference animals
- Diagnostic specificity : Proportion of known uninfected reference animals that test negative in the assay
- Diagnostic sensitivity : Proportion of known infected reference animals that test positive in the assay
- Comparison with existing diagnostic test – Final Threshold determination

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Content of the Principles and Methods of Diagnostic Test Validation

- Stage 3: Reproducibility
  - Definition: ability of a test method to provide consistent results when applied to aliquots of the same samples tested at different laboratories
  - Provides additional data for the estimation of the repeatability
  - Provides data on the ruggedness if the test method has been developed as a diagnostic kit.

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Content of the Principles and Methods of Diagnostic Test Validation

- Stage 4: Programme implementation
  - Extensive application of the test method in different laboratories,
  - Interpretation of tests results, and
  - International recognition

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Content of the Principles and Methods of Diagnostic Test Validation

3. Monitoring and maintenance of the validation criteria:

Organisation of regular proficiency testing,
Consideration for other purposes,
Etc.

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OIE Procedure for the validation and certification of diagnostic assays

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Background of the initiative

- Two Consultants Meetings: one in 2002 and a second one in 2003 after the adoption of the Resolution No. XXIX adopted in May 2003
- Resolution No. XXIX, at the 71st General Session of the OIE in May 2003
- The OIE Procedure was launched in May 2005

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Aim and Scope of the Procedure

- Developed to meet the needs of OIE Members, the aim of this procedure is:
  1. to certify a kit as validated fit for purpose.
  2. to produce an OIE register of recognised diagnostic kits (available on the OIE web site).
- All diagnostic tests for diseases, including zoonosis, caused by pathogens present in animals can be validated and certified by the OIE procedure.

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OIE Procedure for validation and certification of diagnostic assays

Briefly 1/2

- Procedure based on the submission of a dossier by a kit manufacturer wishing to have its kit certified by the OIE.
- Fees requested for the initial assessment and then annual fee if kit included in the OIE Register
- Reassessment of the validation data of the kit included in the OIE Register every 5 years
- Dossier, that has to be filled in, downloadable from the OIE website.
- Dossier based on the OIE validation pathway.

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OIE Procedure for validation and certification of diagnostic assays

Briefly 2/2

- Once a dossier has been submitted to the OIE, an administrative revision is carried out to check if the dossier is complete
- Scientific evaluation of the dossier by a group of 2 – 3 independent and internationally recognised experts
- If the kit goes successfully through the procedure, it is proposed by the Biological Standards Commission for inclusion in the Register to the vote of the World Assembly of Delegates
- OIE Register currently comprises 5 diagnostic kits certified (kit for Rabies, BSE/TSE, White Spot Disease, AI)

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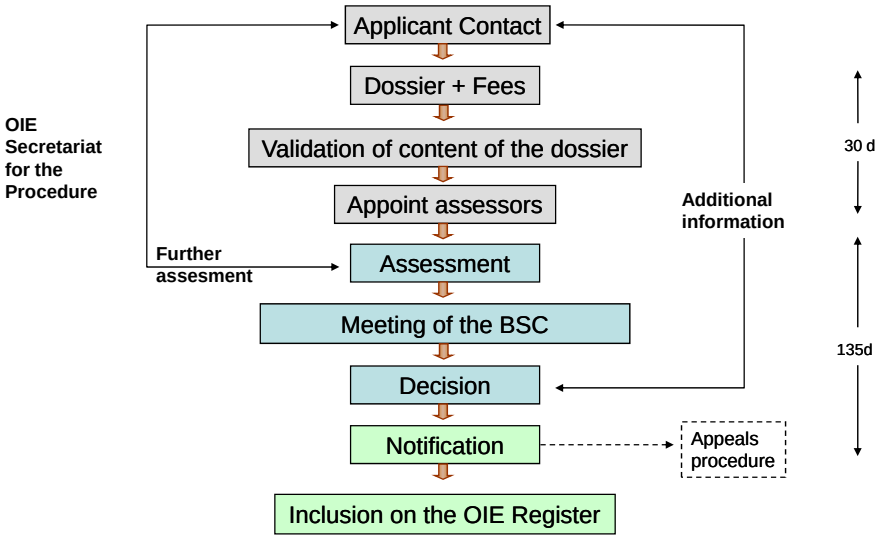
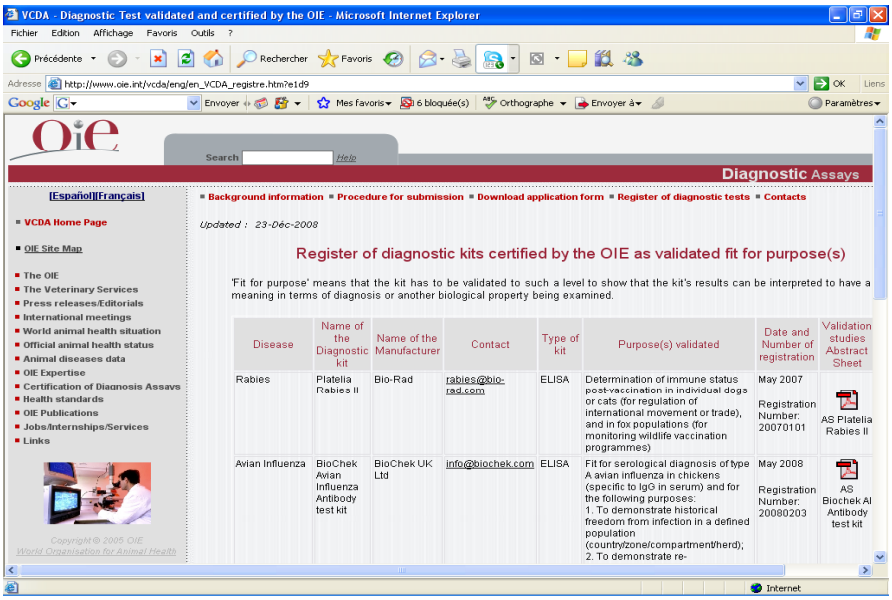
OIE Procedure for validation and certification of diagnostic assays

Outline of all the process



OIE Register available on the OIE Web site



Conclusions

- Framework for a harmonised approach across the world
- Keep on updating the OIE Guidelines and Principles and the Procedure
- Keep on encouraging application of the OIE Standards

Resolution No. XXXII, General Session 2006:

Recognition and implementation of OIE standards for the validation and registration of diagnostic assays by Member Countries

2. Member Countries of the OIE are encouraged to **harmonise their standards for the validation and registration of diagnostic assays with the standards, guidelines and recommendations in the OIE Manual of Diagnostic Tests** and Vaccines for Terrestrial Animals and where such standards are absent or not yet developed, to **apply the standards in the Manual and in the OIE test register for the registration of such products within their countries**.

Thank you for your attention

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