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
OIE Principles and Methods of Diagnostic Test Validation
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)
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.
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.
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
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
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
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
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
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.
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
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.
OIE Procedure for the validation and certification of diagnostic assays
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
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.
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.
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).
OIE Procedure for validation and certification of diagnostic assays

Outline of all the process

1. Applicant Contact
2. Dossier + Fees
3. Validation of content of the dossier
4. Appoint assessors
5. Assessment
6. Meeting of the BSC
7. Decision
8. Notification
9. Inclusion on the OIE Register

Flowchart:
- Applicant Contact → Dossier + Fees → Validation of content of the dossier → Appoint assessors → Assessment → Meeting of the BSC → Decision → Notification → Inclusion on the OIE Register

Timeframes:
- 30 days
- 135 days

OIE Secretariat for the Procedure

Additional information

Appeals procedure
Register of diagnostic kits certified by the OIE as validated fit for purpose(s)

Fit for purpose' means that the kit has to be validated to such a level to show that the kit's results can be interpreted to have a meaning in terms of diagnostic or another biological property being examined.

<table>
<thead>
<tr>
<th>Disease</th>
<th>Name of the Diagnostic kit</th>
<th>Name of the Manufacturer</th>
<th>Contact</th>
<th>Type of kit</th>
<th>Purpose(s) validated</th>
<th>Date and Number of registration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rabies</td>
<td>Platelia Rabies II</td>
<td>Bio-Rad</td>
<td><a href="mailto:rabies@birco-rad.com">rabies@birco-rad.com</a></td>
<td>ELISA</td>
<td>Determination of immune status post-vaccination in individual dogs or cats (for regulation of international movement or trade), and in fox populations (for monitoring wildlife vaccination programmes)</td>
<td>May 2007 Registration Number: 2007/01/01</td>
</tr>
<tr>
<td>Avian Influenza</td>
<td>BioChek Avian Influenza Antibody test kit</td>
<td>BioChek UK Ltd</td>
<td><a href="mailto:info@biocheke.com">info@biocheke.com</a></td>
<td>ELISA</td>
<td>Fit for serological diagnosis of type A avian influenza in chickens (specific to IgG in serum) and for the following purposes: 1. To demonstrate historical freedom from infection in a defined population (country/zone/compartment/herd); 2. To demonstrate re-</td>
<td>May 2008 Registration Number: 20080203</td>
</tr>
</tbody>
</table>

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

Organisation Mondiale
de la Santé Animale

World Organisation
for Animal Health

Organización Mundial
de Sanidad Animal