Vaccine quality assessment support

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The principal aims of the OIE are:

- global animal disease and zoonosis situation,
- disseminate scientific veterinary information,
- international solidarity in the control of animal diseases,
- to improve the legal framework and resources of national Veterinary Services
- within its mandate under the Agreement on Sanitary and Phytosanitary Measures (SPS Agreement) of the World Trade Organization (WTO), to safeguard world trade by publishing health standards for international trade in animals and animal products
OIE Standards and Guidelines
CHAPTER 1.1.5.

PRINCIPLES AND METHODS OF VALIDATION OF DIAGNOSTIC ASSAYS FOR INFECTIOUS DISEASES

INTRODUCTION

Validation is a process that determines the fitness of an assay, which has been properly developed, optimised and standardised, for an intended purpose. All diagnostic assays (laboratory and field assays) should be validated for the species in which they will be used. Validation includes estimates of the analytical and diagnostic performance characteristics of a test. In the context of this chapter, an assay that has completed the first three stages of the validation pathway (see Figure 1 below), including performance characterisation, can be designated as "validated for the original intended purpose(s)." To maintain a validated assay status, however, it is necessary to carefully monitor the assay's performance under conditions of routine use, often by tracking the behaviour of assay controls over time. This ensures that the assay, as originally validated, consistently maintains its performance characteristics. Should it no longer produce results consistent with the original validation data, the assay may be rendered invalid until its intended purpose(s). Thus, a validated assay is continuously assessed to assure it maintains its fitness for purpose through both the assessment of results of the assay controls included with each run and through ongoing assessment during routine use in the targeted population.

Assays applied to individuals or populations have many purposes, such as aiding in: documenting freedom from disease in a country or region, preventing spread of disease through trade, contributing to eradication of an infection from a region or country, confirming diagnosis of clinical cases, estimating infection prevalence to facilitate risk analysis, identifying infected animals toward implementation of control measures, and developing animals for herd, health or immune status post-vaccination. A single assay may be validated for one or more intended purposes by optimising its performance characteristics for each purpose, e.g. setting diagnostic sensitivity (DSs) high, with associated lower diagnostic specificity (DSp) for a screening assay, or conversely, setting DSp high with associated lower DSs for a confirmatory assay.

The ever-changing repertory of new and unique diagnostic reagents and coupled with many novel assay platforms and protocols has precipitated discussions about how to properly validate these assays. It is no longer sufficient to offer simple examples from serological assays, such as the enzyme-linked immunosorbent assay, to guide assay developers in validating the more complex assays, such as nucleic acid detection tests. In order to bring coherence to the validation process for all types of assays, this chapter focuses on the criteria that must be fulfilled during assay development and validation of all assay types. The initiation of assay development as part of the assay validation process may seem counterintuitive, but in reality, these are the required validation criteria (definition of intended purpose), optimisation, and standardisation) that must be assessed in order to achieve a validated assay, comprising steps in the assay development process. Accordingly, the assay development process seamlessly leads into an assay validation pathway, both of which require fulfillment of validation criteria. Further, more detailed guidance is provided in a series of OIE Validation Guidelines that are tailored for several fundamentally different types of assay (e.g., detection of nucleic acids, antibodies, or antigens) and provide more information on specific issues related to the validation of diagnostic assays. For specific information on wildlife

SECTION 3.6.

VALIDATION GUIDELINES

INTRODUCTORY NOTE

The OIE has adopted a formal standard entitled Principles and Methods of Validation of Diagnostic Assays for Infectious Diseases, referred to as the OIE Validation Standard. Its most recent version, adopted in May 2013, may be found on the OIE website as chapter 1.1.5 of the Terrestrial Manual:

http://www.oie.int/fileadmin/Home/eng/health_standards/ahm/GUIDELINE_3.6.1_ANTIBODY_DETECT.pdf

or chapter 1.1.2 of the Aquatic Manual:

http://www.oie.int/fileadmin/Home/eng/health_standards/ahm/current/1.1.2_VALIDATION.pdf

Part 3 of the Terrestrial Manual includes general guidelines for laboratories. These guidelines supplement and give explanatory content in support of the standards included in Parts 1 and 2. The following section of OIE Validation Guidelines is such a supplement, dealing with the use of the OIE Validation Standard and its implementation for specific requirements such as different types of assay (antibody, antigen or nucleic acid detection), and an elaboration of some of the tools used in validation studies (measurement of uncertainty, statistical approaches, reference panels). There is also a guideline addressing some of the particular challenges in validating tests for wildlife species. All of the guidelines have been written by experts in the respective fields, and have been subjected to an extensive process of consultation in arriving at the final tests. These validation guidelines are available on the on-line version of the Manuals and are not included in the printed version.

None of these guidelines should be used in isolation. Each is designed to complement and inform the application of the OIE Validation Standard to specific situations.

Guideline 3.6.1. Development and optimisation of antibody detection assays:

http://www.oie.int/fileadmin/Home/eng/health_standards/ahm/GUIDELINE_3.6.1_ANTIBODY_DETECT.pdf

Guideline 3.6.2. Development and optimisation of antigen detection assays:

http://www.oie.int/fileadmin/Home/eng/health_standards/ahm/GUIDELINE_3.6.2_ANTIGEN_DETECT.pdf

Guideline 3.6.3. Development and optimisation of nucleic acid detection assays:

http://www.oie.int/fileadmin/Home/eng/health_standards/ahm/GUIDELINE_3.6.3_NAD_ASSAYS.pdf

Guideline 3.6.4. Measurement of uncertainty:

http://www.oie.int/fileadmin/Home/eng/health_standards/ahm/GUIDELINE_3.6.4_MEASUREMENT_UNCERT.pdf

Guideline 3.6.5. Statistical approaches to validation:

http://www.oie.int/fileadmin/Home/eng/health_standards/ahm/GUIDELINE_3.6.5_STATISTICAL_VALIDATION.pdf

Guideline 3.6.6. Selection and use of reference samples and panels:

http://www.oie.int/fileadmin/Home/eng/health_standards/ahm/GUIDELINE_3.6.6_REFERENCE_SAMPLES.pdf

Guideline 3.6.7. Principles and methods for the validation of diagnostic tests for infectious diseases applicable to wildlife:

http://www.oie.int/fileadmin/Home/eng/health_standards/ahm/GUIDELINE_3.6.7_WILDLIFE.pdf

OIE Terrestrial Manual 2013

OIE Validation Guidelines 2014
SOP Registration Diagnostic kits

Standard Operating Procedure for OIE
Registration of Diagnostic Kits
Guide and Administrative Forms (2012)

Applicant contact
Application form + fees
Administrative screening of the application form
Evaluation by a panel of experts of the application form
Opinion of the relevant Specialist Commission
Decision of the OIE Director General:
Positive: to the vote of the World Assembly of Delegates
Negative: Appeal Procedure
Vote of the World Assembly of Delegates
Manual of Diagnostic Tests and Vaccines for Terrestrial Animals

- **Part 1** General standards
  - Section 1.1. Introductory chapters
    - Chapter 1.1.6. *Principles of veterinary vaccine production*
    - Chapter 1.1.7. *Tests for sterility and freedom from contamination of biological materials*

- **Part 2** OIE Listed Diseases and Other Diseases of Importance to International Trade

- **Part 3** General guidelines
  - Guideline 3.3. The application of biotechnology to the development of veterinary vaccines
'The Selection Committee for the OIE international call for tender relating to the establishment of a Rabies Vaccine Bank in will convene on Tuesday 29 November 2011 to commence the technical appraisal.'
Request for support to assess the Quality of a Vaccine

OIE Reference Laboratories and Collaborating Centres

Directly: from Veterinary Service of a Member Country
Indirectly: request to DG OIE to propose an expert

in vivo, in vitro, dossier evaluation
Request for support to assess the Quality of a Vaccine

CODA-CERVA - OIE Collaborating Centre

Subject: Analysis of the results obtained from the study of the FMD vaccines in the Laboratory CC in Country XXXX and the National Veterinary Ref Centre (Country YYYY).

1) Documents received

The following documents were received:
- Three reports from the Laboratory XXX dated 01/12/1999, 13/12/1999 and 07/07/2000 describing the virus neutralisation test (VNT) results after vaccination with the FMD vaccines produced in Company AA or Institute BB, in Country ZZZZ;
- One report from the National Veterinary Ref Centre of the Country YYYY describing the ELISA results after vaccination with the FMD vaccine produced in Institute BB, in Country ZZZZ;
- One report from the National Veterinary Ref Centre of the Country YYYY describing the ELISA results after two vaccination experiments using two different batches from the FMD vaccine produced in Company AA, in Country ZZZZ.

2) Analysis of the reports and the results presented

2.1. Serological results after two vaccination experiments using two different batches from the FMD vaccine produced in Company AA, in Country ZZZZ.

There are differences in the results obtained by both laboratories (Laboratory CC in Country XXXX and the National Veterinary Ref Centre, Country YYYY). Two different serological tests (VNT and ELISA) are used by the two reference centres and two out of three FMDV strains used in both tests are different, making the results of both laboratories not simply comparable. According to the VNT, vaccine batch N°K (tested in animals i-j) would give a slightly better protection than vaccine batch N°L (tested in animals v-w) while the ELISA is predicting the opposite (batch N°L better than batch N°K). This difference is difficult to explain apart from the fact that the VNT only detects
Is there a need to steer, harmonise and improve this expert advice process?

- **Guidelines <-> Freedom to Operate**
  - How to reply / operate

- **Forms**
  - Harmonise advice / Indicate minimum information needed and information lacking
    - Vaccine strains <-> field strains (vaccine matching)

- **Responsibilities Expert - OIE / Risks**
  - Related to future use of reports.

- **Disclaimers: standard ?**
Request for support to assess the Quality of a Vaccine

EUROPEAN COMMISSION
HEALTH & CONSUMERS DIRECTORATE-GENERAL
Directorate D — Animal Health and Welfare
D1-Arsenal Health and Standing Committees

Brussels, May 2010

SANCO/7070/2010

EXPERT OPINION ON VACCINE AND/OR DIAGNOSTIC BANKS FOR MAJOR ANIMAL DISEASES

STRATEGIC PLANNING OPTIONS FOR EMERGENCY SITUATIONS OR MAJOR CRISES

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Thank you