The OIE Manual of Diagnostic Tests and Vaccines for Terrestrial & Aquatic Animals

VMP Focal point training

MAPUTO

3 – 5 December 2013

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Scientific and Technical Department
The OIE Specialist Commissions and their mandate

The Terrestrial Manual - overview
  - Diagnostic Tests
  - Vaccines

The Aquatic Manual - overview
  - Diagnostic Tests
  - Vaccines
Terrestrial Animal Health Code – mammals, birds and bees

Aquatic Animal Health Code – fish, molluscs and crustaceans

Manual of Diagnostic Tests and Vaccines for Terrestrial Animals

Manual of Diagnostic Tests for Aquatic Animals

OIE Quality Standard and Guidelines for Veterinary Laboratories: Infectious Diseases
Specialist Commissions

- Terrestrial Animal Health Standards Commission
  "Code Commission"

- Scientific Commission for Animal Diseases
  "Scientific Commission"

- Biological Standards Commission
  "Laboratories Commission"

- Aquatic Animal Health Standards Commission
  "Aquatic Animals Commission"
Biological Standards Commission

"Laboratories Commission“

- Six Members elected by the World Assembly of Delegates for a 3-year term (e.g. 2012)
- Approves OIE Reference Laboratories/OIE Collaborating Centres/Laboratory Twinnings
- Provides scientific advice for Standards related to diagnostics for eventual inclusion in the Terrestrial Code
- Develops and sets International laboratory standards – diagnostics, vaccines, etc. (Terrestrial Manual)
- Promotes the preparation and distribution of reagents
Putting faces to names

http://www.oie.int/en/international-standard-setting/specialists-commissions-groups/laboratories-commission-reports/commission-members-details/
Terrestrial Manual
- Overview
• Describes internationally agreed laboratory standard methods for disease diagnosis, and

• Describes also, when relevant, the requirements for the production and control of vaccines and other biological products

➢ Is the companion volume to the Terrestrial Animal Health Code
• First published in 1989 and since then every 4 years in paper version.
• The last printed version is the 2012, 7th edition
• Available on the OIE website – includes all updated chapters:

    http://www.oie.int/international-standard-setting/terrestrial-manual/access-online/
General Process for developing Chapter for the *Terrestrial Manual*

1. Review by the BSC with the help of the editorial team
2. DELEGATES & Relevant Reference Laboratories and other peer reviewers

Assembly

Adoption of the Chapter

Inclusion on the next edition of the *Manual/OIE website*

Comments

Authors (Experts)

Consultant Editor

Biological Standards Commission (BSC)/ Consultant Editor
Minimum requirements for vaccine production facilities
Quality control of vaccines

Your role in providing expert opinion is crucial!
Divided into different parts:

- **Part 1**: 10 introductory chapters on general issues of interest to veterinary laboratories

- **Part 2**: 113 Chapters on specific diseases (OIE listed diseases and other diseases of public health or trade importance)

- **Part 3**: General Guidelines

- **Part 4**: OIE Reference Experts and disease index
Part 1 – Introductory chapters:

1.1.1. Collection, transmission and storage of diagnostic specimens (13)
1.1.2. Transport of specimen of animal origin (13)
1.1.3. Biosafety and biosecurity in the veterinary diagnostic microbiology laboratory and animal facilities
1.1.4. Quality management in veterinary testing laboratories
1.1.5. Principles and methods of validation of diagnostic assays for infectious diseases (13)
1.1.6. Principles of veterinary vaccine production (including diagnostic biologicals)
Part 1 – Introductory chapters (contd):

1.1.7. Tests for sterility and freedom from contamination of biological materials

1.1.8. *Minimum requirements for vaccine production facilities (under study)*

1.1.9. *Quality control of vaccines (under study)*

1.1.10. International standards for vaccine banks
Structure

Part 2 – 113 Chapters on specific diseases:

OIE listed diseases + other diseases of global importance:

Subdivided by:

- Multiple species (3)
- Apidae (3)
- Aves
- Bovidae (2)
- Equidae (6)
- Leporidae
- Ovidae and Caprinae (2)
- Suidae (1)
- Other Diseases (1)

(x) = updated in 2013
Structure

Part 3 – General Guidelines

4.1 Laboratory methodologies for bacterial antimicrobial susceptibility testing *
4.2 Biotechnology in the diagnosis of infectious diseases *
4.3 The application of biotechnology to the development of veterinary vaccines
4.4 The role of official bodies in the international regulation of veterinary biologicals

* Approved in May 2012
Part 2 – Chapters on specific diseases:

Each disease chapter (except FMD) is developed following this template:

- Summary
- A. Introduction
- B. Diagnostic techniques
- C. Requirements for vaccines and diagnostic biologicals
- References
OIE *Terrestrial Manual* and Diagnostic tests
Relevant parts in the *Terrestrial Manual*:

- Several **introductory chapters** of the *Terrestrial Manual* are relevant for diagnostic tests.

- Considering the importance to validate diagnostic tests, the introductory chapters on the **general principles for the validation of diagnostic assays** (1.1.5) are of special interest.

- In each disease-specific chapter, the **Part B** is on the diagnostic techniques and provides detailed descriptions of the **prescribed** and alternative tests.
Three possible categories of tests described in the part B of the disease-specific chapters:

1. Prescribed tests,
2. Alternative tests, and
3. Other tests
Prescribed tests are required by the *Terrestrial Code* for the testing of animals before they are moved internationally.

Printed in **blue** in the relevant disease-specific chapters.

All the prescribed tests are listed in the table: «*list of tests for international trade* », page XI in each of the two volumes.
Alternative tests are suitable for the diagnosis of disease within a local context, and can also be used in the import/export of animals after bilateral agreement.

The alternative tests are also listed in the table: «list of tests for international trade», page XI in each of the two volumes.
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.
**Table 1. Test methods available for the diagnosis of equine infectious anaemia and their purpose**

<table>
<thead>
<tr>
<th>Method</th>
<th>Population freedom from infection/efficiency of eradication policies</th>
<th>Individual animal freedom from infection</th>
<th>Confirmation of clinical cases</th>
<th>Prevalence of infection – surveillance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agar gel immunodiffusion</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Enzyme-linked immunosorbent assay</td>
<td>++</td>
<td>++</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Immunoblot</td>
<td>–</td>
<td>++</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Polymerase chain reaction</td>
<td>–</td>
<td>++</td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td>Virus isolation/horse inoculation</td>
<td>–</td>
<td>–</td>
<td>+</td>
<td>–</td>
</tr>
</tbody>
</table>

Key: +++ = recommended method; ++ = suitable method; + = may be used in some situations, but cost, reliability, or other factors severely limits its application; – = not appropriate for this purpose.

Although not all of the tests listed as category +++ or ++ have undergone formal standardisation and validation, their routine nature and the fact that they have been used widely without dubious results, makes them acceptable.

Example: Equine Infectious Anaemia
Where the *Terrestrial Code* requires that tests are carried out for international movement, the *Terrestrial Manual* should provide a recommended laboratory method.
OIE Terrestrial Manual and Vaccines
Relevant parts in the *Terrestrial Manual*:

- Several *introductory chapters* of the *Terrestrial Manual* are relevant for the vaccines (production and quality) and more will be developed.

- Chapter 1.1.6, *Principles of Veterinary Vaccine Production* is of special interest.

- In the relevant *disease-specific chapters*, the Part C is on the Requirements for Vaccines and Diagnostic Biologicals – several diseases have just been reviewed, e.g. FMD, Rabies, CSF, RVF
**Background:** A reliable supply of pure, safe, potent and effective vaccines is essential for maintenance of animal health and the successful operation of animal health programmes

**Objective:** to ensure the production and availability of uniform and consistent vaccines of high quality

**Content:** General requirements and procedures
Summary of the content:

- **Nomenclature**: for this chapter, the term “vaccine” includes “all products designed to stimulate active immunisation of animals against disease, without regard to the type of microorganism or microbial toxin from which they may be derived or that they contain”

- **Quality Assurance / Production facilities & the importance of their inspection / Master Seed & Master Cell Stocks / Ingredients / Consistency of Production / Safety & Efficacy Tests / Batch/serial release for Distribution / Labelling / Biotechnology-derived vaccines**
Summary of the content (contd):

Two appendixes:

1. Risk analysis for biologicals for veterinary use (provides only general considerations)

3. Risk analysis for veterinary vaccines:
   Introduction – Principles – Manufacturing practices – Registration in the importing country – Categorisation of veterinary vaccines – Vaccinovigilance – Risk communication
General Template of the Part C which was used until now and is still present in some disease-specific chapters

<table>
<thead>
<tr>
<th>Section</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Seed Management</td>
<td>a) Characteristics of the seed</td>
</tr>
<tr>
<td></td>
<td>b) Method of culture</td>
</tr>
<tr>
<td></td>
<td>c) Validation as a vaccine</td>
</tr>
<tr>
<td>2. Method of Manufacture</td>
<td>a) Identity</td>
</tr>
<tr>
<td></td>
<td>b) Sterility</td>
</tr>
<tr>
<td></td>
<td>c) Safety</td>
</tr>
<tr>
<td>3. In-process control</td>
<td>d) Potency</td>
</tr>
<tr>
<td></td>
<td>e) Duration of protection</td>
</tr>
<tr>
<td>4. Batch control</td>
<td>f) Stability</td>
</tr>
<tr>
<td></td>
<td>g) Preservatives</td>
</tr>
<tr>
<td></td>
<td>h) Precautions</td>
</tr>
<tr>
<td>5. Tests on the final product</td>
<td>a) Safety</td>
</tr>
<tr>
<td></td>
<td>b) Potency</td>
</tr>
</tbody>
</table>
1. Background
   0 Availability, rationale, intended use

2. Outline of production and minimum requirements for vaccines
   a) Characteristics of the seed
      a) Biological criteria
      b) Quality criteria
      c) Validation of the vaccine strain
   b) Method of manufacture
      0 Procedure
      0 Requirements for ingredients
      0 In process controls
      0 Final product batch tests
   c) Requirements for registration
      0 Manufacturing process
      0 Safety requirements
      0 Efficacy requirements
      0 Potency requirements

3. Specific topics (e.g. oral vaccine)
The Aquatic Animal Health Code
Objective: a uniform approach to the diagnosis of aquatic diseases listed in the Aquatic Code

Diagnostic tests are used to comply with standards for international movement / trade of aquatic animals

Manual is produced every 1 - 2 years, updates are on-line

Available in English and Spanish
Unlike terrestrial animals, crustaceans, amphibians, fish and molluscs don’t often show specific clinical disease signs.

Therefore the best suited diagnostic is detection of the pathogen.

The methods are mainly direct, indirect methods, e.g. antibody detection, are generally not accepted.
Molluscs and crustaceans don’t produce antibodies.

General approach: pathogen isolation and identification, or

Antigen detection by immunological or molecular techniques

PCR is recommended for detection and confirmation but not for screening to prove absence of disease.
Divided in two parts:

- **Part 1:** 3 chapters of general interest for veterinary laboratories

- **Part 2:** specific diseases
  - Amphibians: 2 diseases
  - Crustacéans: 10 diseases (3 new in 2012)
  - Fish: 11 diseases (2 new in 2012)
  - Molluscs: 9 diseases (2 new in 2012)
Quality management in veterinary testing laboratories
Principles and methods of validation of diagnostic assays for infectious diseases
Methods for disinfection of aquaculture establishments
The chapters of Part 2 follow this structure:

- Scope
- Disease information
- Sampling
- Diagnostic methods
- Rating of tests against purpose of use
- Tests recommended for the declaration of disease freedom
- Corroborative diagnostic criteria
<table>
<thead>
<tr>
<th>Method</th>
<th>Targeted surveillance</th>
<th>Presumptive diagnosis</th>
<th>Confirmatory diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ova/milt</td>
<td>Fry/fingerlings</td>
<td>Juveniles</td>
</tr>
<tr>
<td>Gross signs</td>
<td>na</td>
<td>d</td>
<td>d</td>
</tr>
<tr>
<td>Histopathology</td>
<td>na</td>
<td>d</td>
<td>d</td>
</tr>
<tr>
<td>Immunoperoxidase stain</td>
<td>na</td>
<td>c</td>
<td>c</td>
</tr>
<tr>
<td>Transmission EM</td>
<td>na</td>
<td>d</td>
<td>d</td>
</tr>
<tr>
<td>Immuno-EM</td>
<td>na</td>
<td>d</td>
<td>d</td>
</tr>
<tr>
<td>Cell culture</td>
<td>na</td>
<td>a</td>
<td>a</td>
</tr>
<tr>
<td>Antigen-capture ELISA</td>
<td>na</td>
<td>a</td>
<td>a</td>
</tr>
<tr>
<td>Antibody-capture ELISA</td>
<td>na</td>
<td>d</td>
<td>d</td>
</tr>
<tr>
<td>PCR-REA</td>
<td>na</td>
<td>d</td>
<td>a</td>
</tr>
<tr>
<td>PCR sequence analysis</td>
<td>na</td>
<td>d</td>
<td>d</td>
</tr>
</tbody>
</table>
Thank you for your attention