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

Regional seminar for OIE National Focal Points for Veterinary Products, Tokyo, Japan, 3 - 5 December 2014

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Outline

• OIEs International Standards
• Procedure for developing new manual chapters
• The Terrestrial Manual - overview
  • Diagnostic Tests
  • Vaccines
• The Aquatic Manual - overview
The OIE Codes and Manuals

- 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
Aquatic Animal Health Standards Commission
“Aquatic Animals Commission”

Compiles information on diseases of fish, molluscs, crustaceans and amphibians and recommends appropriate prevention and control methods for these diseases.


Biological Standards Commission
“Laboratories Commission”

Establishes or approves methods for:
• diagnostic of diseases of mammals, birds and bees
• defining quality criteria of biological products such as vaccines, used for disease control purposes

Oversees production and adoption of the Manual of Diagnostic Tests and Vaccines for Terrestrial Animals.

Advises the Director General in supervising the global network of OIE Reference Laboratories and Collaborating Centres (284 worldwide in 2013).
Process for:

Establishing or updating international standards

FP support

OIE INTERNATIONAL STANDARD

Assembly

Adoption

DELEGATES

Comments

Draft text

Advice of experts or other Specialist Commissions

Review

Specialist Commissions

ISSUE

COMMITTEE, COMMISSIONS, DELEGATES

OIE INTERNATIONAL STANDARD
<table>
<thead>
<tr>
<th>Month</th>
<th>Event Description</th>
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<tbody>
<tr>
<td>May</td>
<td>General Assembly</td>
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<tr>
<td>September</td>
<td>Commission meetings</td>
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<tr>
<td>October</td>
<td>Release of Commission Reports</td>
</tr>
<tr>
<td>October to January</td>
<td>Period for submission of country comments</td>
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<tr>
<td>February</td>
<td>Commission meetings</td>
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<tr>
<td>March</td>
<td>Release of Commission Reports</td>
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<tr>
<td>March to May</td>
<td>Period of preparation for May General Assembly</td>
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**The International Commission**, Made up of the 178 Chief Veterinary Officers of Member Countries, analyse and adopt the international standards, as well as analysing and adopting recognition of countries and zones.

**Code Commissions meet in Paris** The experts of the Specialized Commissions meet to analyze the comments received from the May General Assembly and those received from Member Countries, not yet considered.

**Commission Report is published** The Commission publishes in the website, new proposed Chapters as well as the resulting modifications to the Code, based on country comments.

**Countries examine:** Member Countries examine the Commission Report, discuss them with interested stakeholders and prepare national responses to the Commission. Countries also share their positions, through their Regional Office with other countries in the Region. They send their comments to the OIE headquarters before the end of January.

**Commission meets in Paris** The Code Commission meet in Paris. They analyze Member Country comments received on draft Chapters. They also examine the reports of the various Ad hoc groups of experts and prepare new texts for comment and others for adoption.

**Commission Report is published** The Commission publishes in the website, the proposed texts for adoption in May, based on country comments and expert advise.

**Countries examine Commission report** They discuss the Code report with their stakeholders and prepare their position for the General Assembly. They also share their national positions through their Regional Office with countries of the region.
OIE Terrestrial Manual Overview
Accompanies the *Terrestrial Animal Health Code*

- Describes internationally agreed standard laboratory methods for disease diagnosis
- Describes requirements for the production and control of vaccines and other biological products
- First published in 1989, updated every 4 years, most recent print: 7th edition of 2012
- Freely available in full and up to date online at [http://www.oie.int/en/international-standard-setting/terrestrial-manual/access-online/](http://www.oie.int/en/international-standard-setting/terrestrial-manual/access-online/)
Terrestrial manual - structure

Divided into 4 parts, presented in 2 volumes:

- **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
Volume 1

Introduction (How to use this *Terrestrial Manual*)
List of tests for International trade
Common abbreviations used in this *Terrestrial Manual*
Glossary of terms
Contributors
<table>
<thead>
<tr>
<th>Part 1</th>
<th>General standards</th>
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<tbody>
<tr>
<td>Section 1.1.</td>
<td>Introductory Chapters</td>
</tr>
<tr>
<td>Chapter 1.1.1.</td>
<td>Collection, submission and storage of diagnostic specimens</td>
</tr>
<tr>
<td>Chapter 1.1.2.</td>
<td>Transport of specimens of animal origin</td>
</tr>
<tr>
<td>Chapter 1.1.3.</td>
<td>Biosafety and biosecurity in the veterinary diagnostic microbiology laboratory and animal facilities</td>
</tr>
<tr>
<td>Chapter 1.1.3a.</td>
<td>Standard for managing biorisk in the veterinary laboratory and animal facilities *</td>
</tr>
<tr>
<td>Chapter 1.1.4.</td>
<td>Quality management in veterinary testing laboratories</td>
</tr>
<tr>
<td>Chapter 1.1.5.</td>
<td>Principles and methods of validation of diagnostic assays for infectious diseases</td>
</tr>
<tr>
<td>Chapter 1.1.6.</td>
<td>Principles of veterinary vaccine production (including diagnostic biologicals)</td>
</tr>
<tr>
<td>Chapter 1.1.7.</td>
<td>Tests for sterility and freedom from contamination of biological materials</td>
</tr>
<tr>
<td>Chapter 1.1.8.</td>
<td>Minimum requirements for vaccine production facilities (under study)</td>
</tr>
<tr>
<td>Chapter 1.1.9.</td>
<td>Quality control of vaccines (under study)</td>
</tr>
<tr>
<td>Chapter 1.1.10.</td>
<td>International standards for vaccine banks</td>
</tr>
</tbody>
</table>
Terrestrial Manual – Part 2

- 113 Chapters on specific diseases:
  OIE listed diseases + other diseases of importance to international trade

- Subdivided by:
  - Multiple species (7)
  - Apinae (1)
  - Aves (3)
  - Bovinae (3) (end vol.1)
  - Equidae (1)
  - Leporidae (1)
  - Caprinae (2)
  - Suidae (1)
  - Other Diseases (4)

(x) = updated in 2014
Structure of the guidelines 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
Terrestrial Manual – Part 3

General Guidelines

3.1 Laboratory methodologies for bacterial antimicrobial susceptibility testing
3.2 Biotechnology in the diagnosis of infectious diseases
3.3 The application of biotechnology to the development of veterinary vaccines
3.4 The role of official bodies in the international regulation of veterinary biologicals
3.5 Managing biorisk: examples of aligning risk management strategies with assessed biorisks *
3.6 OIE Validation Guidelines *

* Approved in May 2014
OIE Validation Guidelines

3.6.1 Development and optimisation of antibody detection assays
3.6.2 Development and optimisation of antigen detection assays
3.6.3 Development and optimisation of nucleic acid detection assays
3.6.4 Measurement uncertainty
3.6.5 Statistical approaches to validation
3.6.6 Selection and use of reference samples and panels
3.6.7 Principles and methods for the validation of diagnostic tests for infectious diseases applicable to wildlife

3.6.8 Comparability of assays after minor changes in a validated test method (under study)
Part 4  OIE Reference Experts and Disease Index

List of OIE Reference Laboratories

Alphabetical list of diseases
Terrestrial manual – forthcoming changes

- Minimum requirements for vaccine production facilities (Chapter 1.1.6)
  ⇒ revised draft out for comments until January

- Quality control of vaccines (future chapters 1.1.8 and 1.1.9)
  ⇒ currently with the experts for redrafting

Your role in providing expert opinion is crucial!
Where to find draft chapters

1. International Standard Setting
   - Overview
   - Terrestrial code
   - Terrestrial manual
   - Aquatic code
   - Aquatic manual
   - Specialists commissions & groups
     - Code Commission & Reports
     - Scientific Commission & Expertise
     - Laboratories Commission & Reports
   - Implications of private standards

2. Overview
   - Founded in 1949, the OIE Biological Standards Commission (BSC), composed of six elected members, is concerned with developing internationally agreed standards for laboratory diagnostic tests and vaccines for OIE-listed animal diseases of mammals, birds and bees. To achieve this, its major activities are:

3. Overview
   - To establish or approve methods for diagnosing diseases of mammals, birds and bees and for manufacture and testing of biological products, such as vaccines; and to advise OIE on the appropriate use of diagnostic tests and vaccines;

4. Overview
   - An important element in this is the development and supervision of the OIE Register of Diagnostic Assays;
   - To oversee production of the Manual of Diagnostic Tests and Vaccines for Terrestrial Animals;
   - To select OIE Reference Laboratories for diseases of mammals, birds and bees, and to communicate with these laboratories as a source of specialist expertise;
   - To promote the international standardisation of diagnostic tests, including the preparation and distribution of standard reagents.

Neither the OIE nor the Commission distributes reagents directly, but provides contact points in the
OIE Terrestrial Manual
and
Diagnostic Tests
Diagnostic tests in the *Terrestrial Manual*

Relevant parts in the *Terrestrial Manual*:

- Several introductory chapters of the *Terrestrial Manual* are relevant for diagnostic tests.
- Introductory chapter on general principles for validation of diagnostic assays (1.1.5) of special interest.
- In each disease-specific chapter Part B is on the diagnostic techniques and provides detailed descriptions of relevant tests.
Diagnostic tests in disease specific chapters

Three possible categories of tests are described in Part B of the disease-specific chapters:

1. Prescribed tests,

2. Alternative tests, and

3. Other tests
Prescribed 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 prescribed tests are listed in the table: « list of tests for international trade », page XI in each of the two volumes of the Terrestrial Manual.
Alternative tests / Other tests

• Alternative tests: suitable for diagnosis of disease within a local context; can be used in 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.

• Often other tests are described, which may be of practical value in local situations or which may still be under development.
Test evaluation – fitness for purpose
new approach

Table 1. Test methods available for the diagnosis of equine infectious anaemia and their purpose

<table>
<thead>
<tr>
<th>Method</th>
<th>Purpose</th>
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<tbody>
<tr>
<td></td>
<td>Population freedom from infection/efficiency of eradication policies</td>
</tr>
<tr>
<td>Agar gel immunodiffusion</td>
<td>++</td>
</tr>
<tr>
<td>Enzyme-linked immunosorbent assay</td>
<td>++</td>
</tr>
<tr>
<td>Immunoblot</td>
<td>–</td>
</tr>
<tr>
<td>Polymerase chain reaction</td>
<td>–</td>
</tr>
<tr>
<td>Virus isolation/horse inoculation</td>
<td>–</td>
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</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
Relation between *Manual* and *Code*

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
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.

- Chapters 1.1.6 *Principles of Veterinary Vaccine Production* (under revision) and 1.1.8 Minimum requirements for vaccine production facilities and 1.1.9 Quality Control of Vaccines (*new*) are 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 in 2013
Chapter 1.1.6

Principles of Veterinary Vaccine Production

- **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.
### Disease-specific chapters and vaccines

General Template of the Part C which was used until now and is still present in some disease-specific chapters

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
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</thead>
</table>
| 1. Seed Management | a) Characteristics of the seed  
|   | b) Method of culture  
|   | c) Validation as a vaccine |
| 2. Method of Manufacture | a) Identity  
| 3. In-process control | b) Sterility  
| 4. Batch control | c) Safety  
| 5. Tests on the final product | d) Potency  
|   | e) Duration of protection  
|   | f) Stability  
|   | g) Preservatives  
|   | h) Precautions  
|   | a) Safety  
|   | b) Potency |
New outline of vaccine chapters

1. Background
   • Availability, rationale, intended use

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

3. Specific topics (e.g. oral vaccine)

   Implemented for:
   • FMD
   • Rabies
   • CSF
Manual of diagnostic tests for aquatic animals

- **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 published on-line in real time
- Available in English and Spanish
General considerations

• Amphibians, crustaceans, fish and molluscs often do not show specific clinical disease signs
• Best diagnostic method: detection of the pathogen
• Methods mainly direct; indirect methods, e.g. antibody detection, are generally not accepted
• Molluscs and crustaceans do not produce antibodies
• General approach: Pathogen isolation and identification, or Antigen detection - immunological or molecular techniques
• PCR is recommended for detection and confirmation but not for screening to prove absence of disease
Aquatic Manual - Structure

• **Part 1**: general chapters for veterinary laboratories
  • Quality management in veterinary testing laboratories
  • Principles and methods of validation of diagnostic assays for infectious diseases
  • Methods for disinfection of aquaculture establishments

• **Part 2**: specific disease chapters by
  • Amphibians: 2 diseases
  • Crustaceans: 10 diseases (1 new in 2014)
  • Fish: 12 diseases (4 new in 2014)
  • Molluscs: 9 diseases (1 new in 2014)
Aquatic manual – structure of disease chapters

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 5.1. Methods for targeted surveillance and diagnosis

<table>
<thead>
<tr>
<th>Method</th>
<th>Targeted surveillance</th>
<th>Presumptive diagnosis</th>
<th>Confirmatory diagnosis</th>
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</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>
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<tr>
<td>Antigen-capture ELISA</td>
<td>na</td>
<td>a</td>
<td>a</td>
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<tr>
<td>Antibody-capture ELISA</td>
<td>na</td>
<td>d</td>
<td>d</td>
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<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>
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</tbody>
</table>
Where to find information

International Standard Setting

- Terrestrial code
- Terrestrial manual
- Access online
- Aquatic code
- Aquatic manual
- Specialists commissions & groups
- Implications of private standards

Manual of Diagnostic Tests and Vaccines for Terrestrial Animals

The complete edition in paper format is available in English. The Spanish version is expected to become available in paper and electronic format by 2013.

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Thank you for your attention!