



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

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Outline



- OIEs International Standards
- The OIE Specialist Commissions and relevant mandates
- Procedure for developing new manual chapters
- The Terrestrial Manual - overview
 - Diagnostic Tests
 - Vaccines
- The Aquatic Manual - overview



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OIEs International Standards



OIE is the international standard setting body for animal health and welfare recognised by WTO

OIE set international standards for

- Surveillance, detection, notification and control
- Trade in animals and animal products
- Laboratories, vaccine manufacture, medicines
- Quality and governance of Veterinary Services
- Legislation



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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







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Specialized Commissions



<p>Terrestrial Animal Health Standards Commission "Code Commission"</p> <p>Responsible for updating the <i>Terrestrial Animal Health Code</i> annually; proposes new standards for adoption by the World Assembly of Delegates.</p> <p>Responsible for ensuring that the Code reflects current scientific information.</p> 	<p>Scientific Commission for Animal Diseases "Scientific Commission"</p> <p>Assists in identifying the most appropriate strategies and measures for the following:</p> <ul style="list-style-type: none"> disease surveillance disease prevention and control examining Members' request regarding their official animal health status, for countries that wish to be included on the OIE official list of countries or zones free from certain diseases 	<p>Aquatic Animal Health Standards Commission "Aquatic Animals Commission"</p> <p>Compiles information on diseases of fish, molluscs, crustaceans and amphibians and recommends appropriate prevention and control methods for these diseases.</p> <p>Responsible for updating the <i>Aquatic Animal Health Code</i> and the <i>Manual of Diagnostic Tests for Aquatic Animals</i>; and for proposing new standards for adoption by the World Assembly of Delegates.</p> 	<p>Biological Standards Commission "Laboratories Commission"</p> <p>Establishes or approves methods for:</p> <ul style="list-style-type: none"> diagnostic of diseases of mammals, birds and bees defining quality criteria of biological products such as vaccines, used for disease control purposes <p>Oversees production and adoption of the <i>Manual of Diagnostic Tests and Vaccines for Terrestrial Animals</i>.</p> <p>Advises the Director General in supervising the global network of OIE Reference Laboratories and Collaborating Centres (284 worldwide in 2013).</p> 
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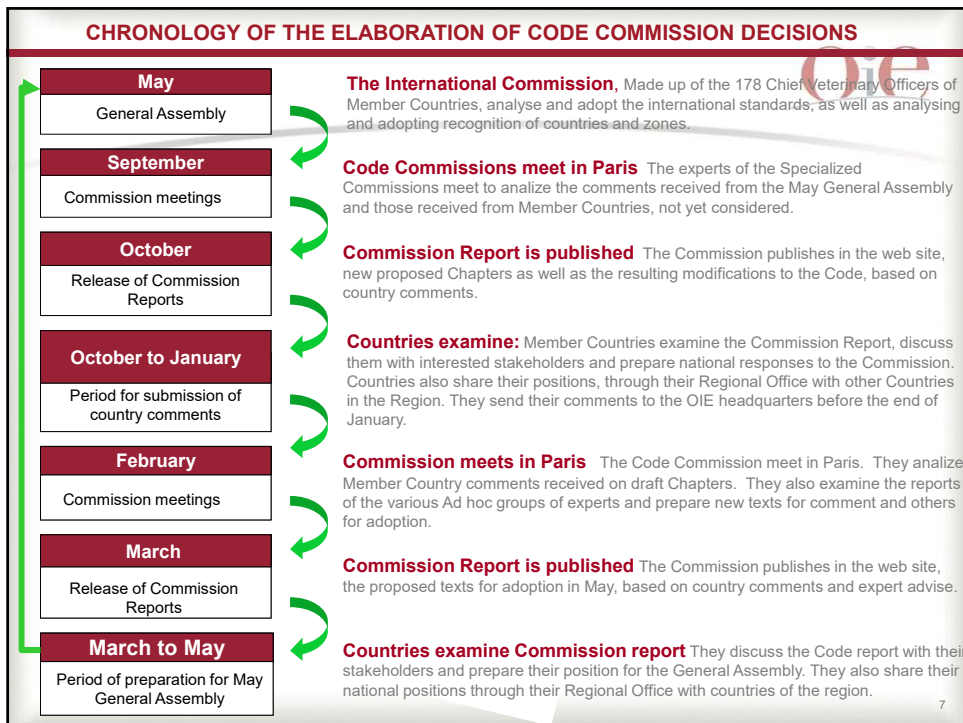
Process for:

Establishing or updating international standards



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Terrestrial manual - Purpose



- 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
- Available in full and up to date on line at <http://www.oie.int/en/international-standard-setting/terrestrial-manual/access-online/>

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Terrestrial manual – forthcoming changes



- Minimum requirements for vaccine production facilities
- Quality control of vaccines

➔ Your role in providing expert opinion is crucial!



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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



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Terrestrial Manual – Part 1



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



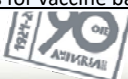
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Terrestrial Manual – Part 1



Part 1	General standards
Section 1.1.	Introductory Chapters
Chapter 1.1.1.	Collection, submission and storage of diagnostic specimens
Chapter 1.1.2.	Transport of specimens of animal origin
Chapter 1.1.3.	Biosafety and biosecurity in the veterinary diagnostic microbiology laboratory and animal facilities
Chapter 1.1.3a.	Standard for managing biorisk in the veterinary laboratory and animal facilities *
Chapter 1.1.4.	Quality management in veterinary testing laboratories
Chapter 1.1.5.	Principles and methods of validation of diagnostic assays for infectious diseases
Chapter 1.1.6.	Principles of veterinary vaccine production (including diagnostic biologicals)
Chapter 1.1.7.	Tests for sterility and freedom from contamination of biological materials
Chapter 1.1.8.	Minimum requirements for vaccine production facilities (under study)
Chapter 1.1.9.	Quality control of vaccines (under study)
Chapter 1.1.10.	International standards for vaccine banks



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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



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Terrestrial Manual – Part 2



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



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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*

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Terrestrial Manual – Part 3



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)*



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Terrestrial Manual – Part 4



Part 4 OIE Reference Experts and Disease Index

List of OIE Reference Laboratories

Alphabetical list of diseases



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OIE *Terrestrial Manual*
and
Diagnostic Tests



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Diagnostic tests in the *Terrestrial Manual*



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 Part B is on the diagnostic techniques and provides detailed descriptions of relevant tests.



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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



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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*.



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Alternative tests / Other tests



- 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.
- Often other tests are described, which may be of practical value in local situations or which may still be under development.



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Test evaluation – fitness for purpose new approach



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

Method	Purpose			
	Population freedom from infection/ efficiency of eradication policies	Individual animal freedom from infection	Confirmation of clinical cases	Prevalence of infection – surveillance
Agar gel immunodiffusion	++	++	++	++
Enzyme-linked immunosorbent assay	++	++	+	+
Immunoblot	-	++	++	-
Polymerase chain reaction	-	+/-	+	-
Virus isolation/horse inoculation	-	-	+	-

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

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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.



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OIE *Terrestrial Manual* and Vaccines



The slide features the OIE logo at the top right. In the center, there is a photograph of laboratory glassware, including three vials with blue caps and a syringe. Below the photograph, the text 'OIE *Terrestrial Manual* and Vaccines' is displayed in a bold, serif font. At the bottom center, there is a small graphic of a '90 OIE ANIMAL' logo.

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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 *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



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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



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Chapter 1.1.6 - Content



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



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Chapter 1.1.6 - Content



Summary of the content (contd):

Two appendixes:

1. Risk analysis for biologicals for veterinary use (provides only general considerations)
2. Risk analysis for veterinary vaccines:
Introduction – Principles – Manufacturing practices – Registration in the importing country – Categorisation of veterinary vaccines – Vaccinovigilance – Risk communication



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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

1. Seed Management	→	a) Characteristics of the seed b) Method of culture c) Validation as a vaccine
2. Method of Manufacture		a) Identity b) Sterility c) Safety d) Potency
3. In-process control		e) Duration of protection f) Stability
4. Batch control	→	g) Preservatives h) Precautions
5. Tests on the final product	↘	a) Safety b) Potency



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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
 - a) Biological criteria
 - b) Quality criteria
 - c) Validation of the vaccine strain
 - b) Method of manufacture
 - Procedure
 - Requirements for ingredients
 - In process controls
 - Final product batch tests
 - c) Requirements for registration
 - Manufacturing process
 - Safety requirements
 - Efficacy requirements
 - Potency requirements
- Implemented for:
- FMD
 - Rabies
 - CSF
3. Specific topics (e.g. oral vaccine)



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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



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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



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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)



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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



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Rating of tests against purpose



Table 5.1. Methods for targeted surveillance and diagnosis

Method	Targeted surveillance				Presumptive diagnosis	Confirmatory diagnosis
	Ova/milt	Fry/fingerlings	Juveniles	Adults		
Gross signs	na	d	d	d	d	d
Histopathology	na	d	d	d	b	d
Immunoperoxidase stain	na	c	c	c	c	c
Transmission EM	na	d	d	d	c	b
Immuno-EM	na	d	d	d	c	b
Cell culture	na	a	a	a	a	b
Antigen-capture ELISA	na	a	a	a	a	a
Antibody-capture ELISA	na	d	d	c	c	d
PCR-REA	na	d	a	d	c	a
PCR sequence analysis	na	d	d	d	c	a



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Where to find information



The screenshot shows the OIE website interface. The main navigation menu includes 'Home', 'About us', 'Our scientific expertise', 'Support to OIE members', 'Animal health in the World', 'International Standard Setting', 'Animal welfare', 'One Health', and 'Publications and documentation'. The 'International Standard Setting' menu is highlighted with a red circle. Below it, the 'Terrestrial manual' section is visible, with 'Terrestrial code' and 'Access online' also circled in red. The main content area features the 'Manual of Diagnostic Tests and Vaccines for Terrestrial Animals' (7th Edition, 2012) with a detailed description and a 'View format' link. The page footer includes 'Contact: scientific Dept@oie.int' and 'Copyright © OIE 2014'.

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Thank you for your attention!



WORLD ORGANISATION FOR ANIMAL HEALTH
Protecting animals, preserving our future

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