Structure of the OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals

Regional Seminar for OIE National Focal Points for Veterinary Laboratories
Jeju, Republic of Korea, 5-7 April 2016

Dr. Peter Daniels
Member, Biological Standards Commission

- Describes internationally agreed laboratory standard methods for disease diagnosis, and
- Describes the requirements for the production/control of vaccines and other biological products.
Where the *Terrestrial Code* requires a test to be carried out for international movement *or other designated purpose*, the *Terrestrial Manual* should provide a recommended laboratory method.

Disease of animals, birds and bees
First published in 1989 and since then every 4 years in printed version.

The most recent version (the Seventh) is the 2012 edition.

Importantly, the Manual is now available on the OIE website - includes all updated chapters:

www.oie.int
For the media

- First Session of the OIE “Improved Animal Welfare Programme”
- OIE launches pilot project to design efficient control methods for Peste des Petits Ruminants, a devastating disease of goats and sheep
- OIE Regional Vaccine Bank for Asia provides 50,000 rabies vaccines to Lao PDR

OIE Videos

View all press releases
Access all media resources

Highlights

Turkish Thrace as FMD free zone

Overview

- Application of compartmentalisation
- Devising import measures

Terrestrial code

- Access online
- Access manual

Aquatic code

- Access online
- Access manual

Scientific and Technical Review

Most recent issues:
- Antimicrobial resistance in animal and public health, April 2012
- Plurithematic issue, Vol. 30 (3), December 2011
- Models in the management of animal diseases, Vol. 30 (2), August 2011

Bulletin online (OIE Magazine): Latest issue
OIE TERRESTRIAL MANUAL

STRUCTURE

DIVIDED INTO 4 PARTS, PRESENTED IN 2 VOLUMES:

Volume I

Part 1
- 11 introductory chapters

Part 2
- 113 Chapters on specific diseases

Part 3
- General Guidelines

Part 4
- OIE Reference Experts and disease index

Volume II
Content, Part 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
Content, Part 1
General standards

Horizontal chapters on
> Management of veterinary laboratories
> Collection, submission and storage of diagnostic specimens
> Transport of specimens of animal origin
> Biosafety and biosecurity: Standard for managing biological risks in the veterinary diagnostic laboratory and animal facilities
> Quality management in veterinary testing laboratories
> Principles and methods of validation of diagnostic assays for infectious diseases
> Principles of veterinary vaccine production (include. diag. biologicals)
> Tests for sterility and freedom from contamination of biological materials
> Minimum requirements for vaccine production facilities
> Quality control of vaccines
> International standards for vaccine banks
Any chapters adopted between printed editions are added to the web version, thus the on-line English version is always the most recent

Manual of Diagnostic Tests and Vaccines for Terrestrial Animals 2015

Summary

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

Part 1

Section 1.1. General standards

Chapter 1.1.0 Management of veterinary laboratories (NB: Version adopted in May 2015)
Chapter 1.1.1 Collection, submission and storage of diagnostic specimens (NB: Version adopted in May 2013)
Chapter 1.1.2 Transport of specimens of animal origin (NB: Version adopted in May 2013)
Chapter 1.1.3 Biosafety and biosecurity: standard for managing biological risk in the veterinary diagnostic laboratory and animal facilities (NB: Version adopted in May 2015)
Chapter 1.1.4 Quality management in veterinary testing laboratories (NB: Version adopted in May 2012)
Chapter 1.1.5 Principles and methods of validation of diagnostic assays for infectious diseases (NB: Version adopted in May, 2013)
Chapter 1.1.6 Principles of veterinary vaccine production (NB: Version adopted in May 2015)
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)
Content, Part 2
OIE Listed Diseases and Other Diseases of Importance

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

Subdivided by:
- Multiple species
- Apinae
- Aves
- Bovinae
- Equidae
- Leporidae
- Caprinae
- Suidae
- Other Diseases
Chapter 1.1.4. Quality management in veterinary testing laboratories (NB: Version adopted in May 2012)
Chapter 1.1.5. Principles and methods of validation of diagnostic assays for infectious diseases (NB: Version adopted in May 2013)
Chapter 1.1.6. Principles of veterinary vaccine production (NB: Version adopted in May 2015)
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

Part 2

Section 2.1. OIE Listed Diseases and Other Diseases of Importance to International Trade

Multiple Species

Chapter 2.1.1. Anthrax (NB: Version adopted in May 2012)
Chapter 2.1.2. Aujeszky’s disease (NB: Version adopted in May 2012)
Chapter 2.1.3. Bluetongue (NB: Version adopted in May 2014)
Chapter 2.1.3b. Crimean-Congo haemorrhagic fever (NB: Version adopted in May 2014)
Chapter 2.1.4. Echinococcosis/hyalidrosis
Chapter 2.1.4b. Epizootic haemorrhagic disease (NB: Version adopted in May 2014)
Chapter 2.1.5. Foot and mouth disease (NB: Version adopted in May 2012)
Chapter 2.1.6. Heartwater
Chapter 2.1.8. Leishmaniosis (NB: Version adopted in May 2014)
Chapter 2.1.9. Leptospirosis (NB: Version adopted in May 2014)
Chapter 2.1.10. New World screwworm (Cochliomyia hominivorax) and Old World screwworm (Chrysomya bezziana) (NB: Version adopted in May 2013)
Chapter 2.1.11. Paratuberculosis (Johne’s disease) (NB: Version adopted in May 2014)
Chapter 2.1.13. Rabies (NB: Version adopted in May 2013)
Chapter 2.1.15. Rinderpest (NB: Version adopted in May 2015)
Chapter 2.1.16. Trichinellosis (NB: Version adopted in May 2012)
Chapter 2.1.17. Trypanosoma evansi infections (including surra) (NB: Version adopted in May 2012)
Chapter 2.1.18. Tularemia
Chapter 2.1.20. West Nile fever (NB: Version adopted in May 2013)

Section 2.2. Apinae

Chapter 2.2.1. Introductory note on bee diseases (NB: Version adopted in May 2013)
Chapter 2.2.2. Acarapisos of honey bees
Chapter 2.2.3. American foulbrood of honey bees (NB: Version adopted in May 2014)
Chapter 2.2.4. Nosemosis of honey bees (NB: Version adopted in May 2013)
Historically three categories of tests have been described in the disease-specific chapters:

1. Prescribed tests,
2. Alternative tests, and
3. Other tests

- Good for international movement
- Good for local/bilateral context
- Other diagnostic purposes
Prescribed tests were those 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.
<table>
<thead>
<tr>
<th>Method</th>
<th>Purpose</th>
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<tbody>
<tr>
<td>Population freedom from infection</td>
<td>Individual animal freedom from infection prior to movement</td>
</tr>
<tr>
<td>Agent identification</td>
<td></td>
</tr>
<tr>
<td>Culture</td>
<td>-</td>
</tr>
<tr>
<td>Detection of immune response</td>
<td></td>
</tr>
<tr>
<td>Serological ELISA</td>
<td>-</td>
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</tbody>
</table>
Purpose of the test(s) - 6 columns
- Population freedom from infection
- Individual animal freedom from infection prior to movement
- Contribute to eradication policies
- Confirmation of clinical cases
- Prevalence of infection - surveillance
- Immune status in individual animals or populations post-vaccination
Chapters on specific diseases - Each disease chapter is developed following this template:

- Summary
- A. Introduction
- B. Diagnostic techniques
  - Identification of the Agent
  - Serological Tests
- C. Requirements for vaccines
- References
(Section B, Diagnostic Techniques) ... should require the inclusion ... of current molecular tests such as PCR-based approaches (including real-time PCR), specifying primer sequences and reaction conditions.

The text should state the stage of validation of the assay as defined in Chapter 1.1.5 Principles and methods of validation of diagnostic assays for infectious diseases.

Where relevant to the purpose of the tests ..., partial or whole genome sequencing should be included with a description of the appropriate methodology.
General Template of **Part C** has been used 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
   - e) Duration of protection
   - f) Stability
   - g) Preservatives
   - h) Precautions
3. In-process control
4. Batch control
5. Tests on the final product
   - a) Safety
   - b) Potency
Content, Part 3
General Guidelines (Recommendations)

General Guidelines (Recommendations)

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
3.6 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
Chapter 2.9.1. Bunyavirus diseases of animals (excluding Rift Valley fever and Crimean-Congo haemorrhagic fever) (NB: Version adopted in May 2014)
Chapter 2.9.2. Camelpox (NB: Version adopted in May 2014)
Chapter 2.9.3. Campylobacter jejuni and Campylobacter coli
Chapter 2.9.4. Cryptosporidiosis
Chapter 2.9.5. Cysticercosis (NB: Version adopted in May 2014)
Chapter 2.9.7. Listeria monocytogenes (NB: Version adopted in May 2014)
Chapter 2.9.8. Mange (NB: Version adopted in May 2013)
Chapter 2.9.9. Salmonellosis (NB: Version adopted in May 2010)
Chapter 2.9.10. Toxoplasmosis
Chapter 2.9.11. Verocytotoxigenic Escherichia coli

Part 3
General Guidelines
Guideline 3.1. Laboratory methodologies for bacterial antimicrobial susceptibility testing (NB: Version adopted in May 2012)
Guideline 3.3. The application of biotechnology to the development of veterinary vaccines (NB: Version adopted in May 2010)
Guideline 3.4. The role of official bodies in the international regulation of veterinary biologicals (NB: Version adopted in May 2008)
Guideline 3.5. Managing biorisk: examples of aligning risk management strategies with assessed biorisks (NB: Version adopted in May 2014)
Guideline 3.6. OIE Validation Guidelines
Guideline 3.6.2. Development and optimisation of antigen detection assays (NB: Version adopted in May 2014)
Guideline 3.6.3. Development and optimisation of nucleic acid detection assays (NB: Version adopted in May 2014)
Guideline 3.6.5. Statistical approaches to validation (NB: Version adopted in May 2014)
Guideline 3.6.6. Selection and use of reference samples and panels (NB: Version adopted in May 2014)
Guideline 3.6.7. Principles and methods for the validation of diagnostic tests for infectious diseases applicable to wildlife (NB: Version adopted in May 2014)
Guideline 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
Content, Part 4

OIE Reference Experts and Disease Index
- List of OIE Reference Laboratories
- Alphabetical list of diseases
Mechanisms for Standard Setting
World Assembly of Delegates

Forms

Permanent Working Groups

Regularly updates progress made in the field of expertise:

1. Animal welfare
2. Food safety
3. Wildlife

Ad Hoc Groups

As needed

Director General

Forms

Recommendations

Prepare recommendations on specific topics:

Examples:

- Tuberculin
- Whole genome sequencing
- Biobank

Advise on current issues

Provide recommendations

Specialist Commissions
DEVELOPING AND UPDATING OF INTERNATIONAL STANDARDS

- **Issue / problem identified** by Delegates, OIE Commission, other international/regional organisations
  - New scientific information, e.g. from research or disease outbreak
  - New diseases – emerging diseases
  - New approach to control, e.g. vaccination
- **Addressed by appropriate Commission** as a new or revised standard
  - Using **Working Groups** and **Ad hoc** Groups, if needed, for specialist tasks, e.g. rabies, BSE, new diagnostic technologies, tuberculosis...
OIE STANDARD SETTING PROCESS

1. Commissions, Delegates

ISSUE / PROBLEM

Specialist Commissions

Review

Advice of experts or other Specialist Commissions

Draft text

1. Delegates

2. World Assembly

Adoption

Once adopted, OIE standards are applicable in all OIE Member Countries

Focal Points please help the Delegate comment!!

OIE Delegate and National Focal Points

OIE INTERNATIONAL STANDARD
The Biological Standards Commission relies heavily on external expertise:

- OIE Reference Labs and Collaborating Centers
- Subject matter experts

Ad hoc Groups

Country comments

**Focal points please help!**
The World Assembly of Delegates, Made up of the 180 Chief Veterinary Officers of OIE Members, analyse and adopt the international standards, as well as analyse and adopt recognition of countries and zones.

Specialised Commissions (Terrestrial and Aquatic Codes) meet in Paris The experts of the Specialised Commissions meet to analyse the comments received from the May General Session and those received from Members, not yet considered.

Commission Report is published The Commission publishes on the web site, new proposed Chapters as well as the resulting modifications to the Code and Manual, based on country comments.

Countries examine Commission report Members examine the Commission Report, discuss it with interested stakeholders and prepare national responses to the Commission. Countries also share their positions, if needed, through the Regional Bureau of the respective Regional Commission (with other countries in the Region). They send their comments to the OIE Headquarters before the end of December.

Commission meets in Paris The Code Commission meet in Paris. They analyse 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 on the web site, the proposed texts for adoption in May, based on country comments and expert advise.

Countries examine Commission report They discuss the Commission report with their stakeholders and prepare their position for the General Session. They also share their national positions through the Regional Bureau of the respective Regional Commission with countries of the region.
SUMMARY OF CRITICALLY IMPORTANT POINTS:-

○ OIE Delegates should realise and accept their responsibility to participate actively in the debate and setting of international standards because..........

○ Once a standard is adopted the Delegate is obligated to support the adopted standard

○ Focal points have an important role in the standard setting procedure, through the preparation of comments for the Delegate for new or revised OIE standards
<table>
<thead>
<tr>
<th>Commission</th>
<th>Responsibilities</th>
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<tbody>
<tr>
<td>Scientific Commission for Animal Diseases</td>
<td>Assists in identifying the most appropriate strategies and measures for disease surveill., prevention, control.</td>
</tr>
<tr>
<td>Aquatic Animal Health Standards Commission</td>
<td>Compiles information on aquatic diseases and recommends appropriate prevention and control methods for these diseases.</td>
</tr>
</tbody>
</table>
| Biological Standards Commission                | Establishes/approves methods for:  
  - diagnostic of terrestrial animals diseases  
  - defining quality criteria of biological products (vaccines)  
  Oversees production and adoption of the *Terrestrial Manual*.  
  Advises the Director General in supervising the global network of OIE Reference Centers. |

Examines Members’ request regarding their official animal health status, for MCs that wish to be included on the OIE official list of countries or zones free from certain diseases.
CURRENT MEMBERS OF THE BSC

Dr Beverly Schmitt
(President)
UNITED STATES OF AMERICA

Dr Franck Berthe
(1st Vice-President)
ITALY

Dr Hualan Chen
(2nd Vice-President)
CHINA (PEOPLE’S REP. OF)

Dr Mehdi El Harrak
(Member)
MOROCCO

Dr Anthony Fooks
(Member)
UNITED KINGDOM

Dr Peter Daniels
(Member)
AUSTRALIA
Routine Work of the BSC

(See Reports of Meetings)

- **Manual of Diagnostic Tests and Vaccines for Terrestrial Animals**: Overall structure and review process for the Terrestrial Manual
- **Oversight of OIE Reference Centres**
  - Applications for the status of OIE Reference Centre
  - Changes of experts at OIE Reference Centres
- **Ad hoc Groups - Proposed future ad hoc Groups**
  - Ad hoc Group on High Throughput Sequencing and Bioinformatics and Computational Genomics (HTS-BCG): implementation of the work plan
- **Ad hoc Group on a Replacement International Standard for bovine tuberculin**
- **International Standardisation/Harmonisation: Diagnostic tests**: OIE Register of diagnostic kits
- **Harmonization with other Commissions**
- **Liaison with/awareness of other international developments**
NEW PROJECT: OIE GENOMIC SEQUENCE PLATFORM (1)

Background

- Growing reliance on generating and using sequence information
- Concurrent ever-increasing trend toward global open information systems
- Crucial and far-reaching implications for veterinary laboratories and the traditional notification and management of infectious diseases and food-borne infections
- The OIE considers that sequence and sequence analysis data should be an integral and necessary part of the analysis and the reporting of diagnostics at the international level.
NEW PROJECT: OIE GENOMIC SEQUENCE PLATFORM (2)

Creation of an OIE platform for the collection and management of genomic sequences in animal health (reports)

- The OIE intends to make full use of the unique worldwide Reference Centre network’s competence and expertise as the key to developing policies and practices for the management and use of sequence information in the framework of WAHIS with direct access for Reference Centres
NEW PROJECT: CREATION OF A BIOBANK

- The OIE aims to create a veterinary biobank network to optimise the occasions for cooperation in sharing biological resources, including reference reagents, within the OIE Reference Centre network.

- This network will be fully connected and open to other biobanks when relevant.
Thank you for your attention

Organisation mondiale de la santé animale

World Organisation for Animal Health

Organización Mundial de Sanidad Animal
NEW ACTIVITIES

- Reference Centres commitment to disseminate quickly new relevant scientific information to the OIE, and support OIE publications through contributions or peer reviews to ensure the scientific accuracy and robustness of its information
- PVS Pathway Laboratory Mission
- National Focal Points for Veterinary Laboratories
FUTURE PLANS OF THE BSC

2016 - 2020

- Manual of Diagnostic Tests and Vaccines for Terrestrial Animals

  Web edition of the Terrestrial Manual is the most up-to-date version
  What is the necessity of continuing to publish a printed edition?

- Harmonising the chapter titles in the Terrestrial Manual and the Terrestrial Code revisited
  Limiting the discrepancy in naming chapters between the Terrestrial Animal Health Code (Terrestrial Code) and the Terrestrial Manual

- Submission of new test methods and validation data
  Form in in preparation and will be used when submitting a new test method for consideration for inclusion in the Terrestrial Manual (based on Chapter 1.1.5 Principles and methods of validation of diagnostic assays for infectious diseases)

- Review of new and pending applications for laboratory twinning projects
  As of August 2015, 26 projects have been completed
  34 are underway (10 new projects are approved and due to start based on fund availability)

- Project to establish a virtual OIE Biobank
  Further develop the concept of establishing a virtual OIE biobank
  Need to harmonise the system with other existing initiatives

- Biosafety/Biosecurity
  Preparing guidelines based on Agreement 15793 (CWA 15793) on Laboratory Biorisk Management to an ISO deliverable (ISO 35001 document)
  For all laboratories and related facilities that handle, store, transport, or dispose of biological agents or toxins, including veterinary laboratories
Member Countries approved the undertaking of periodic evaluations of OIE Reference Centres to ensure their on-going compliance with expected quality management systems, standards and ToRs.

Biological Standards Commission has developed a structured approach to monitoring Reference Centres through the annual reports; visits to laboratories will be proposed.