



The OIE Relevant Standards and Guidelines for Veterinary Medicinal Products

REGIONAL SEMINAR OIE NATIONAL FOCAL POINTS FOR VETERINARY PRODUCTS

BEIRUT, LEBANON 7- 9 NOVEMBER 2017

Dr Mária Szabó

OIE Science and New Technologies Department, Paris, France

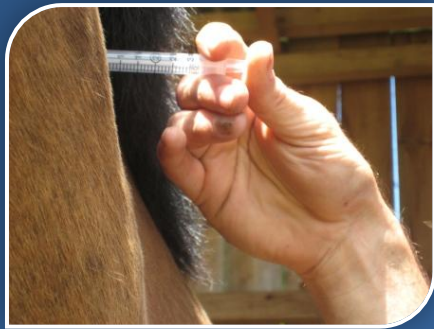


WORLD ORGANISATION FOR ANIMAL HEALTH

Protecting animals, preserving our future

Outline

- ➔ **Veterinary legislation** Chapter 3.4 The role of Official Bodies in the International Regulation of Veterinary biologicals (Terrestrial Animal Health Manual)
- ➔ **Standards and guidelines** related vaccines and recent updates
- ➔ **Standards and guidelines** related to antimicrobial resistance (AMR)
- ➔ **Currently no OIE standards or guidelines** related to antiparasitic products



Standards and Guidelines Related to Vaccines

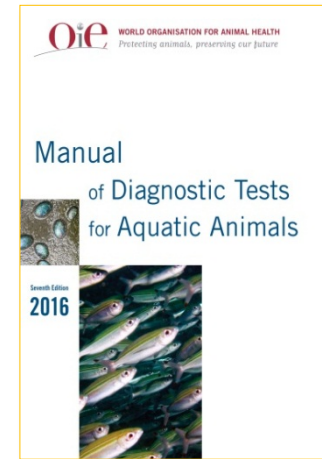
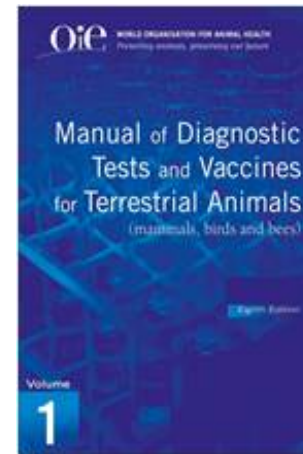
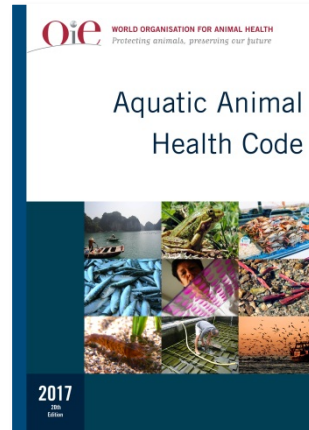
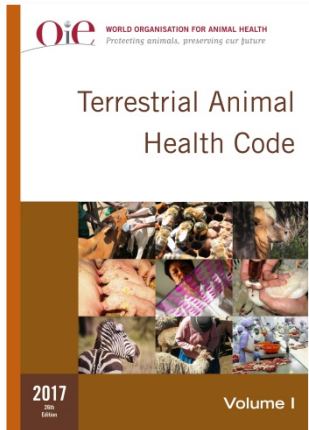
The OIE Standards

CODES

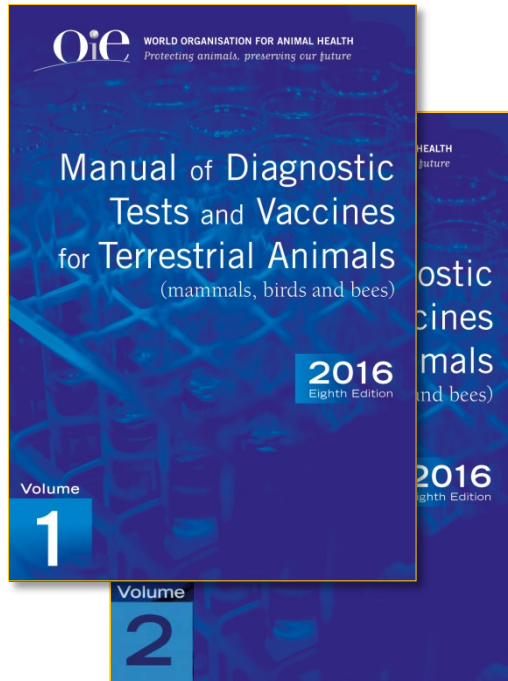
- Terrestrial
- Aquatic

MANUALS

- Terrestrial
- Aquatic



Terrestrial Manual – present



3.7 Recommendations for the Manufacture of Vaccines (new)

Now available online, and the printed version is scheduled for release late 2018

can be purchased directly at pub.sales@oie.int,

<http://www.oie.int/en/international-standard-setting/terrestrial-manual/access-online/>

84th General Session in May 2016

- **Resolution No. 13** Amendments to the *Manual of Diagnostic Test and Vaccines for Terrestrial Animals (Terrestrial Manual)*:

3.7.Recommendations for the **manufacture of vaccines**

- 3.7.1. Minimum requirements for the organisation and management of a vaccine manufacturing facility (**new**)
- 3.7.2. Minimum requirements for the production and quality control of vaccines (**new**)
- 3.7.3. Minimum requirements for aseptic production in vaccine manufacture (**new**)

Terrestrial Manual - Relevant standards

Provides generic and specific guidance on vaccine production and testing:

- **Chapter 1.1.8** Principles of veterinary vaccine production (including diagnostic biologicals) (New version adopted in 2015)
- **Chapter 1.1.9** Tests of biological materials for sterility and freedom from contamination. Developed in consultation with VICH counterparts. The revised chapter incorporating Member Countries' comments ADOPTED in 2017)

Terrestrial Manual: Chapter 1.1.8 (1)

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 and assured quality
- **Contents:** General requirements and procedures
- **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”*

Terrestrial Manual: Chapter 1.1.8 (2)

Summary of the contents:

VACCINE PRODUCTION :

1. Quality Assurance
2. Production facilities
3. Documentation of manufacturing process and record keeping
4. Production
5. Process validation
6. Stability tests
7. Test to demonstrate safety and efficacy of a vaccine

http://www.oie.int/fileadmin/Home/eng/Health_standards/tahm/1.01.08_VACCINE_PRODUCTION.pdf

Terrestrial Manual: Chapter 1.1.8 (3)

Summary of the contents (cont'd)

7.1. SAFETY TEST

- 7.1.1. Target animal safety tests
- 7.1.2. Increase in virulence tests
- 7.1.3. Assessing risk to the environment

7.2. EFFICACY TEST

- 7.2.1. Laboratory efficacy
- 7.2.2. Interference test
- 7.2.3. Field (safety and efficacy)
 - 7.2.3.2. Additional requirement for live rDNA products

8. Updating the Production Outline (materials and methods)

http://www.oie.int/fileadmin/Home/eng/Health_standards/tahm/1.01.08_VACCINE_PRODUCTION.pdf

Terrestrial Manual: Chapter 1.1.8 (4)

Summary of the contents (cont'd)

Quality Controls (QC) in vaccine production :

- **Principle** (The independence of quality control from production is considered fundamental to the satisfactory operation)
- **Batch/serial release for distribution**
 - Batch/serial purity test
 - Batch/Serial safety test
 - Batch/Serial potency test
- **Other certification and tests**
 - Tests or certification on starting materials or finished products
 - Purity
 - Freedom from extraneous agents
 - TSE certification for material of animal origin

Terrestrial Manual: Chapter 1.1.8 (4)

Summary of the contents (continued)

Quality Controls (QC) in vaccine production :

- **Inspection** of Production Facilities: The onsite inspections should be carried out on a regular basis.
- Monitor the manufacturing and quality control procedures.
- Assess conformance to current good manufacturing practices standards (e.g., EU GMP, United States Code of Federal Regulations, PIC/S)
- PIC/S :The Pharmaceutical Inspection Cooperation Scheme

Terrestrial Manual: Chapter 1.1.8 (5)

Summary of the contents (cont'd)

Two Appendices:

- 1. Risk analysis for biologicals for veterinary use** (provides general considerations)
- 2. Risk analysis for veterinary vaccines:**

Introduction – Principles – Manufacturing practices – Information to be submitted when applying for Marketing Authorisation (MA) in the importing country – Categorisation of veterinary vaccines – Vaccinovigilance – Risk communication

http://www.oie.int/fileadmin/Home/eng/Health_standards/tahm/1.01.08_VACCINE_PRODUCTION.pdf

85th General Session in May 2017

Terrestrial Manual: Chapter 1.1.9

Tests for sterility and freedom from contamination of biological materials intended for veterinary use

Approved by the **Biological Standards Commission** sent to Member Countries for second-round comment and proposal for adoption in May 2017. **Adopted during the 85th General Assembly.**

Successful implementation of this Standard will be dependent on different stakeholders, such as National Focal Points for Veterinary Products for OIE Delegates contributed to the development of this Standard and how manufacturers put into practice.

VICH Biologicals Quality Monitoring Expert Working Group (BQM-EWG) provided inputs-to be harmonized as much as possible in the future with VICH extraneous agents guidelines.

Outline of vaccine section of the disease chapters(1)

1. Background

2. Outline of production and minimum requirements for vaccines

2.1. Characteristics of the seed

1. Biological characteristics
2. Quality criteria (*sterility, purity, freedom from extraneous agent*)
3. Validation of the vaccine strain
4. Emergency procedure for provisional acceptance of new master seed virus

2.2. Method of manufacture

- Procedure
- Requirements for ingredients
- In process controls
- Final product batch tests (*sterility, identity, safety, batch potency*)

2.3. Requirements for authorisation/registration/licencing

3. *Specific topics (the e.g. oral vaccine, toxoid, specific requirements for biotechnology based vaccines)*

Outline of vaccine section of the disease chapters (2)

Production and minimum requirements for vaccines

2.3. Requirements for authorisation/registration/licencing

- 2.3.1. Manufacturing process
- 2.3.2. *Safety requirements*
- 2.3.3. Efficacy requirements
- 2.3.4. Vaccines permitting DIVA strategy (DIVA vaccines permit differentiation of infected versus vaccinated animals)
- 2.3.5. Duration of immunity
- 2.3.6. Stability

Terrestrial Manual – Part 3 related to veterinary medicinal products

Specific 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

<http://www.oie.int/international-standard-setting/terrestrial-manual/access-online>

Recent Updates (1)

Waiving or not waiving Target Animal Batch Safety Tests (TABST)?

- The OIE Biological Standard Commission, concluded that, rather than completely eliminating all references to the TABST, references to the TABST in the *Terrestrial Manual* should be revised to include a note that the prescribed TABST **could be eliminated** in situations **where other quality control measures are in place**.
- BSC implemented its decision regarding TABST by modifying chapters 1.1.8 and 2.7.2 and would add two sentences to all relevant disease chapters when they are updated.

“Safety tests in target animals are not required by many regulatory authorities for the release of each batch or serial. Where required, standard procedures are generally conducted using fewer animals than are used in the safety tests required for licensing.”

Recent Updates (2)

Reasons

- Potential variability of quality assurance systems employed by manufacturers in OIE Member Countries
- Potential for residual toxicity of some vaccines

It would be **inappropriate to completely eliminate all references to the TABST** in OIE guidelines such as the *Terrestrial Manual*

Recent Updates (3)

Request for an refined OIE definition of **thermostable** or **thermoresistant** vaccines

- Benefit of access to: science–based, pragmatic standards to objectively characterise the thermotolerant properties of vaccines
- There is much interest in characterising the thermotolerant properties of existing vaccines and **developing new formulations**
- **Need** revised pertinent definition(s) for thermotolerant vaccines to revise or expand the *OIE Manual's* definition on thermotolerance
- **Need to** define relevant parameters of thermotolerance for label claims for various types of veterinary vaccines (e.g conventional live or killed vaccine or a **new generation thermotolerant vaccine**)

Recent Updates (3)

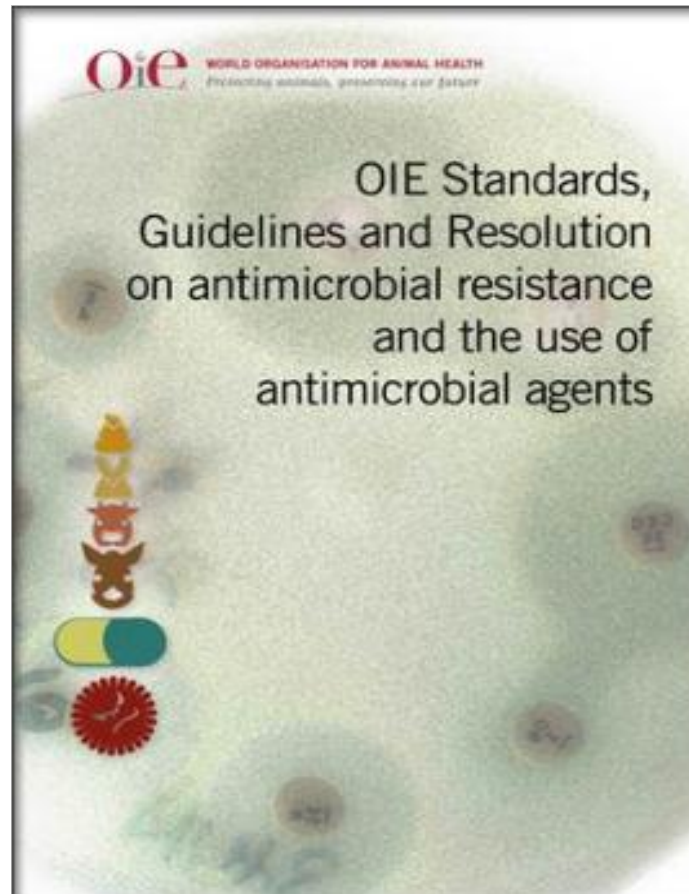
Biological Standards Commission :

Developed a draft glossary definition on thermotolerant vaccine in the Terrestrial Manual : the revised glossary would be circulated with the draft chapters for first-round comment to Member Countries



Standards and guidelines related to antimicrobial resistance (AMR)

Standards and guideline related to antimicrobial resistance



http://www.oie.int/fileadmin/home/eng/Media_Center/docs/pdf/PortailAMR/EN-book-AMR.PDF

Standards and guideline related to antimicrobial resistance

OIE Terrestrial Animal Health Code

Antimicrobial use in terrestrial animals

- **Chapter 6.6.**
Introduction to the **recommendations** for controlling antimicrobial resistance
- **Chapter 6.7.**
Harmonisation of national antimicrobial resistance **surveillance and monitoring** programmes
- **Chapter 6.8.**
Monitoring of the quantities and usage patterns of antimicrobials agents used in food producing animals
- **Chapter 6.9.**
Responsible and prudent use of antimicrobial agents in veterinary medicines
- **Chapter 6.10.**
Risk analysis for antimicrobial resistance arising from the use of antimicrobial agents in animals

<http://www.oie.int/international-standard-setting/terrestrial-code/access-online>

Standards and guideline related to antimicrobial resistance

OIE Standards - Aquatic Animal Health Code

Antimicrobial use in aquatic animals

- **Chapter 6.1.**
Introduction to the **recommendation** for controlling antimicrobial resistance
- **Chapter 6.2.**
Principles for **responsible and prudent use** of antimicrobial agents in aquatic animals
- **Chapter 6.3.**
Monitoring of the quantities and usage patterns of antimicrobial agents used in aquatic animals
- **Chapter 6.4.**
Development and **harmonisation** of national antimicrobial resistance **surveillance and monitoring programmes** for aquatic animals
- **Chapter 6.5.**
Risk analysis for antimicrobial resistance arising from the use of antimicrobial agents in aquatic animals

<http://www.oie.int/international-standard-setting/aquatic-code/access-online> line

Standards and guidelines related to antimicrobial resistance

- The OIE International Committee unanimously adopted the **List of Antimicrobial Agents of Veterinary Importance** at its 75th General Session in May 2007 (Resolution No. XXVIII).
- This list was further updated and adopted in May 2013 and May 2015 by the World Assembly of OIE Delegates. **Next update** foreseen to address in the **WHO list of critically important antimicrobials**
- [List of antimicrobial agents of veterinary importance](http://www.oie.int/fileadmin/Home/eng/Our_scientific_expertise/docs/pdf/Eng_OIE_List_antimicrobials_May2015.pdf)

http://www.oie.int/fileadmin/Home/eng/Our_scientific_expertise/docs/pdf/Eng_OIE_List_antimicrobials_May2015.pdf

Standards and Guidelines Related to Antimicrobial Resistance

- **Criterion 1.** Response rate to the questionnaire regarding Veterinary Important Antimicrobial Agents
- **Criterion 2.** Treatment of serious animal disease and availability of alternative antimicrobial agents

Standards and Guidelines Related to Antimicrobial Resistance

- Veterinary **Critically Important** Antimicrobial Agents (**VCIA**): are those that meet BOTH criteria 1 **AND** 2
- Veterinary **Highly Important** Antimicrobial Agents (**VHIA**): are those that meet criteria 1 **OR** 2
- Veterinary **Important** Antimicrobial Agents (**VIA**): are those that meet **NEITHER** criteria 1 OR 2

Recent Resolution on AMR :

Adopted by the World Assembly of OIE Delegates during their 85th General Session 21 – 26 May 2017 :

- **No. 38** Global action to alleviate the threat of antimicrobial resistance: progress and opportunities for future activities under the 'One Health' initiative



Antiparasitics

Antiparasitics

- Trypanocides**Specific Monograph**

The screenshot shows the OIE website interface. At the top, there is a navigation bar with the OIE logo and text in three languages: 'Organisation Mondiale de la Santé Animale', 'World Organisation for Animal Health', and 'Organizacion Mundial de Sanidad Animal'. There are also language options for 'Français | English | Español', a 'Log in' button, and a 'Sign in online' button. Below this is a red navigation bar with 'Home', 'Catalogue', 'Subscription', and 'Distributors' links, a search bar, and a 'My Shopping Cart (0)' button. The main content area is titled 'Excerpt of product info' and contains the following text:

Product title : **Animal trypanosomosis: making quality control of trypanocidal drugs possible**
Author(s) : O.B. Sutcliffe, et al.
Summary :
No. 12092014-00040-EN
African animal trypanosomosis is arguably the most important animal disease impairing livestock agricultural development in sub-Saharan Africa. In addition to vector control, the use of trypanocidal drugs is important in controlling the impact of the disease on animal health and production in most sub-Saharan countries. However, there are no internationally agreed standards (pharmacopoeia-type monographs or documented product specifications) for the quality control of these compounds. This means that it is impossible to establish independent quality control and quality assurance standards for these agents.
Keywords
African animal trypanosomosis – Diminazene – Homidium – Isometamidium – Monograph – Pharmacopoeia – Quality assurance – Quality control – Trypanocidal drug – Trypanocide.
• Read more
• 091209201400040ensutcliffe813830.pdf

At the bottom right of the excerpt, there is a '< Retour' link.

http://web.oie.int/boutique/index.php?page=ficprod&id_prec=1309&id_produit=1458&lang=en&fichrech=1&PHPSESSID=9374551d777d42d410d15c3c97ddd102

- Future plan based on the feedback of previous Focal Point training seminars: work on guidelines for prudent use of antiparasitic products, subject to future direction from OIE Delegates (and Focal Points) from Member Countries.

Conclusion

- We need to continue to **work together** to have **high quality, practical global standards and guidelines** for veterinary medicinal products
- **We need to build the capacity** to respond to the new challenges, for example by potentially developing an OIE guideline on prudent and responsible use of antiparasitics

Conclusion

- **We need to build the capacity** to respond to the new challenges, like how we respond to emerging diseases ?
- How can the OIE contribute in helping you to implement the standards and guidelines ?

Thank you for your attention!



WORLD ORGANISATION FOR ANIMAL HEALTH
Protecting animals, preserving our future

