



OIE INTERNATIONAL STANDARD SERA RECOGNITION AND LOOKING TO THE FUTURE

A. M. Nicola, M.V., MSc
OIE Biological Standards Commission Member

*World Association of Veterinary Laboratory Diagnosticians
19th International Symposium,
Chiang Mai, Thailand, 21 June 2019*



WORLD ORGANISATION FOR ANIMAL HEALTH *Protecting animals, preserving our future*

Biological Standards Commission (BSC)

Coordinates a programme for the preparation, validation and distribution of OIE-approved International Reference Standards for antibody assays for infectious diseases of animals.



President
Prof. Emmanuel
Couacy-Hymann



1st Vice-President
Dr Franck Berthe



2nd Vice-President
Dr John Pasick



Member
Prof. Ann Cullinane



Member
Dr Joseph S. O'Keefe

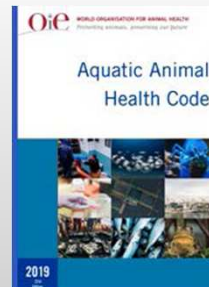
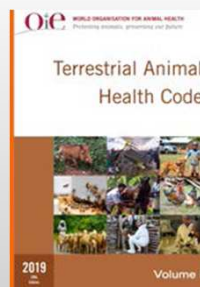
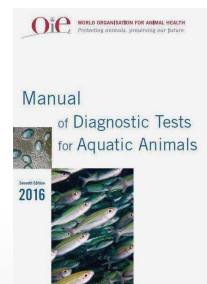


Member
Dr Ana Maria Nicola



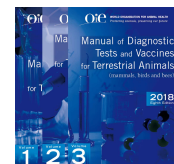
WORLD ORGANISATION FOR ANIMAL HEALTH *Protecting animals, preserving our future*

Standards



WORLD ORGANISATION FOR ANIMAL HEALTH *Protecting animals, preserving our future*

Why a Reference Standards Sera?



International Reference Standards are necessary **to ensure that a given antibody assay is capable of measuring antibody activity to a specified level of diagnostic sensitivity.**

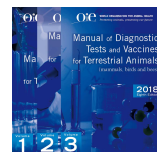
The aim of the programme is to **harmonise diagnostic testing and encourage the mutual recognition of test results for international trade.**

<http://www.oie.int/en/scientific-expertise/veterinary-products/reference-reagents/>



WORLD ORGANISATION FOR ANIMAL HEALTH *Protecting animals, preserving our future*

International Reference Standards



The standards are prepared by an **OIE Reference Laboratory** in accordance with [Guidelines](#) for [antibody](#), [antigen](#) and [polymearase chain reaction \(PCR\) standards](#) drawn-up by the Commission in collaboration with other laboratories.

Such standard preparations are designated by the OIE as **primary reference standards** for use in conjunction with tests described in the OIE *Manual of Diagnostic Tests and Vaccines for Terrestrial Aniamls (mammals, birds and bees)*.



WORLD ORGANISATION FOR ANIMAL HEALTH Protecting animals, preserving our future

Guidelines for the preparation, validation and distribution of antibodies as International Reference Standards for antibody assays for infectious diseases of animals

OIE Guideline

International Reference Antibody Standards for Antibody Assays

1. Introduction

1.1. Purpose

This document provides guidelines for the preparation, validation and distribution of antibodies as International Reference Standards for antibody assays for infectious diseases of animals. In these guidelines, the term "Standards" refers to antibodies unless indicated otherwise. Such standard preparations are designated by the OIE as primary reference standards for use in conjunction with tests described in the OIE *Manual of Diagnostic Tests and Vaccines for Terrestrial Animals*.

1.2. Definitions

1.2.1. Standard Test Protocol

Standard Test Protocol refers to a validated, internationally accepted test procedure, often an "OIE Prescribed Test for International Trade", which is described in the OIE *Manual of Diagnostic Tests and Vaccines for Terrestrial Animals*.

The term International Reference Standard is synonymous with primary reference standard. It represents the standard by which all others are compared and calibrated.

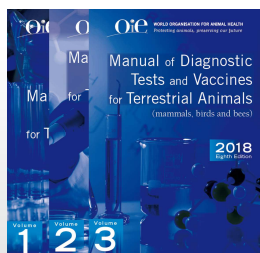
Secondary standards are prepared by direct comparison with the International Reference Standard, and should so far as is possible mimic the characteristics of the primary standard when used in the Standard Test Protocol. A Secondary Standard would typically be prepared by a National Reference Laboratory and be designated as the national or local standard.

Working standards may be synonymous with secondary standards, or they may be tertiary standards calibrated against the secondary standard. Working standards should be available in sufficient quantities for use by diagnostic laboratories to standardise routine daily testing.

1.3. Scope

International Reference Standards are necessary to ensure that a given antibody assay is capable of measuring antibody activity to a specified level of diagnostic sensitivity. Diagnostic sensitivity relates to the risk of a false negative reaction occurring in an antibody assay when in fact an animal is, or has been, infected. International Reference Standards are normally for use by international, national and other reference laboratories in calibrating standard assays and as templates for the production of secondary standards. The secondary or other working standard, and not the international standard, are to be used on a daily basis to standardise testing.

For a limited number of diseases, there has been international agreement on a system of 'International Units' of antibody activity. In such cases the International Reference Standards define the scale of such units. In the vast majority of animal diseases no such system exists, and assay systems, working standards, and test samples are defined relative to the International Reference Standards.



http://www.oie.int/fileadmin/Home/eng/Our_scientific_expertise/docs/pdf/Reagents/A_GUIDELINE_ANTIBODY_STANDARDS.pdf
WORLD ORGANISATION FOR ANIMAL HEALTH Protecting animals, preserving our future

International Reference Standards

They are prepared by **OIE Reference Laboratories** (or other international reference labs) which use an **internationally accepted Standard test Protocol**

Secondary Standards

- ✓ are reagent calibrated by comparison with IRS
- ✓ normally prepared by National Reference Laboratory
- ✓ Commonly represent the **National Standards**

Tertiary standards

- ✓ are reagents calibrated against the Secondary standards
- ✓ usually prepared by normal diagnostic laboratories

are used on a daily basis to standardize testing



WORLD ORGANISATION FOR ANIMAL HEALTH *Protecting animals, preserving our future*

International Reference Standards

Three primary reference standards should be established:

- **a strong positive**
- **a weak positive**
- **a negative**

The weak positive standard **is critical** for providing assurance of the diagnostic sensitivity of the test.



WORLD ORGANISATION FOR ANIMAL HEALTH *Protecting animals, preserving our future*

International Reference Standards Sera

How to prepare them?

Usually **blood serum** which should be free:

- ✓ from haemolysis
- ✓ from excessive lipaemia
- ✓ from *infectious agents (safe)*
it facilitates shipment between countries
- ✓ be produced in specific pathogen free or gnotobiotic animals
- ✓ the wet state be either treated with BEI (binary ethyleneimine) or irradiated at 25–30 kilogray (2.5–3.0Mrad)
- ✓ kept at –78°C./ freeze-dried
- ✓ Bovine sera should be from a BSE-free source



WORLD ORGANISATION FOR ANIMAL HEALTH *Protecting animals, preserving our future*

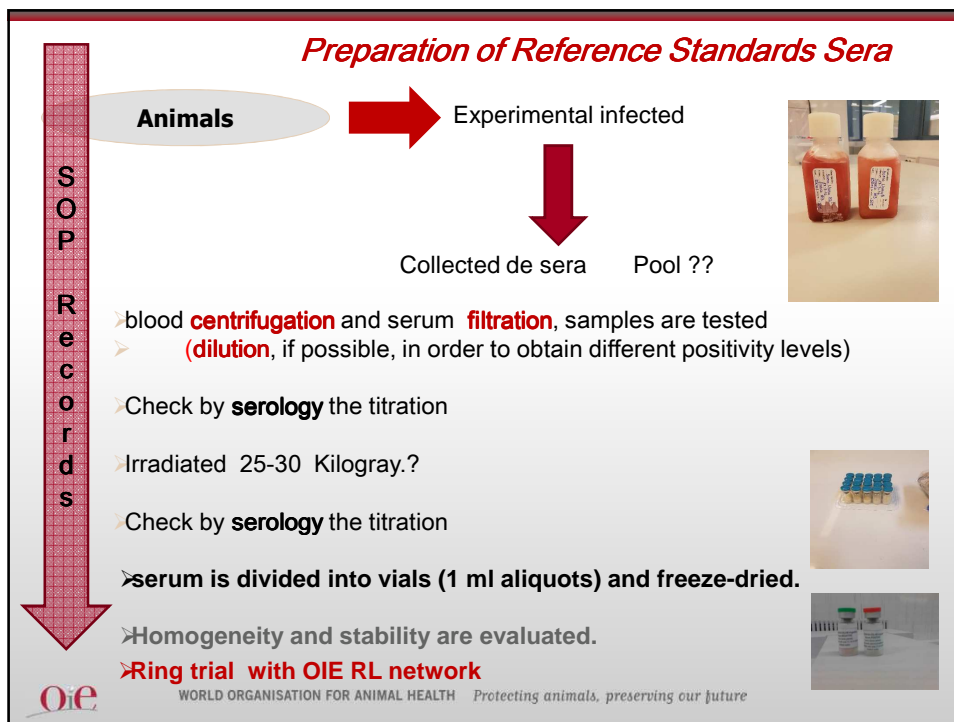
Preparation of Reference Standards

Positive serum

- ✓ It should origin from animals **with a typical humoral immune-response to the selected pathogen** (experimental infection, vaccination and exceptionally from naturally infected animals) *from materials showing the desired level of reactivity without further dilution.*
- ✓ It should be **free from cross-reactive antibodies**
- ✓ It could origin from a single animal or it could derive from a pool of animals



WORLD ORGANISATION FOR ANIMAL HEALTH *Protecting animals, preserving our future*



Preparation of Reference Standards

Evaluation of **homogeneity** of serum aliquots

- 10-15 vials are randomly selected and each one
- is tested **10 times** with both the qualitative and the quantitative method, by the same operator, in the same working conditions and after short intervals
- statistic analysis

Evaluation of **stability** of the sera

5 vials/each temp

	Temp
Dia 0	5 ± 3°C
	22 ± 4°C
	37 ± 1°C
Dia 15	5 ± 3°C
	22 ± 4°C
	37 ± 1°C
Dia 30	5 ± 3°C
	22 ± 4°C
	37 ± 1°C

OIE WORLD ORGANISATION FOR ANIMAL HEALTH *Protecting animals, preserving our future*

Preparation of Reference Standards

Batch control

- The original reference material must begin as one single stock with enough to last at least 5 years.
- This can be kept frozen (preferably at -70°C or below)
- freeze-dried for a minimum 2-year supply (about 500 tests).

Labelling

- OIE logo
- reference standard for (disease) (test)
- specify if strong positive, weak positive or negative
- the name of the Reference Laboratory
- reconstitution method; and storage conditions



Data sheets

ensure that all aliquots are accompanied by an appropriate Data Sheet



WORLD ORGANISATION FOR ANIMAL HEALTH Protecting animals, preserving our future

International Reference Standards

Approval of Reference Standards by Biological Standards Commission



WORLD ORGANISATION FOR ANIMAL HEALTH
Protecting animals, preserving our future

Font size: - + Language: | Français English Español

Keywords Search + Advanced search

Home About us Scientific expertise Solidarity Animal health in the World Standard Setting

Home > Scientific expertise > Veterinary products > Reference reagents

Scientific expertise

- > Overview
- > Collaborating Centres
- > Reference Laboratories
- > Biological threat reduction
- > OFFLU, the animal influenza network
- > Registration of diagnostic kits
- > Veterinary products
 - > VICH Outreach Forum
 - > Antimicrobials
 - > Diagnostic tests
 - > Reference reagents
- > Specific information and recommendations

OIE-approved International Standard Reagents

The OIE Biological Standards Commission coordinates a programme for the preparation, validation and distribution of OIE-approved International Standard Reagents for diagnostic assays for infectious diseases of animals. The standards are prepared by an OIE Reference Laboratory in accordance with Guidelines for antibody, antigen and polymerase chain reaction (PCR) standards drawn-up by the Commission in collaboration with other laboratories. Such standard preparations are designated by the OIE as primary reference standards for use in conjunction with tests described in the OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals (mammals, birds and bees). The aim of the programme is to harmonise diagnostic testing and encourage the mutual recognition of test results for international trade.

Currently available OIE-approved International Standard Reagents

Disease	Test	Available from
African horse sickness	Enzyme-linked immunosorbent assay	Marisa Arias Centro de Investigación en Sanidad Animal, Instituto Nacional de Investigación y Tecnología Agraria y Alimentaria (CISA-INIA), 28130 Valdeolmos, Madrid, Spain Tel: (34-91) 620 23 00 Fax: (34-91) 620 22 47 arias@inia.es / diagnost@inia.es
Aujeszky's disease	Enzyme-linked immunosorbent assay; Virus neutralisation	Dr Marie-Frédérique Le Potter Anses Ploufragan, Laboratoire de Ploufragan/Plouzané Unité de Virologie Immunologie Porcines ZOOPOLE LES CROIX 22440 Ploufragan, France Tel: +33 (0)2 96 01 62 80 Fax: +33 (0)2 96 01 62 94 marie-fredérique.lepotier@anses.fr
Bluetongue	Enzyme-linked immunosorbent assay	Dr Tracy Sturgill

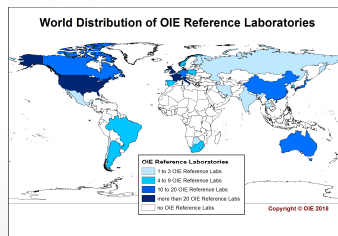
- > WAHIS Interface
- > Online bookshop
- > For the media
- > OIE world conferences
- > Documentary database



WORLD ORGANISATION FOR ANIMAL HEALTH Protecting animals, preserving our future

International Reference Standards

Approval of Reference Standards by Biological Standards Commission



INTERNETWORK

- Registration of diagnostic kits
- Veterinary products
- VICH Outreach Forum
- Antimicrobials
- Diagnostic tests
- Reference reagents
- Specific information and recommendations

Currently available OIE-approved International Standard Reagents

Disease	Test	Available from	
African horse sickness	Enzyme-linked immunosorbent assay	Marisa Anas Centro de Investigación en Sanidad Animal, Instituto Nacional de Investigación y Tecnología Agraria y Alimentaria (CISA-INIA), 28130 Valdeolmos, Madrid, Spain Tel: (34-91) 620 23 00 Fax: (34-91) 620 22 47 anas@inia.es / diagnost@inia.es	
Aujeszky's disease	Enzyme-linked immu Virus neutralisation		Reference Laboratories
		Number	246
		Countries	35
Bluetongue	Enzyme-linked immu	Disease/Topic	105
		Experts	182

African horse sickness
Aujeszky's disease
Bluetongue
Brucella abortus
Brucella melitensis
Brucella ovis
Classical swine fever
Contagious bovine pleuropneumonia
Enzootic bovine leukosis
Equine infectious anaemia
Equine influenza
Equine viral arteritis
Foot and mouth diseases
Infectious bovine rhinotracheitis
Peste des petits ruminants
Rabies
Rinderpest
Swine vesicular disease

OIE INTERNATIONAL STANDARD SERA RECOGNITION AND LOOKING TO THE FUTURE

- A **standard template will be created as an Annex** to the *Guidelines for antibody, antigen and PCR standards* to streamline applications for inclusion of diagnostic standard reagents produced by OIE Reference Laboratories in the list of OIE-approved international standard reagents.
- The guidelines will also be updated to allow OIE Reference Laboratories and other laboratories to participate in the proficiency test** that is required for inclusion of new reagents in the OIE list, provided that the laboratory is accredited for the specific test method.
- The ISS Institute (Italy), OIE Reference Laboratory for trichinellosis, has submitted an application **for inclusion of standard reagents for trichinellosis** in the OIE list. Results of the proficiency test are currently under evaluation.



WORLD ORGANISATION FOR ANIMAL HEALTH Protecting animals, preserving our future

Thank you for your attention



12, rue de Prony, 75017 Paris, France
www.oie.int
media@oie.int - oie@oie.int



Oie WORLD ORGANISATION FOR ANIMAL HEALTH
Protecting animals, preserving our future