Organisation Mondiale de la Santé Animale | World Organisation for Animal Health | Organización Mundial de Sanidad Animal

Quality of Veterinary Medicinal Products

How to ensure the quality of Veterinary Medicinal Products

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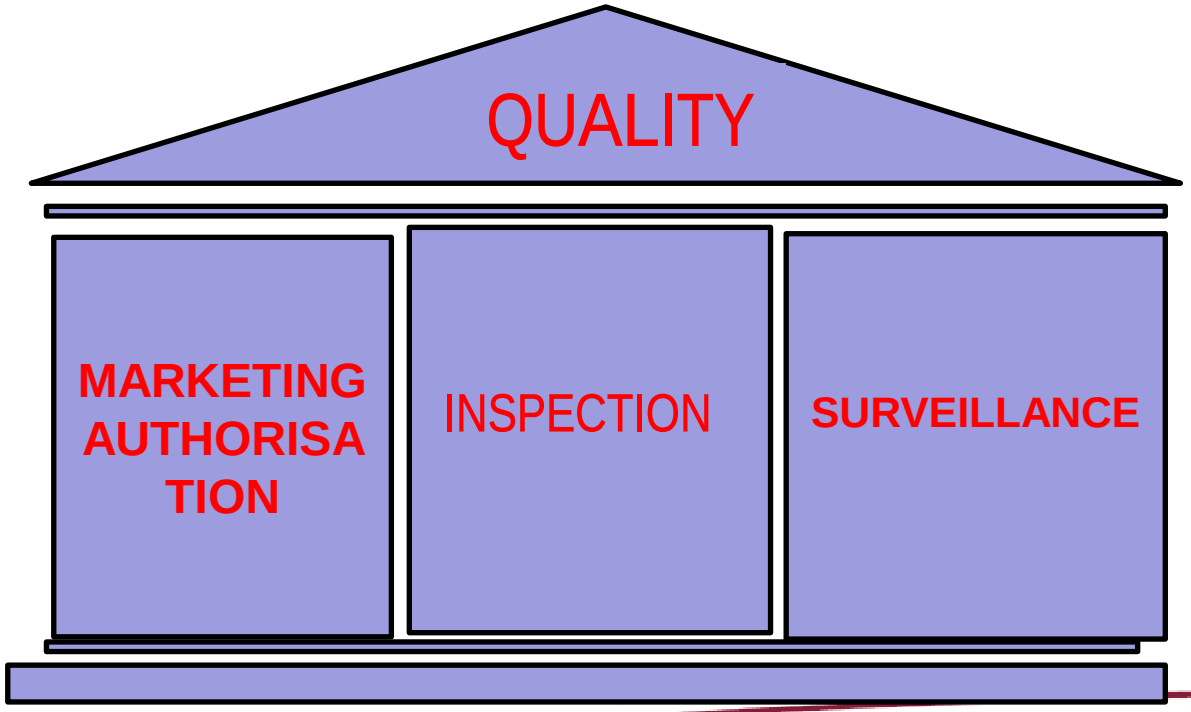
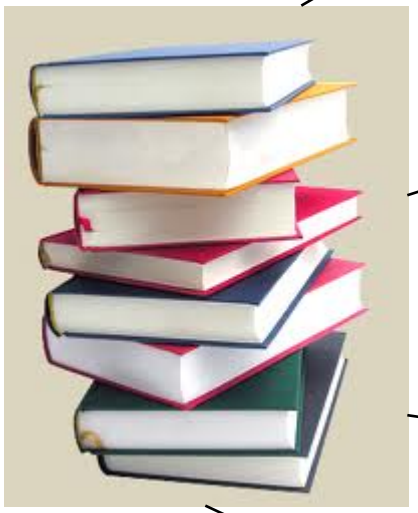
INTRODUCTION

Ensuring the quality of Veterinary Medicinal products (VMPs) is an essential and basic requirement for the good governance of VMPs.

Three Pilars



Marketing Authorisation dossier



- Part 1: Administrative Part
  summary of the dossier

- Part 2: Pharmaceutical quality Part

Constituents, Manufacturing process, Control of starting materials, tests carried out at intermediate stages of the process, finished product …

- Part 3 : Safety and residues tests Part

Toxicology tests (single dose toxicity, repeat dose, effects on reproduction), user safety, environmental risk assessment … (chemical products), administration of one dose, overdose, repeated administration, effects on reproductive performance… (immunological products)

- Part 4 : Efficacy tests

Preclinical and clinical trials…

QUALITY PART

A. Qualitative and Quantitative Particulars of the Constituents :

- Composition : Objective: Describe precisely the product
- Development Pharmaceutics :

Objective: Justify the formula, choice of containers, manufacturing process

B - Description of the Manufacturing Method :

- Description of manufacturing process, GMPs for all sites needed

Objective : quality of finished product is reproducible

QUALITY PART

C - Control of Starting Materials

Objective: Ensure that the product contains starting materials of good and controlled quality

D - Control Tests Carried out at intermediate stages of the Manufacturing Process

E - Tests on the Finished Product

Objectives : Define precisely the specifications of the products, define limits of acceptance

Important for the Quality control by the authorities.

QUALITY PART

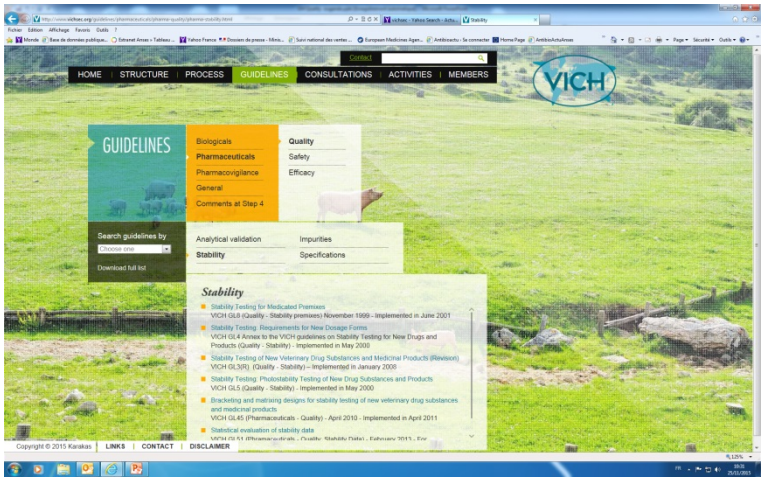
F - Stability Test

Objectives:

- Propose a shelf-life as package for sale, and storage conditions if necessary
- Propose a shef-life after first opening of the immediate packaging
- Propose a shelf-life after dilution or reconstitution
- Propose a shelf-life after incorporation into meal or pelleted feed

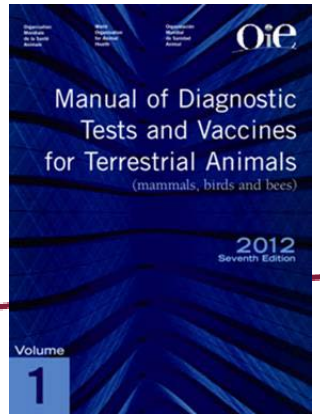
G - Other Information

VICH guidelines available



http://www.vichsec.org/guidelines/biologicals/bio-quality/stability.html

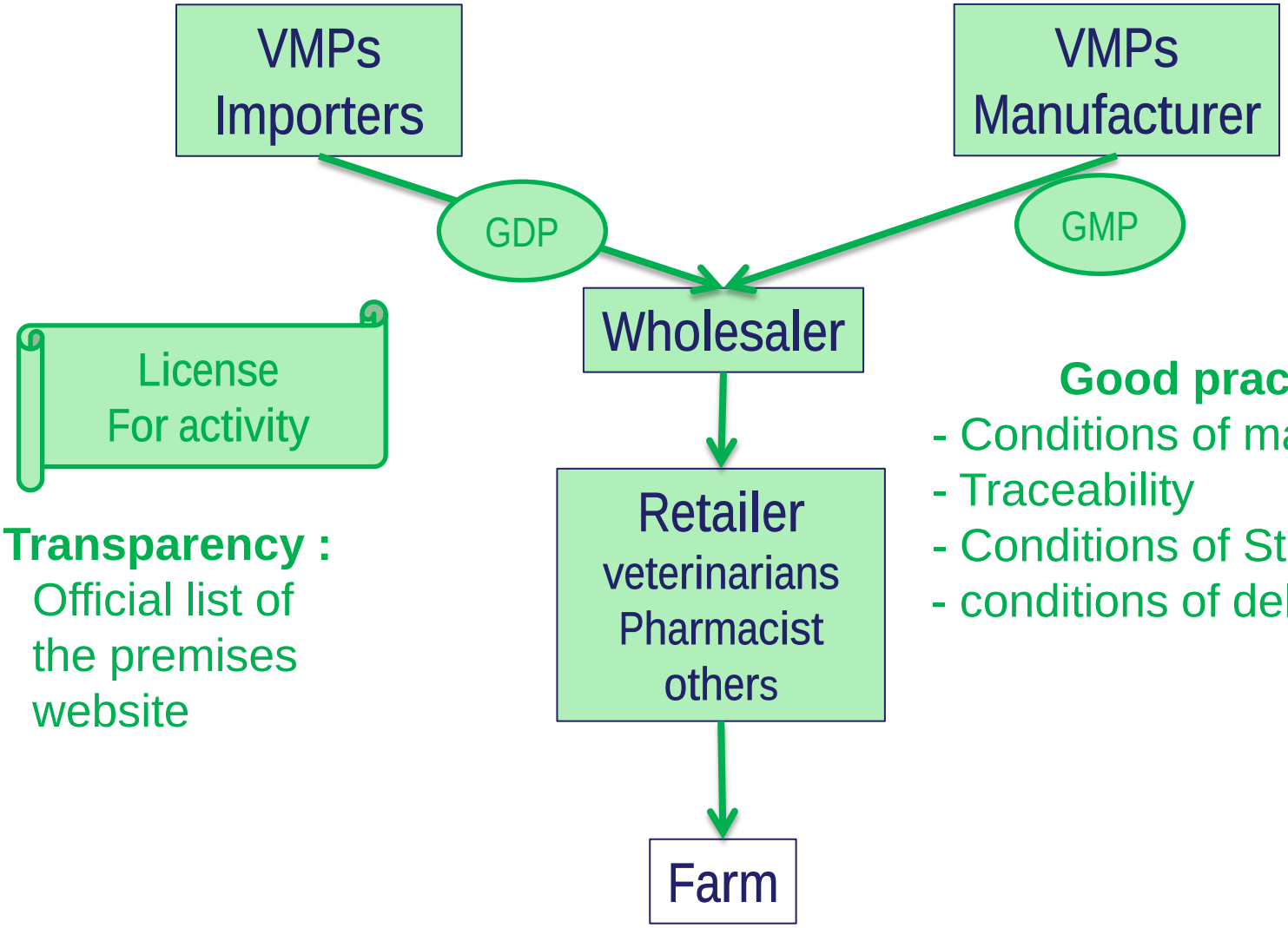
OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals



http://www.oie.int/en/international-standard-setting/terrestrial-manual/

Inspection

Quality during manufacturing, Storage and Distribution



Transparency :

- Official list of the premises
- website

Good practices :

- Conditions of manufacturing
- Traceability
- Conditions of Storage
- conditions of deliverance

An appropriate regulatory framework

⇨ **Need of prior Authorization and periodic control for Veterinary Product companies**

Manufacturer, Importer, Wholesaler…

- These activities should be governed by rules :
  - **Good practices as**
    - Good manufacturing practices (GMP)
    - Good distribution practices (GDP)
    - Good prescription practices …

GMP legislation

- The EU(EEA) Regulatory Framework
  - Areas for Veterinary Legislation:
    - Veterinary Medicinal Products: GMP
    - Veterinary Medicinal Products: **GMP**

    Volume 4 EUDRALEX: Good manufacturing practice (GMP) Guidelines. (near 200 pages)

    http://ec.europa.eu/health/documents/eudralex/vol-4/

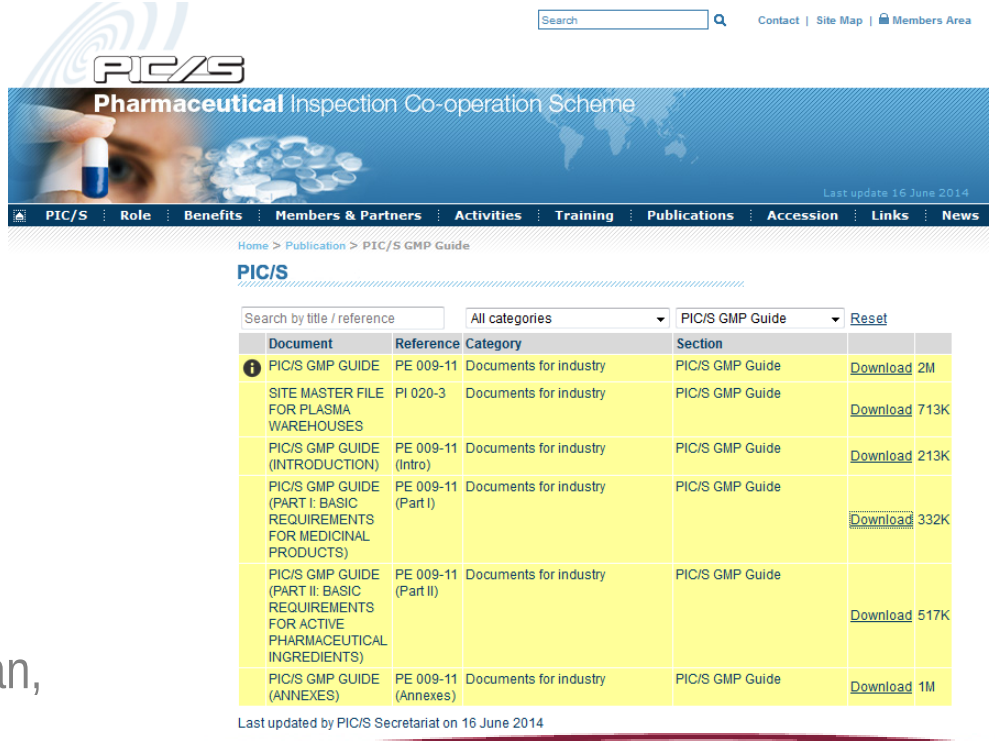
General provisions

- Quality management
- Personnel
- Premises and equipment
- Documentation
- Production
- Quality control
- Work contracted out
- Complaints and product recall
- Self inspection

PIC/S

- The Pharmaceutical Inspection Co-operation Scheme is an international instrument between countries and pharmaceutical inspection authorities, which provide together an active and constructive co-operation in the field of GMP.

- PIC/S' mission is "to lead the international development, implementation and maintenance of harmonised Good Manufacturing Practice (GMP) standards and quality systems of inspectorates in the field of medicinal products."



46 Participating Authorities in PIC/S :
China taipei, Hong Kong, Indonesia, Japan, Korea, Malaysia, Singapore

http://picscheme.org/

GMP at OIE LEVEL

Manual of Diagnostic Tests and Vaccines for Terrestrial Animals 2017

Part 1	**General Standards**
Section 1.1.	**Introductory chapters**
Chapter 1.1.1.	Management of veterinary diagnostic laboratories (NB: Version adopted in May 2015)
Chapter 1.1.2.	Collection, submission and storage of diagnostic specimens (NB: Version adopted in May 2013)
Chapter 1.1.3.	Transport of specimens of animal origin (NB: Version adopted in May 2013)
Chapter 1.1.4.	Biosafety and biosecurity: Standard for managing biological risk in the veterinary laboratory and animal facilities (NB: Version adopted in May 2015)
Chapter 1.1.5.	Quality management in veterinary testing laboratories **(NB: Version adopted in May 2017)**
Chapter 1.1.6.	Principles and methods of validation of diagnostic assays for infectious diseases (NB: Version adopted in May 2013)
Chapter 1.1.7.	Standards for high throughput sequencing, bioinformatics and computational genomics (NB: Version adopted in May 2016)
Chapter 1.1.8.	Principles of veterinary vaccine production (NB: Version adopted in May 2015)
Chapter 1.1.9.	Tests for sterility and freedom from contamination of biological materials intended for veterinary use **(NB: Version adopted in May 2017)**
Chapter 1.1.10.	Vaccine banks (NB: Version adopted in May 2016)

Section 3.7 .	**Recommendations for the manufacture of vaccines**
Chapter 3.7.1.	Minimum requirements for the organisation and management of a vaccine manufacturing facility (NB: Version adopted in May 2016)
Chapter 3.7.2.	Minimum requirements for the production and quality control of vaccines (NB: Version adopted in May 2016)
Chapter 3.7.3.	Minimum requirements for aseptic production in vaccine manufacture (NB: Version adopted in May 2016)

GMP Requirements

Target/activity?

- Manufacturing sites for
  - Pharmaceutical products
  - Medicinal products for clinical trials
- Also, manufacturing sites for
  - Actives ingredients
  - *Autogenous-vaccines*
  - Premixes *for Medicated feeding stuff*
  - Herbal products
  - Homeopathic medicines
- And contract company providing
  - Transport, quality control…

GMP Requirements

Target/product?

- Range of products
  - Sterile
  - Non sterile
  - Biologic
  - Chemical
  - Tablets, oral powder
  - …

Not covered: medical device, reagents, biocides and veterinary food additives

Good Distribution practices (GDP)

Target/activity?

- MAH and distributors
  - Recall and complaints
  - Quality product review
  - Storage condition : cold chain for vaccines
  - Traceability

Surveillance

- Legal Market
- Counterfeit products

Legal Market

Surveillance of the Legal Market

Elaborate a programme of surveillance with a risk analysis and in cooperation with all competent services

Risk based programme

Examples:

- Products used for food producing animals
- Focus on antibiotics and antiparasitics
- Products that present a risk for the users (vet, farmers,etc.)
- biologicals involved in the control of zoonosis
- biologicals involved in the control of regulated diseases
- live vaccines

…

Inspection and control

VMPs Importers

VMPs Manufacturer

GDP

GMP

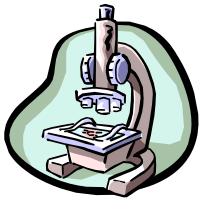
Wholesaler

Retailer
veterinarians
Pharmacist
others

Farm

Sampling

Quality Control



Inspection

Control of :

- Conditions of manufacturing
- Traceability
- Conditions of Storage
- Conditions of deliverance
- List of VMPs (only VMPs authorised)

Sampling

- Done by inspectorates (in wholesalers but also anywhere on the market)

Testing

- Qualitative and quantitative analysis : Active ingredient content
  most often by HPLC (High performance Liquid Chromatography)
- Efficacy for vaccines
- Accredited laboratory or international recognition (OIE Ref. Lab)

Counterfeit products

- Copy of Authorised products
  - Modification of qualitative or quantitative active ingredients
  - Differencies in the labelling

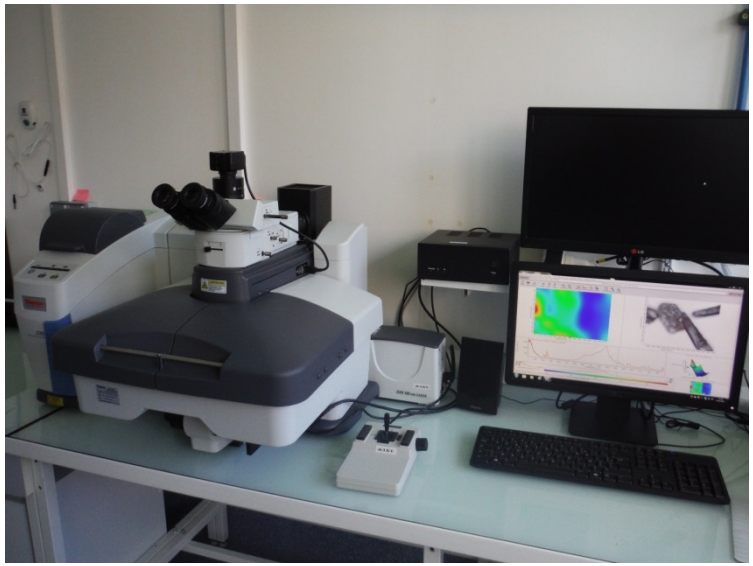
- Need for National, Regional and international cooperation

- Internet sales (a concern)

Counterfeit products

Quality Control Laboratory

- Need for laboratory capacities to identify, analyse counterfeit products



RAMAN SPECTROMETER

At farm level

- Inspectors should verify
  - The absence of counterfeits or unauthorised products
  - The conditions of storage
  - The record keeping
  - The respect of the prescription rules
  - The compliance with the prescription
  - Veterinary medicinal products administered to the animals, dates of administration and respect of withdrawal periods

Conclusion

- *Ensuring quality of Veterinary medicinal products is essential.*
- *Appropriate legislation and Staff (trained inspectors, laboratory capacities) are needed.*
  - *Efficient systems of Authorisation (VMP and companies)*
  - *Transparency and communication*
  - *Efficient Inspectorate body with appropriate power.*
  - *The possibility to survey both the legal and illegal market*

are essential as well as :

The capacity of prosecution and recalling products.

Thank you for your attention

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