

Quality control of veterinary products, Tackling falsified and counterfeit products

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Good Regulatory Practice for the Marketing Authorisation of
Veterinary Products in an African Context

Organising Committee:

BILL & MELINDA
GATES foundation





INTRODUCTION

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

Three Pillars



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VMPs are veterinary important tools, contributing to the improvement of animal and public health worldwide, and to economical development. They have impact on animal safety, user safety, food safety, environmental safety, antimicrobial resistance...

They shall be sure, efficient, safe, and good quality.

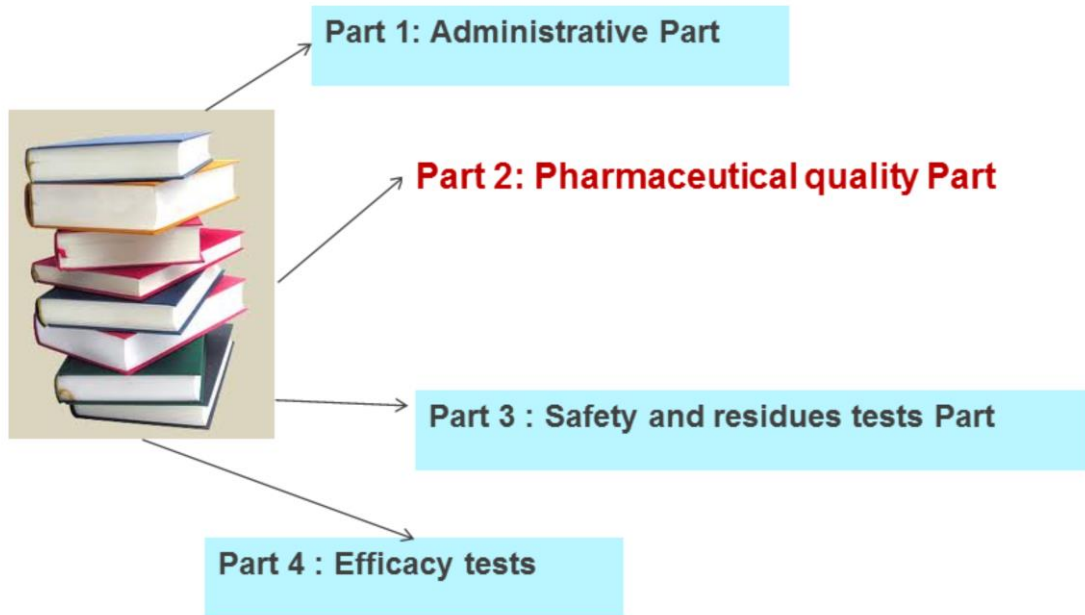
The quality of VMPs is primordial.

Insurance of VMP's Quality is based on 3 pillars :

- 1/ quality requirement and characteristics, methods for analysis and control are defined and validated in the marketing authorisation dossier
- 2/ inspection of manufacturers, wholesalers... is a way to control that VMPs are manufactured, controlled, released and distributed by industry as required in the marketing authorisation in the respect of good practices which are guarantee of good quality
- 3/ surveillance of VMPs put on the market is necessary to detect adverse effects and quality defects (through analysis in an official laboratory).



Marketing Authorisation dossier



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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 ...

The part 2 of the marketing authorisation dossier describes all information concerning the quality of the VMP :

- Detailed composition,
- all the manufacturing process and the control in-process
- Control to conduct on the raw material and all component (including packaging, label control...)
- Control on the finished product for batch release.

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
- Development Pharmaceutics :

C - Control of Starting Materials

E - Tests on the Finished Product

Important for the Quality control by the authorities

F - Stability Test

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- Description of the part 2 concerning the quality of the product

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

C - Control of Starting Materials

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

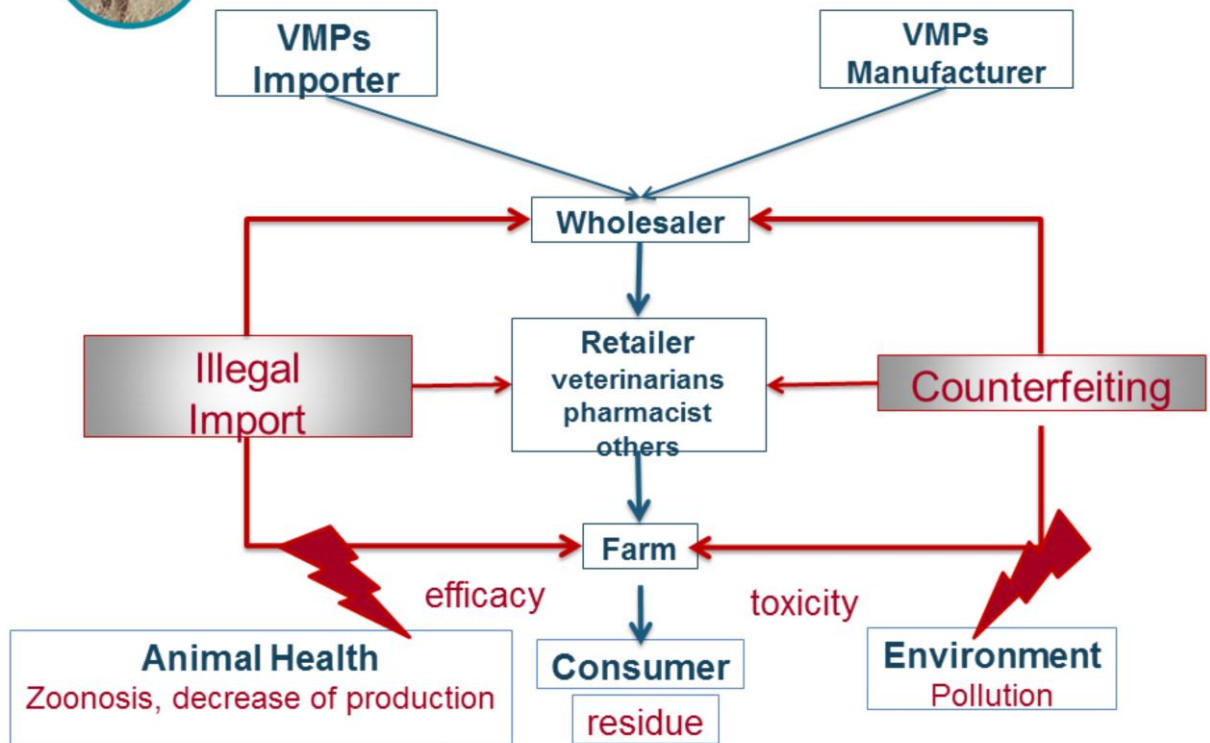
E - Tests on the Finished Product

Objectives : Define precisely the specifications of the products, define limits of acceptance
Important for the Quality control by the authorities

- **F - Stability Test**



VMPs Chain



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Issues to be discussed

- Do you know all the actors involved in the distribution of VMPs in your country ?
- Do you have importer ?
- Do you identify illegal market :
 - Illegal import ?
 - Black market ?
 - Counterfeiting ?

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- Discussion with the attendee to test their knowledge of the VMP chain in their country and if they have identified some problem of illegal import, or falsified and counterfeit products.



Inspection

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Inspection and control

- **Inspectorate Body**
- **Powers of Inspectors**
- **Duties of Inspectors**
 - Impartiality
 - Independence
 - Confidentiality
 - Integrity

***Need for rules
as
good practices***

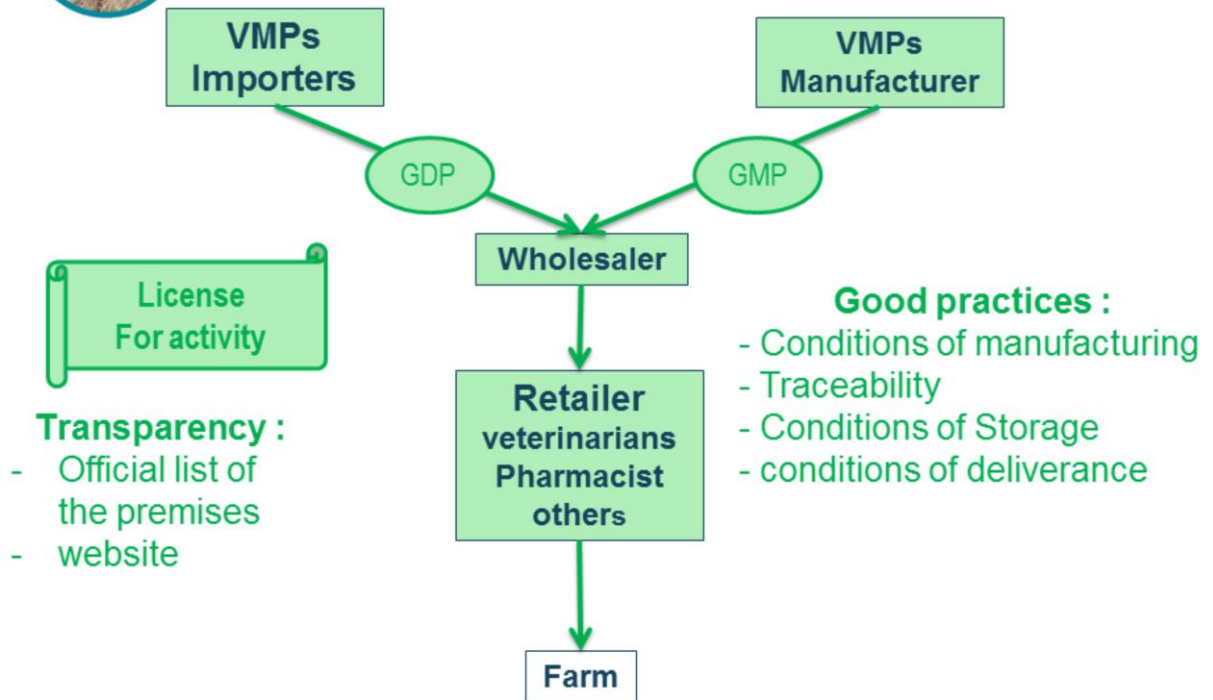
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- For a good governance, each country shall have an inspectorate body.
- The regulation shall clearly define :
 - the composition of this inspectorate body,
 - the power of inspectors :
 - what can they inspect ? How? When ?
 - The modalities to take sample , or to have access to documents...
 - The administrative sanction : recall, destruction of product, suspension or withdraw of marketing authorisation...
 - Their prosecution capacity
 - The duties of inspectors :
 - Impartiality
 - Independence
 - Confidentiality
 - Integrity
- To fight against corruption, link of interest shall be take into account.



Quality during Storage and Distribution



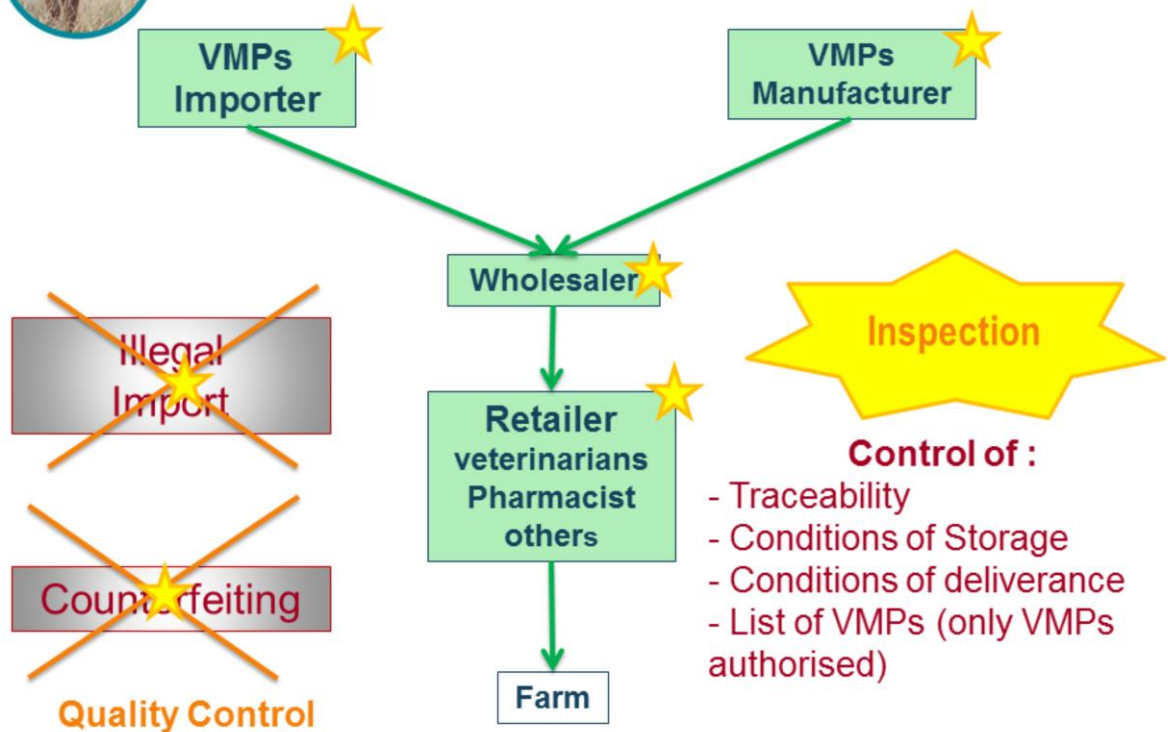
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- The quality of VMPs shall be maintained during all the VMP chain, by the different stakeholders shall ensure that the VMPs they store are authorised by the government, have been bought to an authorised stakeholder and that they sell it to an authorised person.
- At each step the conditions of storage shall ensure that the quality is maintained and be in compliance with the conditions defined in the marketing authorisation.
- Traceability is also very important when recall are necessary to be sure to withdraw from the market all the concerned units of a batch.
- To manage all stakeholder shall observe and implement good practices.
- The Pharmaceutical Inspection Cooperation Scheme (PIC/S) is a structure that currently has 49 participating authorities from all over the world. The PIC/S's main objectives are to lead the international development of recommendations for good practice in the manufacturing and distribution of human and veterinary medicinal products, provide training opportunities to inspectors, ensure that inspection systems are subject to a high level of quality management, and provide inspectors with a framework for exchanges.



Control of VMPs companies



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- Inspection shall be conducted at each level of the VMP chain to control the implementation and respect of the regulation.
- The main objectives of the control shall be :
 1. To verify that only authorised products are manufactured, imported, stored, sold, used....
 2. Ensure good conditions of storage
 3. All the stakeholders are able to organise a recall through a good traceability



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 ...

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- Regular controls shall be conducted to ensure a good governance and all this rules should be defined in a appropriate regulatory framework.



Good Distribution practices (GDP)

Target/activity?

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



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- Good distribution practices are very important and shall cover all activities :
- Reception
- Storage
- Respect of the cold chain (for vaccines, certain antibiotics by example)
- Transport
- Deliverance to the retailers
- Traceability : different system can be implemented : barcode or square code with IT tool offer the possibility to manage traceability.
- The Good Distribution Practices guide adopted by the PICs defines also rules concerning the premises, the staff and their training, the quality management system etc...



Issues to be discussed

- ▶ Do you have an inspectorate body defined in the regulation ?
- ▶ Are they well trained and specialised ?
- ▶ Do they have power :
 - For inspection ?
 - For administrative action ?
 - For prosecution ?
 - For sampling ?
- ▶ Shall the companies be authorised or licenced for their activities ?

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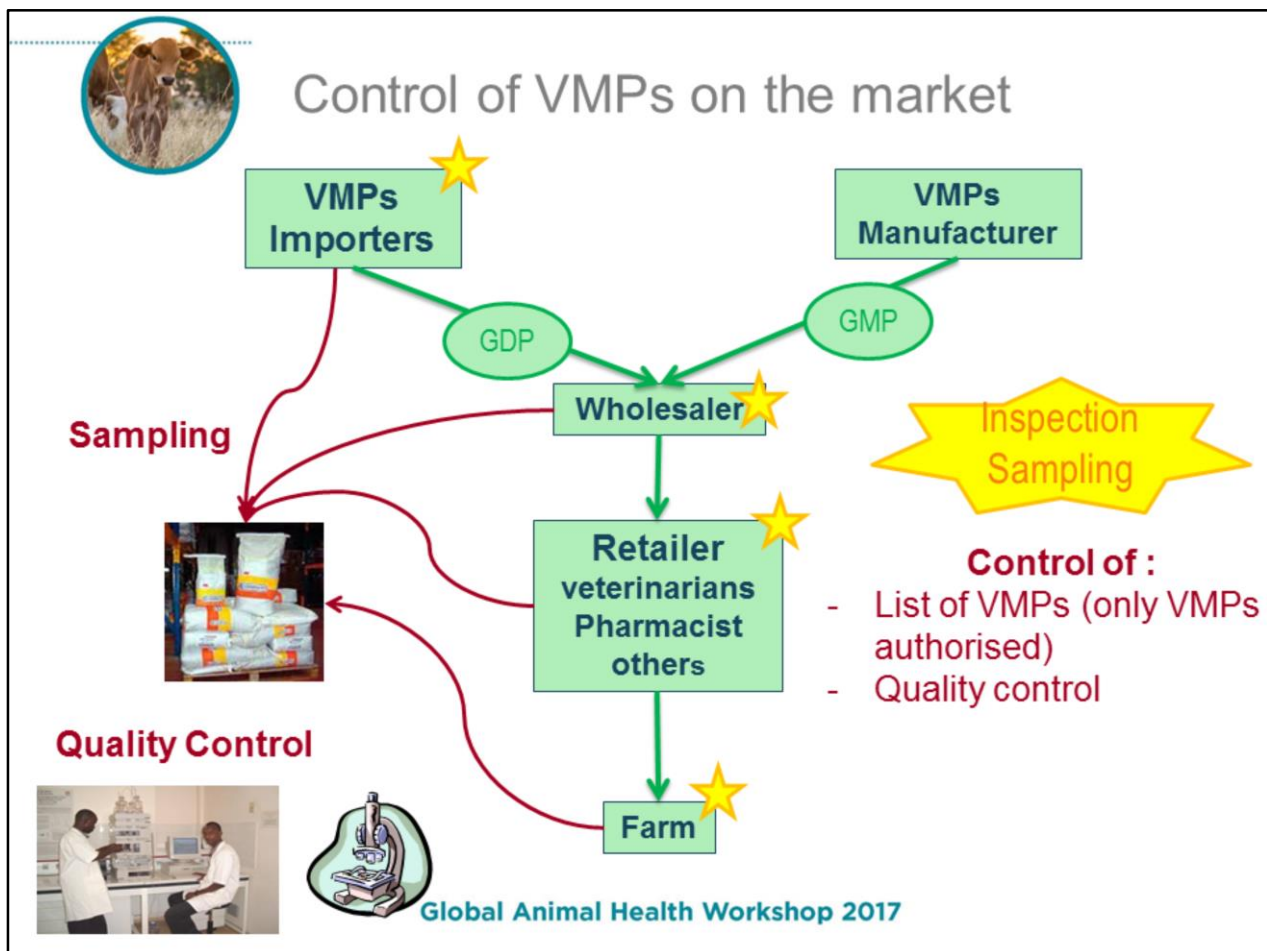


Surveillance

- Legal Market
- Counterfeit products

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- It is also recommended to conduct quality control of the VMPs put on the market
- Sampling should be conducted at all steps of the VMPs chain if that is possible : importer, manufacturer, wholesalers, retailers and at farm.
- The legal framework shall give the power to the inspector for conducting sampling and define the conditions of sampling.
- Countries should have an official laboratory for quality control of VMP. It can be common for quality control of veterinary and human medicines as most of the analysis are similar. This laboratory shall be qualified.



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

...

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- A programme of control shall be defined each year based on a risk analysis.
- The risk analysis depends on the organisation of the VMP chain in the country and of the results and finding of inspection :
 - Majority of import ?
 - Existence of illegal import
 - Existence of counterfeit...
- The risk analysis depends also on the category of product :
 - For food producing animal
 - Sterile or not
 - Antibiotics...
- Another criteria could be the volumes of sales to control first the most used VMPs.



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)

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- Modality of sampling and quality control



Counterfeit products

- ▶ Copy of Authorised products
 - Modification of qualitative or quantitative active ingredients
 - Differences in the labelling
- ▶ Need for National, Regional and international cooperation
- ▶ Internet sales (a concern)

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- Counterfeiting is a really concern which may have direct impact on animal health or human health depending on the nature of the counterfeiting : it could be
 - A modification of the quality of active ingredient : replace by the same ingredient but not the good quality (less expensive), or another active ingredient which residues could be very hazardous for human ;
 - A modification of the quantity of active ingredient : zero active ingredient, or not the good dosage, the adequate quantity which means that the medicines will not be efficient
- Without analysis it is very difficult some time to detect counterfeiting. Sometimes the counterfeit product are identified by their labeling which are not similar to the original one. The control of label are interesting for that and a specific plan of label control could be implemented.
- Counterfeiting, illegal import are illegal activities developed through network and regional cooperation with neighbored countries could be interesting for exchanging information and alerting each other of the existing traffic.
- Sales on internet could also be a concern as the control are not easy and it is sometimes very difficult to identify the actors. Some sampling made by buying VMPs on internet might be also interesting.



Counterfeit products



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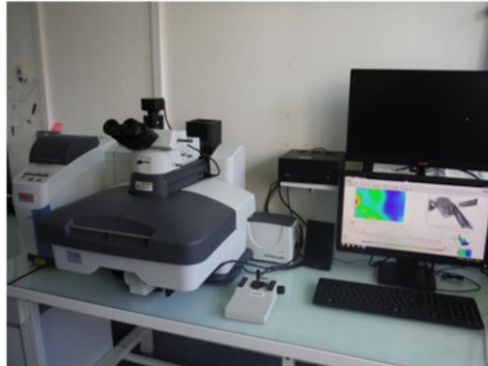
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- Example of counterfeiting : have a look to these two labels
- There are differences in the logo of the company and in the typology of the letter



Quality Control Laboratory

- ▶ Need for laboratory capacities to identify, analyse counterfeit products



RAMAN SPECTROMETER

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- Example of an interesting tool to detect counterfeiting : spectrometry RAMAN
- It gives the possibility to compare quickly the similarity of product's spectrum with a referred spectrum for this product.
- So any differences of quality of the compounds or big differences in quantity of active ingredient could be detected.
- To be efficient, you shall first constitute a library of spectra of good quality product.



A specific issue: retail at village market level



(photos : Dr. Albert Doufissa. Présentation " What is Needed to Improve Availability to Good Quality Veterinary Drugs and Vaccines.")

- ▶ Access to medication is not enough in entire regions
- ▶ Little or no money for assistance to farmers
- ▶ Farmers resignation or no awareness of the importance of quality
- ▶ The size of some packaging remains a problem for many breeders
- ▶ Imports sometimes heavy and slow procedures.



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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



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- Control at farm level are also very important to detect if the farmer use authorised VMPs, if these come from illegal market or not through control of invoices.
- The farmer shall also respect the conditions of storage, administrate the VMPs in compliance with the prescription and record all treatment realised on the animal



Issues to be discussed

- ▶ Do you have qualified laboratory for quality control of VMPs ?
 - For all VMPs ?
 - Vaccines ?
- ▶ Are you confronted to counterfeiting ?
 - Do you have equipments for their analysing ?
- ▶ Do you conduct inspection
 - On retailers?
 - On farm ?

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