I. INTRODUCTION TO GENERAL PHARMACOLOGY

a) Pharmacology

It is defined as a study of drugs properties and all aspect of their use and interaction with the organism (Arturo A.2016). Drugs is any chemical product other than food, that is used to treat, to prevent, to diagnose diseases and control physiological process. The pre requisite knowledge of clinical and non-clinical discipline such as chemistry,biochemistry, biology, physiology, pathology, toxicology and medicine. The study of drugs as experimental science deal with drug properties and their effect on living organism. It tackles the source of drugs (Pharmacognosy), magnitude and time elapsed for observed pharmacological effect (Pharmacodynamic), the relationship between the administered dose, observed tissue concentration and the time in the body (Pharmacokinetics), its use in disease treatment (Therapeutic) and poisoning effect (Toxicology).

b) Terminology

Pharmacokinetic: is a mathematic description of the rate and extent of uptake, distribution and elimination of drug in the body. Pharmacokinetics is the study of drug absorption, distribution, biotransformation (metabolism), and excretion. Pharmacokinetic processes affect the route of administration, doses, dose intervals, and toxicities of drugs given to animals. It gives an insight on the Absorption, Distribution, Metabolism, and Elimination (ADME) principles which are the key processes of the drugs into the body. PK gives a better insight and understanding of the drug withdraw time in producing animal for the sake of preventing residues persistence in tissue or edible product from food producing animals.

Pharmacodynamics: refer to the effect of drugs and their mechanism of action. It includes biochemical and physiological effects. Briefly, PK deals with how the body affects the drug whereas PD deals with how the drug affects the body.

Potency VS efficacy:

Efficacy: is the maximum response a drug can produce/results whereas **Potency** is the measure of the dose that is required to produce the response.

Example:

Drug A produce complete eradication of premature ventricular contraction (PVCs) at a dose of 5mg, a drug B help to achieve the same intention at a dose of 15mg. Therefore, both drugs have the same efficacy but drug A is more potent than drug B which literally mean that it need more of drug B to produce the same effect. Another drug C eradicates PVCs at only 60%; therefore drug C has less efficacy and less potent in therapy of PVCs.

Drug distribution: is a process whereby a drug is carried from the site of absorption to the site of action.

Adverse drug reaction: is any undesirable or unintended reaction/consequences of the drug to the recipients organism. Eg:

i. Ulceration of the GIT following long term administration of corticoids
ii. Immune suppression of the patient following therapy with Steroids

They are classified into Minor, moderate, severe and lethal.

- ***Mild/ minor adverse reactions***: requires no antidote, therapy, nor is prolongation of hospitalization necessary.
- ***Moderate adverse reactions***: this requires a change in drug therapy or dosage regimen, although not necessarily cessation of the drug.
- ***Severe adverse reactions***: potentially life-threatening, causes permanent damage, requires discontinuation of the drug and specific treatment of the adverse reaction.
- ***Lethal adverse reactions***: directly or indirectly contributes to the death of the patient.

Prevention of adverse drug reactions

- ✓ Adverse drug reactions can be minimized but not altogether eliminated by observing the following practices:
  Avoiding all inappropriate use of drugs in the context of patient's clinical condition.
- ✓ Using appropriate dose, route and frequency of drug administration based on patient's specific variables.
- ✓ Taking into consideration previous history of drug reactions including allergic diseases.
- ✓ Ruling out possibility of drug interactions when more than one drug is prescribed,

Side-effects: These are unwanted, but often unavoidable drug effects that are predictable from the drug's pharmacological effects, and occur within therapeutic doses. For instance; the use of Xylazine as premedication and resulted into vomiting as side effect,

Secondary-effects: they are direct consequences of a primary action of the drug, e.g suppression of gastrointestinal bacterial flora by oral administration of tetracyclines resulting in diarrhoea.

Drug toxicity/Over-dosage toxicity: This is predictable toxic effect that occurs with dosage in excess of the therapeutic range. Some over-dosage toxicity may occur because of drug accumulation caused by the patient's ineffective renal excretion or hepatic metabolism (Renal and Hepatic failure respectively).

Lethal dose 50 (LD50): This is a dose that kills 50% of the animals.

Effective dose 50 (ED50): A dose that produces the desired effect in 50% of the subjects is termed the ED50.

The therapeutic index (or margin of safety): The ratio of LD50 to ED50 and is a guide to the drug's safety. The more TI, the safer the drug is.

Teratogenicity: the ability of the drug to cause fetal deformity/ fetal development changes when given to pregnant animals.

Carcinogenicity: is the ability of the drug to induce/cause or promote neoplastic change,

Drugs withdraw time: is a period of time between the last injection and the time when the product in the body tissue falls below the tolerance. In this case, the drug should not be detected in food (milk, meat, eggs or their byproduct).

c) Drug handling and storage

Proper storage facilities improve medication effectiveness and reduce treatment errors. The ideal location for a storage unit is a clean, dry, frost-free area, such as a farm office or utility room. Animal health products should be protected from changes in temperature, sunlight, dust, moisture, animals, and insects. A clean, organized refrigerator makes an ideal drug storage unit. An example of veterinary product that is affected by incorrect storage temperature vaccines containing modified live organisms will have markedly reduced effectiveness if stored at room temperature. Most antibiotics are heat sensitive. Store these products in a refrigerator at a temperature between 2° and 8° C. to maintain potency. Many other products require storage in a cool (below 15° C.) but non-refrigerated location. Check product labels for information on acceptable storage temperature.

Product decomposition may result from exposure to light. Manufacturers package light-sensitive products (e.g. injectable tetracyclines) in lightresistant containers. These should be kept in a lightproof storage unit. Different classes of products (e.g. antibiotics, vaccines, dewormers, etc.) should be stored on separate shelves. This will further reduce the potential for error in product selection; label shelves to maintain an organized storage unit. The later should be locked to prevent access by children or unauthorized individuals.

Photo©RCVS

Inventory management

The on-farm veterinary medicine inventory should be managed according to the following procedures:

- Purchase drugs in quantities which will be used in a reasonable amount of time.
- Check product expiry dates before purchase.
- Clean and reorganize the drug cabinet on a regular schedule.
- Use products with older expiry dates first
- Discard all expired products.

Safe disposal of livestock medicines is essential to protect farm employees, family members, untreated livestock, and the environment from accidental exposure to potentially hazardous chemicals. Many veterinarians and manufacturers will accept returns of products at the location of purchase. It is prohibited to reuse livestock medicine containers as it may be a hazardous. Proper storage and handling of veterinary medicines ensures drug effectiveness and reduces potential for treatment error.

II. CLASSIFICATION AND USE OF DRUGS

1. General consideration

Chemical drugs are generally administered to an animal to combat disease causing agent and try to extend the life of an organism. For any type of drugs to be used /selected; there must be criteria of selection including safety, efficacy, cost, accessibility, etc.

2. Classification of drugs

Drugs can be classified into various categories based on different existed criterions. There is broad classification based on the intention of use therefore can be categorized into antimicrobials, anti-inflammatory, growth promoters, anti-parasitic and insecticides. However, veterinary drugs can be grouped into a very complex system. Detailed classification is as follow:

1. **Antibiotics**: also called antimicrobials, they are used against bacteria pathogens either by killing disease causing organisms or inhibiting their growth and multiplication.
2. **Antiprotozoal**: there are others microorganism that have complex structures that differs from that of bacteria and lender most of the antibiotics ineffective against them. Protozoal diseases such as trypanosomias, babesiosis, Anaplasmosis, coccidisosis, etc are very economical diseases that need serious and specific therapy.
3. **Anti-helminthic drugs**: they majorly act against internal parasites; the later are into three categories: Cestode, nematodes and trematodes.
4. **Anti-inflammatory**: these are specific drugs that are used to minimize/ reduce the inflammatory reaction of the body in the course of infections regardless of the cause of that infection. There are two main types namely Steroidal and Non steroid anti-inflammatory drugs (NSAID vs SAID)
5. **Tranquilizer and Sedatives**: products in this category work efficiently to render animals unconscious and weak (unaggressive). They are used when an animal are exposed to great pain or in case of traumatic condition. They are used in minor surgical operations.
6. **Anesthetics:** Anesthetics work in similar way like sedative and tranquilizer but in an intense way thereby causing complete loss of consciousness. They existed in different forms namely inhalation, injectable and ingestion/PO products.
7. **Antihistamines**: they are class of products that act against allergic reaction in the body caused by histamines and cytokines in the body regardless of the cause.
8. **Corticosteroids**: this is class of drugs that are of paramount important due to the fact that they substitute hormones that increase body energy and regulate fluid in the body in many life threatening conditions. Eg: Cortisol and corticosterone
9. **Hormones**: These are product that are used to control and correct reproductive pattern of animals. They are typically used in case of reproductive failure due to hormonal imbalance.
10. **Vitamins**: they are essential products that are part of nutrition and their deficiency cause many more problem which can be overcome by supply of vitamin, they goes together with minerals(Essential minerals) such as Phosphorus, Potassium, Magnesium, calcium

etc. Phosphorus is also called Energetics due to the fact that they are used to restore energy and provide muscular strength. Its deficiency is often diagnosed in higher producing animals. They are in form of ATP.

11. **Antiseptics & ant maggots**: these are chemical products that exist in different forms. They are used for therapy of wound and works better if combined with other drugs. They are topically and locally used.
12. **Insecticide and Acaracides**: they are applied topically to kill external parasites (lices, ticks, mites) of the skin and their range of toxicity is common if not used with properly.
13. **Infusions**: also known as fluids; Fluid therapy is a very essential lifesaving medication if serves to restore fluid loss. They act quite well if the right type, right dose is given.
14. **Vaccines:** Used for preventive purpose
15. **Antiviral, antifungal and antineoplastic**: they are less common in veterinary practices, but may be used in case they are required and human product can be used as an option especially in small animal. Lastly, Feed supplement such as vitamineral mixture, enzymes, probiotics, calcium supplements, and others are also part of veterinary drugs are essential for production and growth.

a. Antibiotics

Like any other drug, antimicrobial therapy is based upon the selective toxicity of the drug for invading organisms rather than mammalian cells. It is important to select an agent to which the organism is sensitive and to maintain the effective tissue concentrations (above the minimal inhibitory concentration or MIC) until the infection is eliminated. A practical approach is to select an antimicrobial agent where the measured MIC is less than the concentration known as the breakpoint concentration. Sensitivity tests using sensitivity disks can be used to estimate the MIC of specific bacteria and then tables are consulted to see if the MIC is below the breakpoint

It is pointed out that the sensitivity tests and breakpoints are useful indicators for the clinical outcome, but in the whole animal, additional factors like drug binding, drug distribution, and an active immune system affect the outcome so that clinical experience is still essential.

The following are criteria of antimicrobial classification:

a. Mechanism of action
b. Effective spectrum
c. Form of administration
d. Chemical nature/ structure

Simply, the mechanisms of action of antimicrobials are either killing the pathogens or inhibiting their growth and multiplication. This occurs in various way including inhibition of the cell wall

synthesis, inhibition of ribosome function, inhibition of nucleic acid synthesis, inhibition of folate metabolism and inhibition of cell membrane function which stop bacteria pathogen from harming the host cells or kill it at all. The following are class of antibiotics according to the chemical nature or structure.

i. Tetracycline

Tetracyclines possess antibacterial activity by binding to the 30S ribosomal subunit of a susceptible organism. Following ribosomal binding the tetracycline interferes with the binding of aminoacyl-tRNA to the messenger RNA molecule/ribosome complex; this disrupts the bacterial protein synthesis. Tetracycline binds with the 70S ribosomes found in mitochondria and can also inhibit protein synthesis in mitochondria. Tetracyclines are bacteriostatic and illustrate great affectivity against multiplying bacteria. Tetracycline is a broad-spectrum antimicrobial and used for a wide variety of Gram-positive and Gram-negative bacterial infections.

Examples	Chlortetracycline, oxytetracycline, doxycycline, minocycline
Mechanism	Bacteriostatic
Spectrum	Broad spectrum. Exhibits activity against a wide range of Gram-positive, Gram-negative bacteria, atypical organisms such as chlamydiae, mycoplasmas, rickettsiae and protozoan parasites
Examples of use	Tetracyclines are primarily indicated in the treatment of borreliosis, brucellosis (usually in combination with rifampin or streptomycin), chlamydiosis, ehrlichiosis, leptospirosis, listeriosis, rickettsiosis, and tularemia

ii. Fluoroquinolone

Examples	Enrofloxacin, Danofloxacin, Marbofloxacin, Orbifloxacin
Mechanism	bactericidal
Spectrum	Broad spectrum – 3rd generation fluoroquinolones Narrow spectrum – other fluoroquinolones

Examples of use	**Ruminants:** acute respiratory disease, E. coli, Salmonella, Mycoplasma, mastitis, metritis, conjunctivitis **Swine**: Mycoplasma hyopneumoniae, Actinobacillus pleuropneumoniae, E. coli and Pasteurella multocida **Horses:** for infections with bacteria resistant to the first drug of choice; not recommended in young growing horses **Dogs and Cats**: prostatitis, mastitis, rhinitis, pyoderma, otitis, wound infections, peritonitis, osteomyelitis, and soft tissue infections; not recommended for use in animals <8 months of age (or <18 months of age for large breed of dogs to avoid arthropathic effects

iii. β-lactam antibiotics

Examples	Penicillin; Penicillinase-resistant penicillin (methicillin; oxacillin);extended spectrum (ampicillin, amoxicillin); cephalosporins, Carbapenems, Monobactams
Mechanism	Generally bactericidal
Spectrum	Broad-spectrum: carbapenems, 2nd, 3rd and 4th generation cephalosporins; Narrow spectrum: penicillin, 1st generation cephalosporins, monobactams
Example of use	**Ruminants:** Anthrax, listeriosis, leptospirosis, clostridial and corynebacterial infections; streptococcal mastitis, keratoconjunctivitis Swine: erysipelas, streptococcal and clostridial infections **Horses**: Tetanus, strangles, other strep and clostridial infections, foal pneumonia **Dogs and cats**: streptococcal and clostridial infections, UTI **Poultry**: Necrotic enteritis, ulcerative enteritis, intestinal spirochetosis

iv. Sulfonamide

Examples	Sulfadiazine, sulfamethoxazole, sulfadoxine
Mechanism	bacteriostatic
Spectrum	Broad-spectrum; affects Gram-positive and many Gram-negative bacteria, toxoplasma and protozoal agents
Note	Act synergistically (and becomes bactericidal) in combination with diaminopyrimidines (trimethoprim)

v. Aminoglycosides

Examples	Gentamicin, tobramycin, amikacin, streptomycin, kanamycin
Mechanism	Bactericidal (dose dependent)
Spectrum	Broad spectrum but NOT effective against anaerobic bacteria
Examples of use	Due to its toxicity, aminoglycoside use has been clinically limited to severe infections. The more toxic antibiotics in this class have been restricted to topical or oral use for the treatment of infections caused by Enterobacteriaceae. The less toxic aminoglycosedes are used for parenteral treatment of severe sepsis caused by Gram negative aerobes
Side effects	Nephrotoxic and ototoxic
Note	Not effective against anaerobic bacteria

vi. Chloramphenicol

Mechanism	Bacteriostatic
Spectrum	Broad

Examples of use	Anaerobic infections in companion animals, such as serious ocular infections, prostatitis, otitis media/interna and salmonellosis
Side effects	Bone marrow depression, may compromise antibody production if given prior to vaccination. Anaphylaxis, vomiting and diarrhea reported in dogs and cats
Note	Because of its capacity to cause fatal aplastic anemia in humans, chloramphenicol is prohibited in food animals in many countries.

vii. Lincosamides

Examples	Lincomycin, Clindamycin and Pirlimycin
Mechanism	bactericidal or bacteriostatic, depending on the drug concentration, bacterial species and concentration of bacteria
Spectrum	Moderate-spectrum; primarily active against Gram positive bacteria, most anaerobic bacteria and some mycoplasma
Use	Clindamycin has an excellent activity against anaerobes; Swine: dysentery and mycoplasma infections (lincomycin) **Cattle**: used as intramammary infusion in mastitis (pilrimycin); **Dogs and cats**: for infections with Gram positive cocci and anaerobes **Poultry**: for the control of mycoplasmosis (usually in combination with spectinomycin) and necrotic enteritis
Note	NOT for equines

viii. Macrolide

Examples	Erythromycin, Tylosin, Spiramycin, Tilmicosin, Tulathromycin, azithromycine, etc

Mechanism	Bacteriostatic
Spectrum	Narrow (Gram positive bacteria, gram negative coccus and Mycoplasma)
Use	Erythromycin: against Campylobacter jejuni, anaerobic infections Tylosin and spiramycin: Mycoplasma infections Tilmicosin: against Mannheimia, Actinobaciullus, Pasteurella, Mycoplasma
Note	Parenteral use of tylosin in horses has been fatal, while oral administration has no indication for use and might result in enterocolitis. Tilmicosin can be fatal to pigs if given parenterally, and is not recommended for use in goats due to toxicity.

b. Prudent use of Antibiotic

Antibiotics are essentially used to treat bacterial (and some parasitic) infections. Incorrect use of antibiotics leads to bacteria which are resistant to antibiotics. Infections with resistant bacteria are difficult and sometimes impossible to cure leading to poor welfare of animals and humans. Therefore it is important that animals health professionals know how to use antibiotics effectively and responsibly (Animal welfare training manual_WTS,2020). Antibiotics are used to treat or prevent bacterial infections and some parasites. Antibiotics have no or negative effect on viral and fungal infections. However, in most cases, they are used during viral infection to fight against second bacterial infection. They should never be used to compensate malpractices, lack of hygiene and husbandly deficit.

What are the bases to choose antibiotics to use?

Antibiotics choice is based various criteria among which product characteristics are the main to put in account:

1. **Effective spectrum:** this refers to the range of activity of antibiotics, whether narrow or broad. Narrow spectrum antibiotics are used when there is knowledge of the exact causative agent whereas broad spectrum antibiotics are used widely when there is no clue on the causal of infection.

2. **Resistance situation:** Resistant bacteria are able to withstand attack by antibacterial drugs, so that standard treatments become ineffective and infections persist, increasing the risk of spread to others
3. **Effect:** the effect is defined as bactericidal or bacteriostatic
4. **Therapeutic index:** simple means the range from therapeutic effect to toxicity
5. **Tissue penetration:** Ability of the product to enter body tissue Eg: BUB,BBB
6. **Form of administration:** the rout via which the drug is applied(topical, oral, parenteral,
7. **Effect duration:** this stands for how long the drugs take in the body tissue, from absorption till excretion (**ADME principles**). Is either long acting or short acting.

Antibiotics abuse and misuse contribute dramatically to the emerging antimicrobial resistance. Several malpractices play a key role in development of AMR. The following are some of the causes:

- Unspecific use of AB
- Premature termination of therapy
- Sub therapeutic dose
- Extended and repeated use of antibiotics
- Mass treatment

There are other factors to consider when choosing antibiotics to use. Animal related factors such as age, physiological status, species and breed are among the key element to put into account. Furthermore, accessibility of the product on local market is another aspect to consider in this case. Antibiotic sensitivity test is the most appropriate method to identify which drug is most effective /appropriate for a given bacterial infection.

Principle of combination therapy: combination therapy refers to the use of more than one antibiotic to have maximum/ added effect. They should be synergetic rather than being antagonistic.

Eg: Sulfonamide and trimethoprim, Penicillin and streptomycin

Some combinations of antibiotics can intensify side effects, trigger cross-resistance or inhibit each other‘s effect on the bacteria. Bactericidal and bacteriostatic drugs can never be combined.

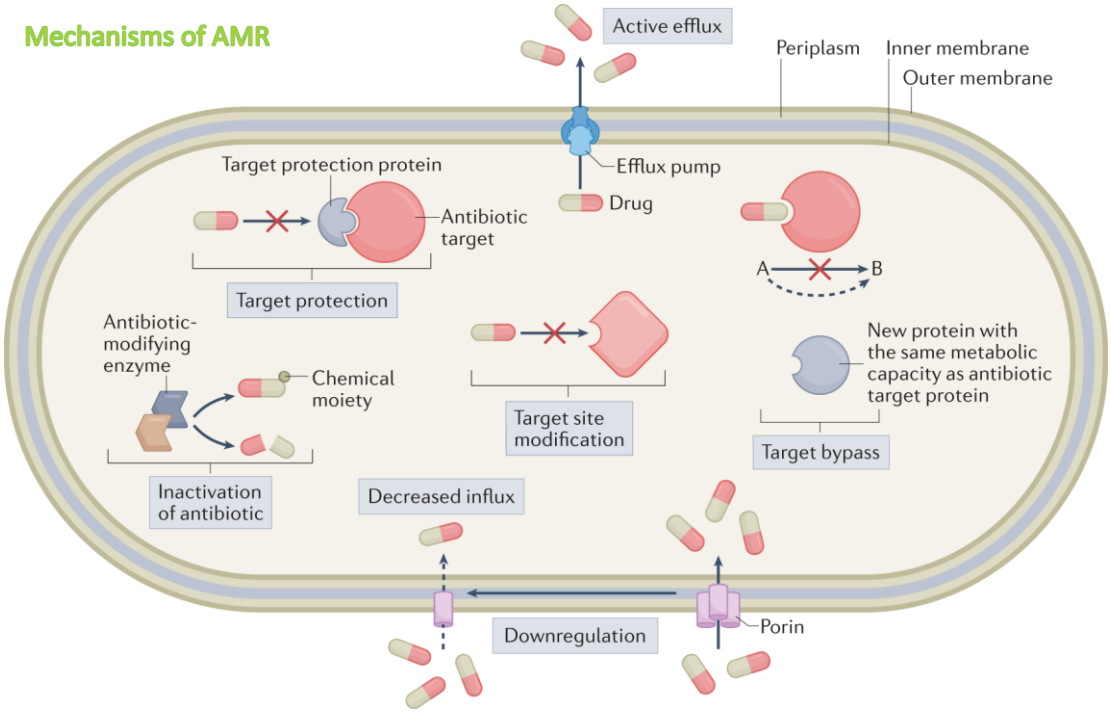
c. Antimicrobial resistance (AMR)

Definition:

It is the failure of drug/antimicrobials to exert its intended action/effect on pathogenic agent that was previously able to affect. Resistant bacteria are able to withstand the effect of the drug which renders the treatment ineffective and brink the risk of continuous spread of the pathogen to other animals.

Public health point of view:

FAO stated that AMR will contribute to 10 million human deaths per year in the world and 10 percent loss of production in the livestock sector in low-income countries by 2050. It is therefore crucial that livestock producers are aware of the risks caused by AMR, not only to protect human health but also to ensure the effectiveness of antimicrobials as a remedy for animal diseases to allow profitable food production. Unnecessary use of antimicrobials in both human and animals allow resistant microbes to survive while susceptible microbes are killed. Some of these resistant microbes are transmitted from animals to humans or vice versa through direct contact, through the food chain in animal products and possibly through the environment.



Note: Giving the right amount of drug is one of the key among many other mitigation measures to fight AMR. The right dose of drug is computed by the following formula:

$$Dose = \frac{\textbf{Body weight(kg)} * \textbf{ Dosage rate}(\frac{\textbf{mg}}{\textbf{kg}})}{\textbf{Conc}[\ ](\frac{\textbf{mg}}{\textbf{ml}})}$$

The body weight should always be counted; the dosage rate of a drug is how much mg of the principal ingredient per 1kg of given specie of animal and it is universal(never change) then the concentration simply means how much mg of the active ingredients we find in 1ml of given drug, always indicated on the bottle.

d. VETERINARY DRUG PRESCRIPTION

Veterinary prescription order is an order issued by a licensed veterinarians authorized drugs distribution to deliver veterinary prescription drugs to a specific client, or authorize pharmacists to dispense such drugs to a specific client.

The purpose of this instruction ***is to optimize the usage of veterinary drugs to prevent, fight against antimicrobial resistance***. Secondary, it has been designed ***to minimize the risk of drug residues in animal food products and lastly***, this was made to ***enable practitioners to fulfill their professional duties towards the customer, the public and the animals.***

Article 3: Prescriber of the veterinary prescription

Only practitioner who are registered in Rwanda council of veterinary doctors under the category of veterinary doctors or veterinary technicians and who do not possess a veterinary pharmacy are authorized to prescribe veterinary prescription drugs. For vet technicians, they must have served for at least 2 years.

The practitioner shall dispense only to the animal's owner or person responsible for the animals he/she is treating and only for conditions of being treated by that practitioner. The practitioner shall supervise the dispensing process.

Content of the prescription:

Article 4 stated that the inscription in the veterinary register must include the following:

- A chronological order number reported on prescription
- The name of the prescriber,address and phone number
- The number of registration certificate with RCVD and the license number as well
- Prescribed drug dosage
- The name and address of the client,

- The quantity delivered
- The manufacturing lot number of the medicine
- The date of issue.

In the clinic, the registration of veterinary prescription should be stored for 5years separately from over the counter drugs, and be easily distinguishable by the professional and paraprofessional staff. In article 5 of the instruction, veterinary prescription drugs should be dispensed only in quantities required for the treatment of the animal(s) for which the drugs are dispensed. The prescription will clearly indicate the name and address of the signatory. The maximum validity period of a veterinary prescription is **three months.**

In article no 6, it is stated that the drugs should be stored under condition recommended by the manufacturer and all drugs should be examined periodically to ensure cleanliness and current dating. The drugs are dispensed in package labelled with the following information:

- The dispensing practitioner's name, address and telephone number;
- The date the drugs is dispensed;
- The animal owner's name and the animal's or herd identification;
- The name, strength and quantity of the drug, directions for its use and any cautionary statement
- Withdraw interval after treatment

The instruction also specified the category of veterinary products to be prescribed only by a veterinary doctor among others:

- Antimicrobials
- Antiparasitic
- Analgesics and anti-inflammatory
- Cytotoxic agents and other systemic therapeutic agents
- Hormones
- Anti-histamines substances
- Atropine and
- Vaccines as veterinary biologicals

This instruction also planned disciplinary sanctions that will not obey any of the articles of this instruction with a possibility of prosecuting and punishing him/her under the penal code.

The committee in charge of veterinary inspection and the disciplinary committee are responsible for ensuring compliance with these instructions by the members of the council.

References

1. Arturo. Veterinary Pharmacology and toxicology front. Vet.Sci.,13 September 2016 Sec. https://doi.org/10.3389/fvets.2016.00082
2. Dowling A. et al. Mode of action and mechanisms of resistance, August 2017 Formatex Research Center. Editors: A. Méndez-Vilas. Web: (PDF) Antibiotics: Mode of action and mechanisms of resistance. (researchgate.net)
3. Information in the above article was derived from the OMAF Factsheet, "Storage and Handling of Livestock Medicines on the Dairy Farm."
4. Royal college of veterinary Surgeon (RCVS) 2020. Requirement for handling of controlled drugs and medicines,
5. Farm Safety Association, Proper storage of veterinary medicines, OMAF Factsheet, "Storage and Handling of Livestock Medicines on the Dairy Farm"
6. Amanda R. and Sally B., 2007. Veterinary pharmacology, practical guide for veterinary nurses. Pharmacy practices Pg 19-25, Elsevier, Edinburgh, UK
7. Riviere, J. Edmond (Jim Edmond), editor. | Papich, Mark G., editor. Title: Veterinary pharmacology and therapeutics / edited by Jim E. Riviere, Mark G. Papich. Tenth edition. | Hoboken, NJ : John Wiley & Sons Inc., 2018.
8. Walter H.Hsu 2008. Handbook of veterinary pharmacology, 1st Edition. Wiley-Blackwell, US
9. WTS. 2020. Animal welfare course module, Responsible use of antibiotics