# Responsible and prudent use of anthelmintic chemicals to help control anthelmintic resistance in grazing livestock species

WORLD ORGANISATION FOR ANIMAL HEALTH
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# Introduction

Antiparasitic resistance is an important challenge across the world, including all World Organisation for Animal Health (OIE) regions. This type of resistance poses a significant threat to animal health and welfare and can result in production losses in food-producing species, thus presenting a challenge for food security. There are currently no OIE guidelines or standards on antiparasitic agents.

The OIE first addressed this subject in the 4th and 5th cycles of its Training Seminars for the OIE National Focal Points for Veterinary Products. During these seminars, which were held worldwide, the OIE sought the views of its 182 Members on the potential need for OIE guidelines and standards on responsible and prudent use of antiparasitic agents. Standards and guidelines for antimicrobial agents already exist. The latter, entitled 'Responsible and prudent use of antimicrobial agents in veterinary medicine', can be found in the *OIE Terrestrial Animal Health Code*, Chapter 6.10., and the *Aquatic Animal Health Code*, Chapter 6.2.

In 2019, the OIE Electronic Expert Group on Antiparasitic Resistance was set up as one of the outcomes of the Training Seminars for Focal Points for Veterinary Products with the goal of producing a publication on the responsible and prudent use of antiparasitic agents to help control antiparasitic resistance. As part of this initiative, the Electronic Expert Group on Antiparasitic Resistance developed two surveys that were conducted in Africa; the Americas; Asia and the Pacific; Europe and the Middle East in 2020 and 2021 to assess antiparasitic agents and resistance and the prudent use of anthelmintic chemicals, respectively. The results are incorporated into this document, which focuses on anthelmintic resistance in grazing livestock. This publication could become the basis for OIE standards for responsible and prudent use of antiparasitic agents if such standards are considered warranted.

Cattle sale yards, Central Australia

Alpine goats on pasture. Goat gastrointestinal nematodes often develop resistance to anthelminthics.
As goats are very sensitive to gastrointestinal nematodes, it limits the use of grazing.

## Objectives of responsible and prudent use

Responsible and prudent use of anthelmintic chemicals includes implementing practical measures and recommendations intended to improve animal health and welfare while preventing or reducing the emergence, selection and spread of anthelmintic-resistant organisms in animals and humans and minimising residues in animal products for human consumption.

Such measures include:

- **ensuring the rational use of anthelmintic chemicals in animals** with the purpose of optimising their efficacy and safety;
- **complying with the ethical obligation and economic need** to keep animals in good health;
- **preventing and reducing anthelmintic resistance in parasites** within animal host populations, in the environment and between animals and humans;
- **maintaining the efficacy and usefulness of anthelmintic chemicals** used in animal and human medicine;
- **protecting consumer health** by ensuring the safety of food of animal origin with respect to residues of anthelmintic chemicals.

# Responsible and prudent use of anthelmintic chemicals to help control anthelmintic resistance

## Introduction

Helminth parasites (worms, helminths) of livestock can significantly decrease the production of meat, milk and fibre, as well as negatively impact animal traction used for land cultivation. Anthelmintic chemicals are antiparasitic agents that are a vital tool in parasite control. However, resistance to anthelmintic chemicals has emerged globally and now poses a significant threat to animal health and productivity. Prudent use of chemical and non-chemical means to manage anthelmintic resistance is a global goal. The aim of this document is to promote the prudent use of the few classes of anthelmintic chemicals that remain available for parasite control, with an emphasis on their use in food-producing ruminants such as sheep, goats and cattle. This paper covers definitions, the global extent of anthelmintic resistance and causes of resistance. It also discusses challenges that are central to resistance, such as the diagnosis of parasitism and resistance, livestock parasite management to reduce resistance, and the regulation of pharmaceutical anthelmintic chemicals. Lastly, this paper identifies gaps in essential knowledge and skills and highlights research and training needs. Its purpose is to inform advisors to animal food and fibre producers and farmers globally, equipping them with knowledge and skills that will foster prudent use of these important tools.

## Anthelmintic resistance

Anthelmintic resistance is the genetic ability of parasites to survive treatment with an anthelmintic chemical that has generally been effective against those parasites in the past. Helminths of ruminants that demonstrate resistance include roundworms (nematodes), tapeworms (cestodes) and flukes (trematodes). For nearly all these parasite species, livestock are infected by the ingestion of infective immature stages of the parasites during grazing. Anthelmintic resistance becomes a problem when an increasing percentage of a parasite population carries resistance genes, allowing increasing numbers of resistant parasites to survive and re-infect animals in a herd or flock. The gradual development of anthelmintic resistance is an evolutionary process within a given parasite population in response to chemical exposure that exerts selection pressure, killing sensitive parasites but allowing others with some resistance to survive. However, the speed, range and extent of the development of resistance can be greatly influenced by certain management factors. Risk factors that encourage an increase in the development of resistance are discussed subsequently in this paper.

Anthelmintic resistance is a One Health issue and is a major concern for farmers and consumers who rely on livestock, such as cattle, sheep and goats, to produce meat, milk and fibre. Parasitic diseases must be managed to maintain animal health and welfare and prevent subsequent production losses. In addition, resistance has been found in nematode parasites of horses and dogs. Anthelmintic resistance can negatively impact human health as some of these parasites are zoonotic (e.g. hookworms in dogs and some ruminant roundworms, such as *Trichostrongylus* spp. and liver flukes).

The level of government regulation of anthelmintics is a global challenge in the management of anthelmintic resistance. In some countries, anthelmintic chemicals are available only by prescription so their use can be more closely monitored by a veterinarian. However, according to OIE regionally distributed surveys, in most countries these chemicals are sold over the counter and do not require veterinary professional oversight, which may contribute to their overuse or inappropriate use.

The major classes of broad-spectrum anthelmintic chemicals available for use in livestock include:

- benzimidazoles
- imidothiazoles/tetrahydropyrimidines
- macrocyclic lactones
- salicylanilides
- amino-acetonitrile derivatives
- spiroindoles.

Within these classes, each anthelmintic chemical is characterised by a similar spectrum of activity (i.e. a range of parasite genera/species controlled) and a common mode of action. For example, doramectin and moxidectin are both macrocyclic lactones with similar spectra of activity and mechanisms of action. Parasites resistant to one member of a chemical class can be assumed to also be resistant to other chemicals in the same class to varying degrees.

In addition to those listed here, some other chemical classes with narrow activity spectra are used for specific cases in some countries. Triclabendazole, while a benzimidazole, does not follow this pattern. It is effective only against liver flukes (*Fasciola* spp.) and appears to have a different mode of action to other benzimidazoles. Additionally, not all classes or individual actives within a class of anthelmintic chemicals are available in all countries.

Anthelmintic chemicals are formulated into veterinary medicinal products (VMPs), which are registered for sale and intended for use in animals. Across classes, anthelmintic chemicals are available as VMPs in a wide range of dosage forms, including oral pastes, boluses (continuous or sequential release), drenches, medicated feeds, subcutaneous injections and topical applications. The route of administration can impact the pharmacological features of an anthelmintic chemical.

A herd of cattle in the northern zone at the Senegal River in the dry season.
The animals are positive for gastrointestinal polyparasitism (schistosomiasis, strongyloses, fascioliasis).

## Global state of anthelmintic resistance

Because ruminants are important in food production systems in every occupied region of the world, the development of anthelmintic resistance is a global threat to animal and human health, animal welfare and food security. The degree of anthelmintic resistance varies across the globe, but in most countries its true prevalence is unknown due to cost, time and the absence of national systems or other resources required for adequate surveillance. Livestock production systems both within and across continents may also be different, and generalised statements regarding the prevalence and causes of anthelmintic resistance cannot necessarily be applied globally. Resistance is also dynamic, meaning that it occurs over time and is influenced by many factors, such as the history and intensity of anthelmintic chemical use and other management factors. Such factors can impact when, where and how quickly resistance emerges. Generally, the same biochemical mechanisms of resistance within anthelmintic chemical classes and parasite species occur across the world, suggesting the same drivers (e.g. selection pressures, genetic variants in parasites) exist in many environments. Lastly, the diagnosis of resistance is not straightforward and may be performed sporadically using various diagnostic tools depending on the target host and parasite species. Therefore, differences in both global prevalence and regional reporting may reflect real differences, underestimates resulting from infrequent testing, or the inability of many animal health services to monitor resistance and collect such information. For more information on production systems and anthelmintic resistance across each global region, see Appendix 1.

The most common occurrence of anthelmintic resistance globally is found in roundworms of ruminants, predominantly small ruminants, and extends to a wide range of anthelmintic chemical classes. Resistance in liver flukes has also been described in several regions. Table I lists parasite species in ruminant hosts for which resistance has been reported.

**Table I.** Major parasite species for which anthelmintic resistance has been reported in ruminants

| Parasite | Sheep | Goat | Cattle |
|---|---|---|---|
| Nematodes | | | |
| *Haemonchus contortus* | ● | ● | |
| *Haemonchus placei* | | | ● |
| *Teladorsagia circumcincta* | ● | ● | |
| *Ostertagia ostertagi* | | ● | ● |
| *Trichostrongylus axei* | ● | ● | ● |
| *Trichostrongylus* (intestinal species) | ● | ● | |
| *Cooperia spp.* | | | ● |
| Trematodes | | | |
| *Fasciola hepatica* | ● | ● | ● |
| *Fasciola gigantica* | ● | ● | ● |

It is likely that resistance can develop to any anthelmintic chemical class. The extent of resistance (i.e. the percentage of helminths surviving treatment) and prevalence of resistance (the percentage of farms where resistance is present) to an anthelmintic chemical class in a particular parasite species varies widely. Examples from field investigations in specific geographical locations describe parasite populations in which resistance to most or all anthelmintic classes occurs simultaneously. Alternatively, in some situations, lack of efficacy of an anthelmintic chemical may be due to lack of good practice compliance rather than a result of resistance development. Systematic detection and monitoring will help in determining if true resistance has developed at a specific location.

## Methods to detect anthelmintic resistance

If anthelmintic resistance is suspected, it is most commonly detected by assessing the efficacy of an anthelmintic chemical against a population of parasites and comparing this efficacy to a threshold or standard and, ideally, a non-treated control group. One method to measure anthelmintic efficacy is a controlled slaughter test, in which animals are treated with an anthelmintic, sacrificed a period of time after treatment and necropsied to count the parasites remaining in the gastrointestinal tract. Although this is an accurate method for determining treatment efficacy, its use is typically limited to laboratory settings.

The most widely applied practical technique in the field to detect anthelmintic resistance of gastrointestinal helminths is the faecal egg count reduction test (FECRT). The FECRT is a mathematical calculation of the reduction in the number of parasite eggs in faecal samples. The mean reduction for a group compared to controls is calculated to derive the efficacy of the treatment, which can then be compared to expected efficacies. The confidence interval of the mean can also be calculated. Faecal samples are taken from individuals in a group of animals both prior to and after treatment with an anthelmintic chemical at its labelled dose, with the duration after treatment dictated by the anthelmintic chemical used. In some cases, an untreated control group is used to account for inherent changes in egg count between the two sampling times. The FECRT is a useful and practical tool that can be used to detect resistance on individual farms. Results can assist in assessing which anthelmintic chemical classes remain effective for a given group of animals.

It is important to assign an efficacy level with which to compare FECRT results so that resistance can be identified. International guidelines, such as those from the World Association for the Advancement of Veterinary Parasitology (WAAVP), have set standards for efficacy in this context. These are a reduction in post-treatment faecal egg count of >90% in cattle or >95% in sheep (associated with a lower limit of >90% for a 95% confidence interval). Faecal egg count reductions lower than these thresholds are classified as resistance. However, levels of resistance will vary from farm to farm within a region and over time, and a FECRT should be performed periodically to determine the effectiveness of a specific anthelmintic chemical at a given location.

Sheep in transhumance in the French Alps

To ensure confidence in the results, individuals should perform the FECRT in a standardised way and repeat the test routinely to assess trends. Methods to standardise the FECRT are described by the WAAVP.

A benefit of using the FECRT, compared to other diagnostic methods for the detection of anthelmintic resistance, is that it can be conducted on a farm without specialised laboratory equipment and with minimal training.

The FECRT method is a valuable tool and the most widely used technique to detect anthelmintic resistance, but there are some limitations to this method:

- Faecal egg counts can be less accurate in cattle compared with small ruminants because the lower egg numbers per gram of cattle faeces are near the limit of detection of standard egg counting methods. Accuracy can be improved by using more sensitive egg counting methods.
- In general, egg counts are not highly correlated to the actual worm burden within the animal.
- Egg shedding can vary widely between animals in a herd or flock. A few animals contribute most of the eggs shed on pasture (i.e. high shedders), while most of the animals have low rates of egg shedding. This variation demonstrates the value of collecting faeces from several members of a group of animals.
- As animals age, faecal egg counts fall owing to the development of host immunity to the parasites.
- The FECRT does not differentiate the parasite species present. Common nematode parasite eggs in cattle, sheep and goats, except for the *Nematodirus* genera, appear identical under light microscopy. Therefore, the information gathered from this test detects the presence or absence of resistance but cannot tell the investigator what species of parasites are contributing to this resistance. Nevertheless, most anthelmintic chemicals are broad spectrum, meaning that results of an FECRT are still helpful in making decisions on parasite control.

It should be noted that the detection of resistance using egg counts relies on the availability of a VMP with known concentrations of an active anthelmintic chemical. Therefore, the quality of a VMP has a large impact on the test results, and use of substandard or falsified preparations will make FECRT results unreliable.

The FECRT has been suggested for detecting the resistance of liver flukes (*Fasciola* spp.), but this approach has not been validated. Alternatively, testing for a decline in faeces *Fasciola* antigen following treatment can be used for assessing the resistance of liver flukes.

This method works similarly to egg count reduction tests except that it uses optical density in a standardised commercial ELISA (enzyme-linked immunosorbent assay) that has been validated against fluke counts. Faecal antigen can be used to detect immature flukes prior to egg production, and the mathematics used to calculate reduced optical density is the same as for the FECRT. Additionally, new diagnostic technologies are being continuously developed, including a variety of different molecular assays for other parasite species, and could be implemented if they become widely available.

# Development of resistance

## How resistance is selected

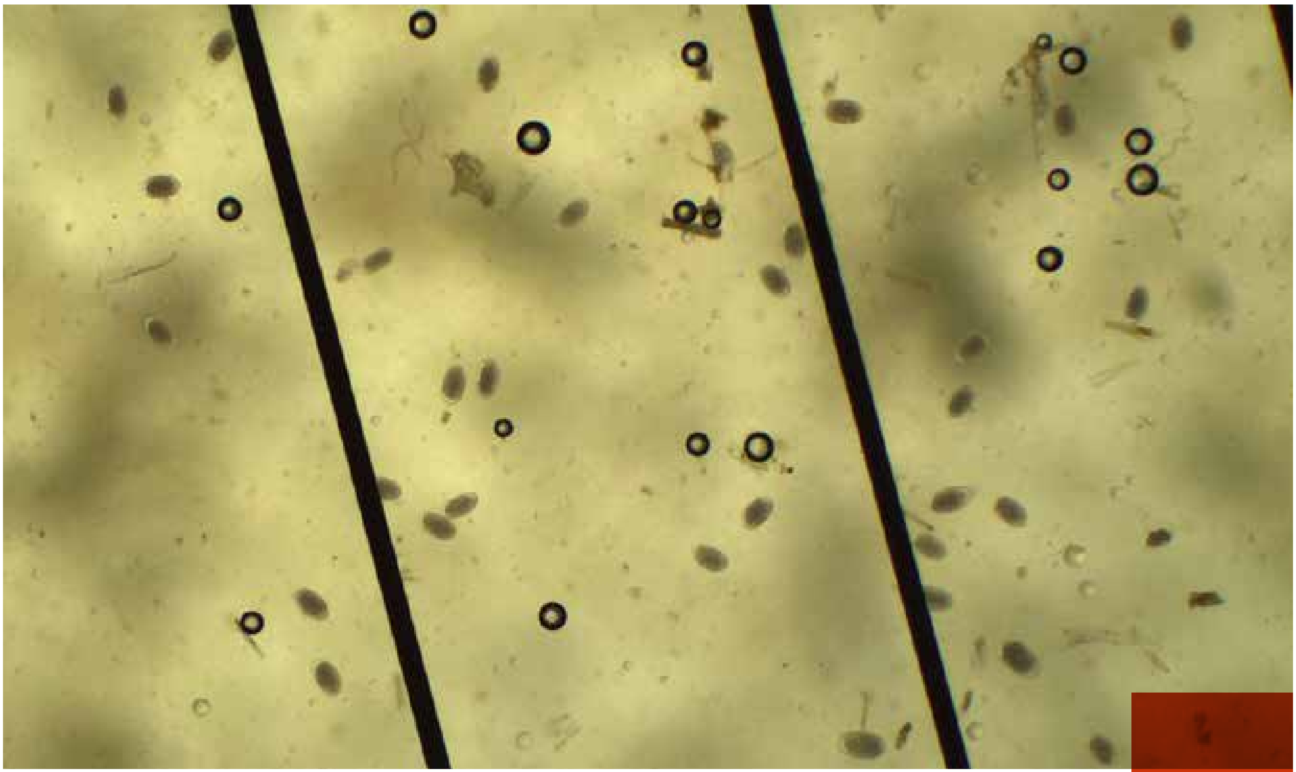
Parasites that survive anthelmintic chemical treatment designed to kill them carry genes that contribute to the resistance phenotype. These are typically in the form of natural variations of one or more genes between individuals in the parasite population. Resistance development further depends on the genes' heritability – how much the resistance phenotype can be attributed to genetic factors versus environmental factors, whether the genes are dominant or recessive and how many genes are involved.

For resistance to establish in a population of nematodes, three conditions must be met.

1. Worms with resistance genes are present before treatment (even at very low levels).
2. The proportion of worms with the resistance genes is amplified due to selection pressure (anthelmintic chemical treatment).
3. The offspring of resistant worms survive and are transmitted to hosts to form the next parasite generation.

The genetic makeup of parasites cannot be controlled, but appropriate management can reduce the selection and transmission of resistant parasites. The example of pasture refugia provides an illustration of how the dynamics of selection and transmission can operate. A refugium is a subpopulation of worms within the larger local population that is not selected by treatment of the host and may include free-living larval stages on pasture. In the absence of selection, these remain susceptible to the anthelmintic chemical. The parasitic stages in the host are not a refugium. When an animal is treated in the correct way and with the correct dose of an anthelmintic chemical, any surviving parasites within the host animal are resistant. These surviving resistant parasites then reproduce and pass eggs onto the pasture; the eggs, along with larvae that develop from them, thus contribute to the pasture population. If that anthelmintic chemical treatment occurred during weather conditions favourable to larval survival (e.g. moist and warm), then the many susceptible worms already on pasture dilute the proportion of resistant worms from the new eggs. However, if treatment occurred during adverse weather conditions (e.g. hot and dry), then the susceptible refugium will be small. When eggs from resistant worms fall onto pasture, their numbers might be low, but they contribute a large proportion to the pasture larvae that infect the next hosts. Thus, the population has the potential to quickly develop resistance to the anthelmintic chemical. As for transmission, if no animals graze the dry paddock for a long period, then all the parasites, including the resistant ones, will die, and the proportion of resistance genes in the population will decline.

Cattle in the dry marshy zone of the north at the Senegal River. The animals are positive for gastrointestinal polyparasitism (schistomsomosis, strongyloidosis, fasciolosis).



Eggs of maîtres-assistantes *Haemonchus contortus* seen on faecal floatation using microscopy

## Risk factors for resistance

Many factors are known to contribute to the selection of anthelmintic resistance within a given livestock population. These factors, and how they work together, are influenced by management systems, host animals, climate and weather patterns, the pharmacology of the anthelmintic chemical and the biology of the parasite species. Biological systems are complex and difficult to understand and predict; much of the available information on risks comes from examining field data and computer-based simulations.

The most important risk factors that can contribute to and increase the rate of anthelmintic resistance development are:

- parasite biology: pre-existing resistance genes, a short and direct life cycle, parasite fecundity;
- anthelmintic chemical dosage form;
- high treatment frequency of anthelmintic chemical use;
- antiparasitic agents given to control one parasite species but potentially selecting resistance in another (e.g. off-target selection of helminths when treating ectoparasite infections);
- loss of refugia for susceptible worms;
- introducing new animals that carry resistant parasites.

Management practices can be used to mitigate many of the risk factors listed above. However, some risk factors, such as parasite biology and fitness, are inherent and cannot be altered with management changes. Changes in management practices should be guided by two goals: to reduce selection pressure by anthelmintic chemicals and to reduce the chance that the offspring of resistant parasites will be transmitted to the next host. Several principles of management and approaches that help to slow the rate of selection for resistance are listed on the next page.

**Know the level of anthelmintic resistance by measuring it.**

- Use a standardised method such as FECRT and repeat over time.
- Use an anthelmintic chemical with efficacy against the parasite species present.
- Reduce treatment frequency where possible.
- Use full doses of a VMP as described on the label.
- Target for treatment only those animals that are infected or vulnerable.
- Use high-quality VMPs.

**Maintain susceptible worm populations.**

- Treat when refugia populations are high (e.g. when the environment is moist and warm).
- Avoid treating and then moving animals to pasture with few infective stages.
- Apply quarantine treatments with a VMP for newly introduced animals to prevent importing resistance.

**Use non-chemical control options.**

- Graze worm-contaminated ground with older livestock or other host species.
- House or tether animals to prevent access to infected pasture.
- Rotate pastures.
- Avoid overgrazing pastures.

**Develop parasite control plans with advisors to apply the recommendations above in ways best suited to the herd and environment.**

Adult mix-breed cows with calves on pasture in the state of Rio Grande do Sul, Brazil

## Availability of quality anthelmintic chemicals

The availability of good-quality anthelmintic chemicals with clear instructions for use is essential for effective treatment. The use of poor-quality anthelmintic chemicals can result in under-dosing, leading to failure to treat the parasitic infection and hastening the development of resistance. Where possible, farmers and producers should purchase VMPs from reputable sources and use products that are appropriately labelled and sealed, and that have been stored properly. The Responsibilities section below discusses the role of the Competent Authority in ensuring high-quality products are available for use.

## Practical methods to control parasites and reduce selection for resistance

The aim of resistance management is to control parasitic disease while minimising the development of resistance. Various countries have approached this issue in a range of practical ways using a variety of methods. The application of these methods depends on the parasites involved, the level of knowledge of parasite epidemiology in the locality, the severity of resistance and the animal management system. Possible methods are provided below as examples of what might be tested and applied in new situations. Specifically, knowledge of parasite epidemiology, anthelmintic chemical options and non-chemical control need to be applied in a strategic parasite control programme. This is referred to as integrated parasite management (IPM). Rather than a single approach, it is likely that farmers will require a combination of options to achieve sustainable control.

For each approach described below, the application is named and followed by a description of how it may be applied, in what situations it has been used or recommended and how it is expected to work to reduce resistance. It may be appropriate to modify these methods to suit the situation. The approaches have been separated into chemical approaches, where the aim is to reduce the rate of selection for resistance, and non-chemical approaches, many of which break the life cycle of the parasites.

### Chemical approaches in the use of anthelmintics

#### Targeted treatment

Targeted treatment includes one or more practical methods to estimate the severity of a parasitic infection and treat only the affected animals that meet predetermined thresholds. This method leaves some animals untreated within a herd, thus preserving refugia and lowering the selection of resistance, but still reduces the parasite load across the host population. One method of targeted treatment is to apply an anthelmintic chemical treatment to animals shedding the most eggs based on faecal egg count or those most clinically affected by parasitism. Examples of addressing the latter population include treating only individual animals below a certain body condition score or those animals with high faecal scores (e.g. dag score, a measure of faecal soiling of the perineal skin and wool due to diarrhoea). Another method is to use FAMACHA©, an on-the-farm test for sheep and goats that evaluates an animal's burden of hematophagous *Haemonchus contortus* (barber pole worm) based on the colour of the inner lower eyelid, which is linked to the degree of anaemia (www.wormx.info/famacha).


A veterinarian evaluates the colour of a sheep's eyelid using a FAMACHA© card to determine the level of infection with *Haemonchus contortus* (barber pole worm)

### Long-acting products versus short-acting products

Long-acting VMPs contain anthelmintic chemicals with longer persistence in the host. These products can therefore continue killing parasites, including new infections, for several weeks after treatment. Long-acting VMPs often have a long elimination phase (i.e. 'tail effect') during which selective pressure from gradually decreasing drug levels allows some resistant worms to survive. There is evidence that longer-acting VMPs tend to select for resistance more quickly than short-acting compounds owing to this tail effect. On the other hand, this effect may be offset by other factors that make long-acting VMPs preferable, such as the ability to achieve equivalent parasite control with fewer treatments. Therefore, it is prudent to use long-acting VMPs only when transmission of resistant parasites is unlikely to occur, such as in high-refugia situations.

### Combination products

Fixed combination VMPs containing active ingredients from two or more anthelmintic chemical classes that target the same parasite species are available in some countries. These combination VMPs may help slow the development of resistance when used together with other management practices in a herd or flock where resistance is still at low levels. In some countries, where resistance levels are high, combinations are used in parasite control programmes. However, experts are concerned that this approach may cause the development of resistance to multiple anthelmintic chemicals concurrently. Furthermore, in some countries, combination products may not be available. Considering the issues noted above, caution in the use of combination anthelmintics is advised. Because of the high prevalence and level of resistance worldwide, combination products should only be used strategically, while retaining susceptible refugia and with ongoing testing and evaluation, to minimise negative impacts on resistance. Additionally, VMPs containing combinations for non-overlapping indications (e.g. a nematocide plus a flukicide) should be used only when treatment for co-infections is needed.

Two or more anthelmintic chemicals given as a combination or given sequentially are often also used for quarantine treatments, whereby animals are dosed when they arrive at a farm and kept in a barn with regular manure disposal. Once parasite clearance is demonstrated via negative faecal egg count, they can be shifted to pasture. In this way, the spread of parasites carrying resistance genes can be avoided.

### Methods of application of anthelmintic chemicals

To reduce selection for resistance, maximising parasite kill is desired. To achieve this, full doses of VMPs should always be applied. Users must follow label instructions, calibrate application devices (such as oral drench applicators) and estimate animal weights so that a group of animals is treated at the volume appropriate for the heaviest animal. Application routes include oral, injectable and pour-on. There are reports that the use of some pour-on formulations of anthelmintic chemicals achieves relative under-dosing and there is concern that this will select for resistance.

## Non-chemical approaches to parasite control

Non-chemical methods of helminth control work by reducing worm burdens, increasing host resilience and immunity, and preventing transmission of parasites. These approaches work in two ways: they 1) reduce selection for resistance by reducing reliance on anthelmintic chemicals and 2) reduce transmission of parasites to the next host by breaking the helminth life cycle.

## Grazing management

A wide variety of grazing management practices may reduce the development of resistance. Certain methods may be better suited to particular herds, environments and production practices. Some examples are listed below.

- **Minimising overgrazing helps decrease an animal's exposure to infective larvae.** Most parasite larvae stay within 6 cm of the ground, so keeping good grass cover and not letting animals eat close to the ground reduces access to larvae. Reducing stocking density is one way to maintain longer grass.
- **Dragging or harrowing pastures to break up manure piles may help with the desiccation of parasite eggs in hot, dry conditions, thus lowering larval numbers.** Collecting and composting faeces can also kill larvae and help prevent transmission.
- **Rotating pastures by grazing with other livestock species that are susceptible to different helminths can help decrease the parasite burden within a herd.** For example, horses grazing a pasture prior to ruminants can lower larval numbers of ruminant parasite species by consuming the larvae with the grass. Co-grazing or rotating pastures between cattle and sheep can also help in this manner, but to a lesser extent, as these livestock species do share some parasite species.
- **Cell grazing regimens can be applied where several fenced grazing areas are available.** In these systems, animals are moved sequentially to new, uninfected paddocks and thus avoid picking up infective stages of parasites. This approach has been successfully applied with sheep in several environments around the world. The most successful examples are from hot climates, where larvae die quickly. For example, animals can graze a pasture for about six days before it becomes infective and return to the same paddock once larvae are dead. This timeframe can be as short as 80 days in hot climates.
- **Liver flukes have snail intermediate hosts that inhabit wet, swampy areas.** The fluke life cycle can be broken in two ways: by preventing contamination of snail habitats by animals' faeces containing fluke eggs and by stopping ruminant ingestion of infective stages (metacercariae) released from snails onto grass near water. Both can be achieved by restricting animal access to these areas with fences, although water troughs may need to be provided if access to open water is restricted.
- **Zero grazing can be an effective way to break the life cycle.** This may be achieved by cutting and carrying forage from areas where animal grazing has not occurred. This is practised in some environments where sheep or goats are kept in a pen or tethered. An extension of this idea is a management system in which animals are kept in yards or indoors and fed grain or hay.
- **Antiparasitic forages may be useful under certain conditions, but more research is needed to demonstrate efficacy.**

## Herd and flock management

Protecting vulnerable animals, such as the young and those with inadequate nutrition or poor health, from exposure to parasite infection is a useful approach in non-chemical control. Grouping animals by age within herds or flocks can also make diagnostic testing for parasites and treatment decisions more efficient. Additionally, having mature animals graze highly contaminated pastures can help reduce parasite eggs without the use of chemicals because, compared with young animals, mature animals have greater immunity to most gastrointestinal parasites. On farms with only mature animals, keeping animals on the best plane of nutrition possible is another way to keep animals healthy and increase their natural ability to endure a low level of parasitism without impacting their production values.

## Genetically immune hosts

Some breeds and lines of animals have superior genetic resilience against parasites and enhanced natural immunity, resulting in lower parasite burdens. This genetic benefit is heritable to varying degrees, and sheep breeding values have been developed to enable selection for rams with lower egg counts. Breeding with males displaying this characteristic and maintaining selection for superior immunity, including by not treating flocks with anthelmintic chemicals, has been effective in developing low-worm flocks in some areas.

*Haemonchus contortus* adult worms on the abomasal mucosa of a sheep at postmortem (France)

## Vaccines

Vaccines can stimulate protective immunity and lower worm burdens in animals. When available, they are a sustainable parasite control option and do not select for resistance. Few parasite vaccines are currently authorised, and when available, they are limited in spectrum (e.g. against *Haemonchus contortus* in sheep, lungworm *[Dictyocaulus viviparus]* in cattle and *Echinococcus granulosus* in ruminants). In general, these vaccines require multiple administrations and, even then, only aid in control and therefore must be used in conjunction with other parasite management tools.

## Integrated parasite management

The management options discussed above, which aim to optimise parasite control while preserving the activity of anthelmintic chemicals, should ideally be integrated into a management regimen. A starting point is understanding how the local weather conditions, geography and climate change can and will impact the efficiency of parasite transmission on pasture. For example, a hot, dry season can desiccate and kill parasite eggs on pasture, thereby reducing transmission to grazing animals. Conversely, warm, wet environments, such as in tropical or sub-tropical geographies, can hasten parasite transmission due to conditions that foster rapid larval development on pasture. This type of information, combined with an understanding of animal management, can contribute to an understanding of parasite epidemiology. This, in turn, is used alongside knowledge of resistance status, the available anthelmintic chemicals and locally relevant non-chemical parasite control options to form the basis of locally developed IPM.

# Responsibilities

## Introduction

In order to achieve the responsible and prudent use of anthelmintic chemicals, common efforts should be undertaken by all stakeholders involved in the authorisation, production, control, importation, exportation, distribution and use of VMPs containing anthelmintic chemicals. This list includes Competent Authorities, the veterinary pharmaceutical industry, wholesale and retail distributors, veterinarians and food animal producers.

All OIE Members should combat the unauthorised manufacture, compounding, importation, advertisement, trade, distribution, storage and use of unlicensed, substandard and falsified veterinary products, including bulk active ingredients, by using appropriate regulatory controls and other measures. Coordination of these activities at the national or regional level is recommended and may support the implementation of targeted actions by stakeholders and enable clear and transparent communication to users.

Flood risk area in the north of Senegal (river region) where schistosomiasis (animal and human) and cattle strongylosis has been raging – EISMV mission in Ndioum, Department of Podor

Helminth diagnosis

## Responsibilities of the Competent Authority

The Competent Authority responsible for granting marketing authorisations for VMPs should establish and implement an efficient regulatory framework to register anthelmintic chemicals for veterinary use and to monitor and regulate the safe and effective use of these chemicals once they are on the market (pharmacovigilance system). Through these actions, the Competent Authority can play a substantial role in promoting the responsible and prudent use of anthelmintic chemicals. In the absence of regulatory systems, monitoring the sale and use of anthelmintic chemicals is difficult to implement without statutory support.

The examination of marketing authorisation applications should include an assessment of the pharmaceutical quality, safety and efficacy of anthelmintic chemicals for the proposed indication. Data on quality should include information about the individual components of the anthelmintic chemical and manufacture of the VMP, as well as data on storage conditions and shelf life. Safety data should address the safety of the anthelmintic chemical not only for the treated animal, but also for people in contact with the anthelmintic chemical or for consumers of food derived from the animal. An assessment of the environmental impact of the proposed use should also be considered. A specific issue for macrocyclic lactones is to consider their potential impact on dung beetles and soil-dwelling organisms following use and disposal.

Efficacy and safety assessments should include laboratory and field data demonstrating the efficacy and safety of the product for the proposed dose and route of administration in the target species. The evaluation may also include consideration of the potential impact of the proposed use of the anthelmintic chemical on the development of resistance. Where appropriate, a Competent Authority may consider extrapolating study results from one species to apply to another species for anthelmintic chemical registration. However, differences in the pharmacokinetic profile of some anthelmintic chemicals exist between species, such as between sheep, goats and cattle. Consequently, drug registration should be based on specific pharmacokinetic studies for each combination of drug and ruminant species.

When assessing applications, the Competent Authority is encouraged to apply the requirements outlined in quality, safety and efficacy guidelines established by the International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products (VICH). Several guidelines, for example, describe tests and methodologies for assessing stability and environmental risk. There are also efficacy guidelines for anthelmintic chemicals used in specific host species. VICH guidelines are listed on the VICH website (vichsec.org/en/guidelines.html). In addition, the WAAVP has published recommended guidelines for determining efficacy that Competent Authorities may find helpful. A list of resources is provided in Appendix 2. Marketing authorisation should be granted based on data submitted by the applicant and only if the criteria for safety, quality and efficacy are met.

Countries that lack the necessary resources to implement an efficient registration procedure for VMPs containing anthelmintic chemicals may need to import these products from another country. When doing so, the following measures should be taken:

- establish effective administrative control mechanisms for the import of these VMPs, including border controls;
- evaluate the validity of the registration procedures of the exporting and manufacturing country, as appropriate, and clearly communicate the outcome of this evaluation;
- develop the necessary technical cooperation with experienced relevant authorities to check the quality of imported VMPs as well as the validity of the labelled conditions of use.

The Competent Authorities of importing countries should request that the pharmaceutical industry provide quality certificates prepared by the Competent Authority of the exporting and manufacturing country, as appropriate.

The label of a registered anthelmintic should clearly specify the indication, dose and administration instructions and display responsible and prudent use warnings and any other special conditions of use. Anthelmintic chemicals need to be stored appropriately to maintain their anthelmintic activity, and clear information about the storage conditions and shelf life should also be provided on the label. In addition to approving appropriate labelling, Competent Authorities should monitor advertising of these products. Advertising should only reflect evidence-based claims, and Competent Authorities should aim to ensure that it complies with relevant legislation and the marketing registration and discourage direct advertising to those not legally entitled to prescribe the anthelmintic chemical, when applicable.

A robust pharmacovigilance process should be in place to allow reporting of adverse findings and to monitor efficacy and safety of VMPs. The information collected through a pharmacovigilance programme, including lack of efficacy and any other relevant scientific data, could form part of the comprehensive strategy to minimise anthelmintic resistance. The Competent Authority should also work to prevent illegal manufacture of anthelmintic chemicals as well as to combat the sale and use of falsified and substandard VMPs. This may be accomplished by establishing a regulatory system with the Competent Authority to randomly sample or perform other post-market surveillance. To enforce this regulation, the Competent Authority should have access to laboratory analysis for independent verification.

Competent Authorities may also help reduce the inappropriate use of anthelmintic chemicals in food-producing species by requiring a veterinary prescription. Anthelmintic chemicals are available as registered VMPs in most countries, but their distribution, availability and use at the farm level varies widely. In many countries, veterinarians are not involved in the decision to use an anthelmintic and these products are available over the counter (i.e. without a veterinary prescription) or can be ordered with limited control via the Internet.

In other countries, such as those in the European Union, anthelmintic chemicals for food-producing animals are generally available only by veterinary prescription. Such restricted use can give veterinarians the opportunity to provide additional information on how to use the anthelmintic chemicals along with other control measures; however, care must be taken to ensure that such measures do not impede the availability of necessary medication to producers and farmers.

## Responsibilities of the pharmaceutical industry

The veterinary pharmaceutical industry is responsible for supplying all the information requested by the national Competent Authority, guaranteeing the quality of this information in compliance with the provisions of good manufacturing, laboratory and clinical practices, and implementing a pharmacovigilance programme. Data should comply with the requirements outlined in quality, safety and efficacy guidelines established by VICH. Ideally, companies should maintain compliance practices, including keeping records of sales, imports, manufacture, licensing and distributor sales. They should also maintain technical expertise so that problems and complaints can be properly addressed.

Labels should be approved by the Competent Authority and should accurately reflect the contents and instructions for use. In addition, companies should consider providing label information directing responsible and prudent use, including information on management of resistant parasites, and developing packaging and container sizes that discourage splitting, illegal labelling and dilution. The veterinary pharmaceutical industry should respect principles of responsible and prudent use and should comply with established codes of advertising standards, including distributing information in compliance with the provisions of the marketing authorisation. Appropriate marketing should be limited to the product claims for which the authorisation was granted.

The pharmaceutical industry is also well placed to collaborate with academia, veterinarians, the Competent Authority and others to educate farmers and other users on the prudent use of anthelmintic chemicals. This training should provide balanced information on appropriate and sustainable parasite management specific to individual farms.

## Responsibilities of wholesale and retail distribution

Distributors have a responsibility to store anthelmintic chemicals securely, record sales and maintain inventories of an authorised VMP. Retail distributors should keep detailed records – including, where applicable, date of supply, name of prescriber, name of user, name of product, batch number, expiration date, quantity supplied and copy of prescription – and attend appropriate training (for example, on appropriate storage conditions) as applicable. They should also provide secure supply lines and warehousing. Selling product in its original container and with original labels is essential, and distributors should also consider operating a container return service or container deposit system to help reduce container reuse.

## Responsibilities of veterinarians

The veterinarian is responsible for promoting public health, animal health and animal welfare, including through identification, prevention and treatment of animal disease. Ideally, veterinarians should engage with local farmers regarding animal health plans, including parasite control using non-chemical control methods, as promoting sound animal husbandry methods can help to reduce the need for anthelmintic products in food-producing animals.

Veterinarians should undertake and maintain training and remain familiar with current scientific thinking on the correct choice, use and administration of anthelmintic chemicals. They can add value by training farmers in anthelmintic chemical choice and use and providing a recording system to clients.

They also have a role on the front line in detecting and reporting safety and efficacy issues to the Competent Authority and testing for and providing localised accounts of anthelmintic resistance.

Appropriate training should be available to veterinarians on IPM, along with basic parasitology as provided in their formal veterinary education. Opportunities should be provided for veterinarians to update their knowledge of current issues regarding anthelmintic resistance, diagnostic methods and the prudent and responsible use of anthelmintic chemicals. Training could be provided by the Competent Authority, the veterinary pharmaceutical industry, academia or independent organisations.

Poultry ascaris

## Responsibilities of food animal producers

Food animal producers, with the assistance and guidance of veterinarians, are responsible for implementing animal health and welfare programmes on their farms in order to promote animal health and food safety. Food animal producers have a direct role in the responsible and prudent use of anthelmintic chemicals in their animals and should be encouraged to work with an advisor, such as a veterinarian, when deciding how to develop a parasite control programme, ideally integrating the following guidelines:

- draw up a health plan with the attending veterinarian that outlines preventive measures;
- use anthelmintic chemicals in accordance with national legislation;
- use anthelmintic chemicals in accordance with the instructions of the advising veterinarian or the product label instructions, including storage conditions and expiry date;
- comply with and record the withdrawal periods (also called 'withholding periods' or 'export slaughter intervals') to ensure that residue levels in animal-derived food do not present a risk for the consumer;
- dispose of unused and expired surplus anthelmintic chemicals under conditions safe for the environment;
- keep animal treatment records, as well as results of diagnostic tests (e.g. faecal egg counts, FECRT results);
- keep adequate records of all anthelmintic chemicals used, including dates and doses given;
- inform the attending veterinarian of recurrent disease problems and reductions in product efficacy;
- report adverse events to the attending veterinarian, Competent Authority and pharmaceutical company, as applicable.

Local breed goat from Crete

Education plays a vital role in the responsible and prudent use of anthelmintic chemicals. Food animal producers should participate in appropriate training programmes as provided by veterinarians, the Competent Authority, the veterinary pharmaceutical industry and other independent organisations to remain updated on current control methods and responsible and prudent use guidelines. Where possible, training programmes should be readily accessible to producers and provide practical advice for individual farms.

# Gaps in knowledge

Although anthelmintic resistance in livestock species is a global issue, there are many gaps in the understanding of its true prevalence, diagnostic tools and other practical management techniques to help slow its spread and help ensure that the currently available anthelmintic chemicals remain as effective as possible in the long term. Competent Authorities, the veterinary pharmaceutical industry, veterinarians, independent organisations and academia should work together where possible to identify the needs of farmers for practical parasite control programmes, as well as to make scientific advances on the topic of parasitology.

Some overarching global needs and gaps in knowledge regarding anthelmintic resistance have been documented via an OIE questionnaire on the status of anthelmintic chemical use and resistance as well as identification of needs to aid in combatting resistance. This survey (survey 1) and another on regulatory processes (survey 2) were completed by National Focal Points for Veterinary Products across all regions in 2020 and 2021. Although these surveys were not fully representative, with occasional regional differences, responses to the questionnaires demonstrated several findings. (Region-specific summaries of responses to the two surveys, including information on resistance and regulation, are provided in Appendix 1.)

In terms of needs, the following points were commonly identified as important:

- the availability of methods of diagnosis;
- the availability of methods for the responsible and prudent use of anthelmintic chemicals;
- lists of locally available anthelmintic VMPs and their indications for use;
- methods of non-chemical control (e.g. breaking parasite life cycles, pasture management based on parasite epidemiology).

Assistant Professor R.M.Akbaev delivers a laboratory seminar for students of the Veterinary Medicine Faculty. K.I.Skryabin Moscow State Academy of Veterinary Medicine and Biotechnology. Department of Parasitology and Veterinary Sanitary

Given the global need for more information on anthelmintic resistance across all sectors, the following two-pronged approach addresses areas where more research and focused training are needed:

### 1 Research and development:

- improved and standardised diagnostic tests, including methods of analysis;
- large-scale prevalence data;
- improved understanding of parasite epidemiology and its application to parasite control;
- trialling and adoption of non-chemical control methods;
- development of novel anthelmintic chemicals;
- vaccine development.

### 2 Focused and standardised training, harmonised across various entities (Competent Authority, veterinarians, pharmaceutical industry and others), that promotes adoption of the responsible and prudent use of anthelmintic chemicals, to include:

- adoption of good practices (e.g. integrated parasite management), including use of diagnostic tests;
- development and sharing of resources, including educational programmes, e-learning tools (complementing the OIE platform) and decision support tools, for all applicable users and stakeholders;
- sharing of laboratory techniques and reference data;
- sharing of local-level evidence of effective management practices;
- equipping advisors with local knowledge and focusing appropriate resources.

Pale sclera due to anaemia in a ram heavily infected with *Haemonchus contortus*

# Appendix 1

## Results of surveys on antiparasitic agents and resistance, and on responsibilities for the prudent use of anthelmintics, 2020 and 2021

The following information summarises the results received from the five OIE regions[1] for the surveys conducted by the OIE in 2020 and 2021: 'Survey on antiparasitic agents and resistance in terrestrial and aquatic animals' (survey 1) and 'Survey on responsibilities for the prudent use of anthelmintics' (survey 2). Responses for survey 1 and survey 2 were received from 119 of 183 countries (65%) and 81 of 183 countries (44%), respectively[2]. Further detail on the number of responses by region compared with the total number of countries in each region is provided in Table AI.

With this limited response rate, it is acknowledged that the results are not representative of each region. Therefore, the information in the survey responses was averaged across each region, and the information presented below reflects region-specific results. Some questions allowed selection of multiple answers. The results do not represent all countries within a region or other data or information available from other sources. (A summary of global needs based on the information identified in survey 1 is provided in the section of the paper entitled 'Gaps in Knowledge'.)

**Table AI.** Number of countries that responded to the OIE's surveys on antiparasitic resistance, by OIE region

| | Survey 1 | Survey 2 | Number of OIE Members |
|---|---|---|---|
| **Africa** | 35 | 16 | 54 |
| **Americas** | | | |
| **OIE Members** | 25 | 24 | 31 |
| **Non-OIE Members** | 1 | 1 | N/A |
| **Asia and the Pacific** | 15 | 18 | 32 |
| **Europe** | 36 | 17 | 53 |
| **Middle East** | 9 (a) | 5 | 12 |

(a) One of the nine responses to this survey came from a country officially in the OIE Africa region.

[1] See Appendix 3 for the distribution of OIE Members by OIE region.

[2] The total number of countries (183) is more than the number of OIE Members (182) for both questionnaires owing to the inclusion of a non-OIE Member in the Americas region. For survey 1, one country was sent the survey by two regions (the Middle East and Africa). However, as the country provided a response in only one region, this did not impact the final global results.

# Africa

## Types of production systems (survey 1)

The results indicated that Africa's animal production systems are dominated by cattle, small ruminants (goats and sheep), poultry, pigs and fish.

## Anthelmintic resistance (surveys 1 and 2)

Responses identified that the status of anthelmintic resistance was largely unknown at both national (25/35) and local (23/35) levels. Similarly, most respondent countries had very little awareness or information available on anthelmintic resistance (21/35) and indicated that veterinarians do not routinely carry out FECRTs to evaluate anthelmintic resistance (12/16).

## Anthelmintic chemical availability, regulatory oversight and pharmacovigilance (surveys 1 and 2)

Regarding the regulatory environment for anthelmintic chemicals, the responses were mostly positive, with most respondent countries indicating that registration practices were complete (23/35) and that the Competent Authority had put in place measures for regulating marketing, labelling and quality control of anthelmintic chemicals (11/16). Most respondent countries reported having appropriate regulatory control systems in place to fight unauthorised production/importation (15/16), Competent Authorities that require certificates of analysis (15/16) and labels containing detailed descriptions of product characteristics and instructions for the correct use of anthelmintic chemicals (15/16).

Although such services are available in some countries, only about half of responses indicated that Competent Authorities had access to quality control and assurance laboratory services (8/16) and applied the guidelines established by VICH (7/16). Drug withdrawal/withholding periods, regulatory surveillance of parasitic diseases and pharmacovigilance were reported as being implemented by less than half of the countries that responded. Anthelmintic chemicals were sold over the counter in most countries (14/16). Additionally, anthelmintic drug containers lacked label information on environmental protection in 10 out of the 16 responding countries.

## Other (surveys 1 and 2)

Most countries indicated that although anthelmintics are sold directly to farmers, veterinarians are still key decision-makers on anthelmintic chemical use (13/16). Most respondent countries reported that veterinarians advise farmers on animal health plans, including parasite control (15/16). Although most respondent countries reported that their veterinarians undertake and maintain training on the choice, use and administration of anthelmintics (9/16), many were still in the process of building capacity (6/16). Only about half of respondent countries indicated that farmers had access to advice on the correct use of anthelmintics (18/35), while 14 out of 16 respondents indicated that products were appropriately stored. Respondents identified an important gap in the region's veterinary capacity to detect and report pharmacovigilance breaches and anthelmintic resistance.

Emaciated cattle at rest in the northern zone at the Senegal River in the dry season. The animals are positive for gastrointestinal helminthic polyparasitism (schistomsomosis, strongyloidosis, fasciolosis)

# Americas

## Types of production systems (survey 1)

The results indicate that animal production systems in the Americas are dominated by cattle, poultry (layers and broilers), commercial swine and sheep.

## Anthelmintic resistance (surveys 1 and 2)

In general, responding countries indicated that the prevalence of anthelmintic resistance was mostly unknown (16/26) or known only for some species (10/26), and there was very little awareness about anthelmintic resistance (15/26). This may be due, in part, to the reported infrequent use of tests to diagnose resistance; only 6 out of 25 respondent countries reported that veterinarians were regularly performing FECRTs. All 26 respondent countries indicated that additional information on methods of prudent and responsible use of anthelmintics would be helpful in improving the control of anthelmintic resistance. Additionally, most respondents (21/26) indicated that information on methods of breaking parasite life cycles would also be helpful.

## Anthelmintic chemical availability, regulatory oversight and pharmacovigilance (surveys 1 and 2)

Most countries reported having regulatory structures with the ability to grant market authorisations (20/25) and combat the unauthorised manufacture of anthelmintics (e.g. importation, advertisement, distribution, storage) through appropriate regulatory controls and other measures (19/25). Most also reported that products bear labels with detailed product characteristics and instructions for use and administration (21/25), are sold in their original containers with original labels (20/25) and are stored correctly (17/25).

Responses also indicated that regulatory authorities infrequently monitor for parasitic diseases (only 4 out of 25 respondents indicated this was performed), infrequently apply pharmacovigilance regarding poor quality and/or misuse of anthelmintics (6 out of 25 respondents indicated this was applied) and lack access to laboratories to analyse product quality (9 out of 25 respondents indicated that this access existed). Additionally, the survey results revealed that anthelmintics in most responding countries were available over the counter (19/25); on-farm use was generally unrestricted or not recorded (15/26); and very few responding countries followed VICH guidelines and other approaches for regional harmonisation (6/25). Based on the responses, indices for evaluating a country's regulatory environment demonstrated significant potential for improvement and suggested many countries would benefit from more robust registration practices, pharmacovigilance and availability of education for farmers.

## Other (surveys 1 and 2)

In most responding countries, veterinarians were reported to be a trusted source of advice for local farmers on animal health plans, including parasite control (18/25). Despite this, the two biggest knowledge gaps identified with respect to parasite control were in diagnosing resistance (22/26) and the availability of in-person extension services (14/22), such as from field professionals or advisors, veterinarians and veterinary paraprofessionals.

## Asia and the Pacific

### Types of production systems (survey 1)

The results indicated that animal production in the region is based on cattle, sheep, pigs and poultry.

### Anthelmintic resistance (survey 1)

Across the region, 8 out of the 15 responding countries had some awareness of the presence of resistance in their country and indicated that, while resistance has been reported, comprehensive data are lacking. FECRTs are not reported as being commonly used in most countries.

### Anthelmintic availability and pharmacovigilance (survey 2)

Respondents indicated that there were strong regulatory and registration processes in place (14/18), that anthelmintic chemicals were appropriately labelled (17/18) and that storage was appropriate (17/18). Levels of compliance and the quality of VMPs were thought to be high (13/18). It was reported that the regulatory authority applied VICH guidelines in half of the responding countries (9/18), and in 6 out of 18 responding countries authorities monitored parasitic diseases. In most cases, anthelmintic chemicals were available over the counter (14/18), and anthelmintic use was monitored in half of the responding countries. While high levels of import control occurred in most responding countries (17/18), there was potential concern that frequent transborder movement of animals for many countries on the Asian continent made the regulation of agricultural chemicals and their use challenging. Pharmacovigilance was practiced in 6 out of 18 respondent countries, and withdrawal periods were respected in the majority (15/18). The responses revealed variability in the region: in some developed economies regulation was tightly controlled, while in others there was less government oversight and effective legislation to manage chemical usage. Based on the indices derived from the responses, there was potential for improvement and many countries would benefit from more robust registration and pharmacovigilance systems.

### Other (surveys 1 and 2)

Veterinarians provided advice in 17 out of 18 responding countries, while in 14 out of 18 responding countries they undertook and maintained training in parasite control, and in 12 out of 18 responding countries they performed FECRTs. Veterinarians reported pharmacovigilance breaches and anthelmintic resistance in half of the responding countries (9/18). Knowledge gaps with respect to anthelmintic resistance concerned diagnosis of resistance (11/15) and access to methods for breaking parasite life cycles (9/15), and many (13/15) identified distribution of prudent use guidelines as a high priority.

## Europe

### Types of production systems (survey 1)

The results indicated that Europe's animal production systems are dominated by cattle, poultry (layers and broilers), commercial swine and sheep.

### Resistance (survey 1)

Due to infrequent use of diagnostic methods (such as the FECRT) in the respondent countries, anthelmintic resistance status was reported as being mostly unknown (20/36) or known for some species (12/36). Routine diagnosis of anthelmintic resistance on advanced farms is performed in 3 out of 36 respondent countries, and there is very little awareness or information on anthelmintic resistance in many countries (13/36). Most respondent countries (35/36) believed that methods of prudent and responsible use of anthelmintics would assist in improving the control of anthelmintic resistance. Scientific expertise was available in 15 out of 35 countries and was well resourced and communicated in 3 out of 35 countries.

### Anthelmintic chemical availability, regulatory oversight and pharmacovigilance (survey 2)

Respondent countries indicated that they have strong regulatory systems for registering and monitoring anthelmintics, including requiring marketing authorisations (16/17), indicating withdrawal periods and maintaining regulatory and quality controls. However, anthelminthics were reported as being available over the counter in 8 out of the 17 responding countries.

In the majority of respondent countries, detailed product characteristics are written on labels, as are instructions for use and administration (16/17) and environmental protection (15/17). Appropriate training on anthelmintic chemicals is available in 11 out of 17 countries, and pharmacovigilance regarding poor quality and misuse of anthelmintic VMPs is applied in 13 out of 17 countries.

Competent Authorities from 16 out of 17 responding countries grant marketing authorisations following efficient registration procedures to evaluate quality, safety and efficacy of anthelmintics and regulate and ensure proper marketing, quality control and labelling.

Additionally, nearly all respondents indicated that the Competent Authority has access to laboratory analysis for verification (15/17) and that import controls at borders are effective (12/17). Wholesale and retail distribution are well organised and controlled, although container return services are available in only 7 out of the 17 countries.

### Others (surveys 1 and 2)

All 17 responding countries indicated that veterinarians provide advice for local farmers on animal health plans, including parasite control. Training in the choice, use and administration of anthelmintics is undertaken by veterinarians in most respondent countries (13/17). Most countries (14/17) responded that veterinarians report pharmacovigilance breaches and anthelmintic resistance, but fewer (9/17) reported that veterinarians conduct diagnostic tests (e.g. FECRT). The two biggest knowledge gaps identified with respect to parasite control were in diagnosis of resistance (26/36) and control methods (12/36).

Salers cows and a Charolese bull on pasture

# Middle East

## Types of production systems (survey 1)

The results indicated that animal production systems in the Middle East are dominated by cattle, sheep, goats and poultry, followed by camels, buffaloes, horses and fish to a lesser extent and varying by country.

## Anthelmintic resistance (survey 1)

Most respondents felt that the status of anthelmintic resistance in their country was mostly unknown at national (7/9) and local levels (8/9), that information was not widely available and that the level of awareness about anthelmintic resistance was limited (7/9).This region also indicated that FECRT use was very low or unknown (7/9). In terms of information needed, countries responded that having a list of available anthelmintics and their indications for use as well as information on methods of prudent and responsible use of anthelmintics would improve the control of anthelmintic resistance.

## Anthelmintic chemical availability, regulatory oversight and pharmacovigilance (surveys 1 and 2)

Regarding the regulatory environment for anthelmintics, country responses were mostly positive, with respondents indicating the presence of comprehensive registration practices (7/9), appropriately labelled products (7/9) and import controls on anthelmintics (5/5). Most also reported that anthelmintic VMPs were properly stored (5/5), that the majority were of good quality when purchased from known providers (6/9) and that regulatory authorities were working to apply existing guidelines established by VICH for the registration of VMPs (4/5).

Responses also indicated that regulatory authorities infrequently monitored for parasitic diseases (only one of the five respondents reported such monitoring was performed). Responses also indicated that there were some anthelmintic chemicals that were illegally marketed or for which the quality was unknown (3/9), and laboratory testing for verification of anthelmintic products was not accessible to the Competent Authority in one of five responding countries. It was reported that anthelmintic chemicals were available over the counter in three of five countries, on-farm use was unrestricted or not recorded in two of five, and the withdrawal periods were respected in three of the five responding countries. Based on the responses, indices for evaluating a country's regulatory environment demonstrated significant potential for improvement and suggested many countries would benefit from more robust registration practices, pharmacovigilance and the availability of appropriate training on anthelmintics.

## Other (surveys 1 and 2)

All five countries that responded to survey 2 indicated that veterinarians advise the local farmers on animal health plans, including parasite control. However, fewer countries indicated that veterinarians maintain training in anthelmintic choice, use and administration (2/5); perform FECRTs (2/5); and detect and report pharmacovigilance breaches (2/5). The most frequently identified knowledge gaps with respect to parasite control were 'diagnosis of resistance' (7/9) followed by 'extension service based on advisors, vets, and veterinary paraprofessionals' (3/9).

# Appendix 2

## Relevant guidelines

### International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products (VICH) Guidelines

VICH Guidelines webpage: vichsec.org/en/guidelines.html

The list of guidelines below includes only those specific to evaluating the efficacy of anthelmintic chemicals. Training and other guidelines that may be applicable, including those on evaluating safety and manufacturing, can be found on the VICH website.

VICH GL7: Efficacy of anthelmintics: General requirements

VICH GL12: Efficacy of anthelmintics: Specific recommendations for bovines

VICH GL13: Efficacy of anthelmintics: Specific requirements for ovines

VICH GL14: Efficacy of anthelmintics: Specific recommendations for caprines

VICH GL15: Efficacy of anthelmintics: Specific recommendations for equines

VICH GL16: Efficacy of anthelmintics: Specific requirements for porcines

VICH GL19: Efficacy of anthelmintics: Specific recommendations for canines

VICH GL20: Efficacy of anthelmintics: Specific recommendations for feline

VICH GL21: Efficacy of anthelmintics: Specific recommendations for poultry

Cows and calves of tropically adapted cattle on supplemental feed in Northern Territory, Australia

## World Association for the Advancement of Veterinary Parasitology Guidelines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# APPENDIX 3

## Distribution of OIE Members by OIE Region

### Africa (54)

1. ALGERIA
2. ANGOLA
3. BENIN
4. BOTSWANA
5. BURKINA FASO
6. BURUNDI
7. CAMEROON
8. CABO VERDE
9. CENTRAL AFRICAN (REP.)
10. CHAD
11. COMOROS
12. CONGO (REP. OF THE)
13. CONGO (DEM. REP. OF THE)
14. CÔTE D'IVOIRE
15. DJIBOUTI
16. EGYPT
17. EQUATORIAL GUINEA
18. ERITREA
19. ESWATINI
20. ETHIOPIA
21. GABON
22. GAMBIA
23. GHANA
24. GUINEA
25. GUINEA-BISSAU
26. KENYA
27. LESOTHO
28. LIBERIA
29. LIBYA
30. MADAGASCAR
31. MALAWI
32. MALI
33. MAURITANIA
34. MAURITIUS
35. MOROCCO
36. MOZAMBIQUE
37. NAMIBIA
38. NIGER
39. NIGERIA
40. RWANDA
41. SAO TOME AND PRINCIPE
42. SENEGAL
43. SEYCHELLES
44. SIERRA LEONE
45. SOMALIA
46. SOUTH AFRICA
47. SOUTH SUDAN (REP. OF)
48. SUDAN
49. TANZANIA
50. TOGO
51. TUNISIA
52. UGANDA
53. ZAMBIA
54. ZIMBABWE

### Americas (31)

1. ARGENTINA
2. BAHAMAS
3. BARBADOS
4. BELIZE
5. BOLIVIA
6. BRAZIL
7. CANADA
8. COLOMBIA
9. COSTA RICA
10. CUBA
11. CURACAO
12. CHILE
13. DOMINICAN (REP.)
14. ECUADOR
15. EL SALVADOR
16. GUATEMALA
17. GUYANA
18. HAITI
19. HONDURAS
20. JAMAICA
21. MEXICO
22. NICARAGUA
23. PANAMA
24. PARAGUAY
25. PERU
26. SAINT LUCIA
27. SURINAME
28. TRINIDAD AND TOBAGO
29. UNITED STATES OF AMERICA
30. URUGUAY
31. VENEZUELA

### Middle East (12)

1. AFGHANISTAN
2. BAHRAIN
3. IRAQ
4. JORDAN
5. KUWAIT
6. LEBANON
7. OMAN
8. QATAR
9. SAUDI ARABIA
10. SYRIA
11. UNITED ARAB EMIRATES
12. YEMEN

### Asia and the Pacific (32)

1. AUSTRALIA
2. BANGLADESH
3. BHUTAN
4. BRUNEI
5. CAMBODIA
6. CHINA (PEOPLE'S REP. OF)
7. FIJI
8. INDIA
9. INDONESIA
10. IRAN
11. JAPAN
12. KOREA (REP. OF)
13. KOREA (DEM. PEOPLE'S REP. OF)
14. LAOS
15. MALAYSIA
16. MALDIVES
17. MICRONEISA (FED. STATES OF)
18. MONGOLIA
19. MYANMAR
20. NEPAL
21. NEW CALEDONIA
22. NEW ZEALAND
23. PAKISTAN
24. PAPUA NEW GUINEA
25. PHILIPPINES
26. SINGAPORE
27. SRI LANKA
28. TAIPEI (CHINESE)
29. THAILAND
30. TIMOR LESTE
31. VANUATU
32. VIETNAM

### Europe (53)

1. ALBANIA
2. ANDORA
3. ARMENIA
4. AUSTRIA
5. AZERBAIJAN
6. BELARUS
7. BELGIUM
8. BOSNIA AND HERZEGOVINA
9. BULGARIA
10. CROATIA
11. CYPRUS
12. CZECH REP.
13. DENMARK
14. ESTONIA
15. FINLAND
16. FRANCE
17. GEORGIA
18. GERMANY
19. GREECE
20. HUNGARY
21. ICELAND
22. IRELAND
23. ISRAEL
24. ITALY
25. KAZAKHSTAN
26. KYRGYZSTAN
27. LATVIA
28. LIECHTENSTEIN
29. LITHUANIA
30. LUXEMBOURG
31. MALTA
32. MOLDOVA
33. MONTENEGRO
34. NETHERLANDS (THE)
35. NORTH MACEDONIA
36. NORWAY
37. POLAND
38. PORTUGAL
39. ROMANIA
40. RUSSIA
41. SAN MARINO
42. SERBIA
43. SLOVAKIA
44. SLOVENIA
45. SPAIN
46. SWEDEN
47. SWITZERLAND
48. TAJIKISTAN
49. TURKEY
50. TURKMENISTAN
51. UKRAINE
52. UNITED KINGDOM
53. UZBEKISTAN

# Notes

# Notes

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