

ANTIPARASITIC RESISTANCE

US FDA'S EXPERIENCE

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Overview

Antiparasitic resistance is an issue for grazing livestock in the United States

- ▣ What is FDA-CVM's experience thus far?
- ▣ What is FDA-CVM's role now and in the future?



FDA-CVM

- **Within FDA, the Center for Veterinary Medicine (CVM) regulates animal drugs (including antiparasitics), animal feed, and veterinary devices.**
- **We make sure an animal drug is safe and effective before approving it**
- **We monitor the safety and effectiveness of animal drugs on the market**



FDA-CVM



Our mission:

“Protecting human and animal health.”

Our vision:

“Excellence. Innovation. Leadership.”

Promoting the sustainable use of antiparasitics is within both our mission and vision.

FDA Approved Antiparasitics: Sheep, Goats, and Cattle

Active Ingredient	Species
Thiabendazole	Sheep, goats, cattle
Morantel tartrate	Goats, cattle
Albendazole	Sheep, goats, cattle
Fenbendazole	Goats, wild sheep, cattle
Levamisole	Sheep and cattle
Ivermectin	Sheep and cattle
Moxidectin	Sheep and cattle
Oxfendazole	Cattle
Doramectin	Cattle
Eprinomectin	Cattle

*This list is current as of September 2015

**Not all products may be currently marketed

FDA Approved Antiparasitics: Horses

- Several older products are approved (including organophosphates and piperazine combinations), but are no longer marketed.
- Commonly marketed, approved products include:

Active ingredients

Ivermectin (\pm praziquantel)

Moxidectin ((\pm praziquantel)

Pyrantel pamoate

Pyrantel tartrate (administered daily in feed)

Fenbendazole (approved at 2 dose regimens)

Oxibendazole

Other benzimidazoles are approved but not commonly used

CVM's Public Meeting

- March 2012, CVM held a Public Meeting: “Antiparasitic Drug Use and Resistance in Ruminants and Equines”
- Hosted 7 internationally-recognized veterinary parasitologists/pharmacologists



CVM's Public Meeting



Topics discussed:

- ✓ **Current state of antiparasitic resistance in the U.S. and worldwide**
- ✓ **How to diagnose and define antiparasitic resistance**
- ✓ **Ways antiparasitic drugs can be used (alone versus in combination) to maximize effectiveness and minimize resistance**

Combination dewormers?

Multiple studies have shown that appropriately chosen combinations of antiparasitics from different drug families, when used appropriately, have the potential to slow the development of resistance.

In regulatory terms, these are combinations with highly/completely overlapping indications

**None are currently approved in the U.S.
We encourage drug companies to investigate such combos for approval.**

CVM'S ARMS initiative

Antiparasitic Resistance Management Strategy (ARMS)

- CVM's initiative to promote sustainable use of anthiparasitic drugs in grazing livestock species
- Launched in September 2012
- 3-pronged approach:
 - ▣ Education
 - ▣ Research
 - ▣ Regulation



Species covered by ARMS



- ❖ **ARMS covers the primary grazing livestock species in the U.S.: cattle, goats and sheep, and horses**
- ❖ **ARMS currently does not cover cats and dogs, swine, poultry, or aquaculture**

Reaching Out



- A primary goal of ARMS is to spread the word regarding antiparasitic resistance and sustainable use of antiparasitic drugs in livestock species
- Education is a priority
 - ▣ ARMS keeps informed on the most recent research worldwide: includes regular review of published literature, and attending scientific meetings (AAVP and WAAVP)
 - ▣ Speaking opportunities – in the US and beyond
 - Recent US examples include at AVMA 2014, 2015
 - VICH Veterinary Outreach Forum February 2013
 - OIE Focal Points meeting (today's presentations)

Progress – what's been done so far?

- Pathway for approval of combination antiparasitics
- Website
- Brochure
- Speaking engagements
- *JAVMA* Commentary
- *Veterinary Parasitology* Special Issue
- Inter-agency and international communication
- Monitoring scientific literature and clinical data



Website

The screenshot shows the FDA website page for Antiparasitic Resistance. The page has a blue header with the FDA logo and navigation links. The main content area is white with a blue sidebar on the left. The sidebar contains a 'Safety & Health' menu with 'Antiparasitic Resistance' highlighted. The main content area has a 'What is antiparasitic resistance?' section with a definition and a list of factors. Below this is an 'Additional Information' section with three links to public meetings and helpful information. The footer contains contact information, social media icons, and a list of links for various FDA services.

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Animal & Veterinary

Home | Animal & Veterinary | Safety & Health

Safety & Health

- Antiparasitic Resistance**
- Report a Problem
- Recalls & Withdrawals
- Product Safety Information
- Animal Feed Safety System (AFSS)
- Antimicrobial Resistance
- Animal Cloning
- Frequently Asked Questions

Antiparasitic Resistance

What is antiparasitic resistance?

Antiparasitic resistance is the genetic ability of parasites to survive treatment with an antiparasitic drug that was generally effective against those parasites in the past. After an animal is treated with an antiparasitic drug, the susceptible parasites die and the resistant parasites survive to pass on resistance genes to their offspring.

Antiparasitic resistance poses a significant threat to animal health and can result in production losses in food-producing species. Researchers have documented antiparasitic resistance in grazing species, such as cattle, small ruminants (sheep and goats), and horses, both globally and within the United States.

Many factors contribute to antiparasitic resistance, including the biology of the parasite; the immune status of the host animal; treatment practices; drug properties; and certain livestock management practices.

What is FDA's Center for Veterinary Medicine doing about antiparasitic resistance?

To help combat this emerging problem, the FDA's Center for Veterinary Medicine started the Antiparasitic Resistance Management Strategy (ARMS). The strategy promotes sustainable use of approved antiparasitic drugs in cattle, small ruminants, and horses. Sustainable use will help ensure that antiparasitic drugs remain effective for as long as possible, thereby slowing the development of antiparasitic resistance in grazing species in the United States.

Additional Information

- FDA's Public Meeting on Antiparasitic Drug Use and Resistance in Ruminants and Equines
- FDA's Public Meeting on Antiparasitic Drug Use and Resistance in Ruminants and Equines - An Overview (PDF - 384KB)
- Helpful Information for Veterinarians - Antiparasitic Resistance in Cattle and Small Ruminants in the United States: How to Detect it and What to do about it (PDF - 794KB)

Page Last Updated: 05/02/2013
Note: If you need help accessing information in different file formats, see Instructions for Downloading Viewers and Players.

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Brochure

Helpful Information for Veterinarians

Antiparasitic Resistance in Cattle and Small Ruminants in the United States: How to Detect It and What to Do About It

Introduction

Internal parasite infections and external parasite infestations harm animal health and can result in significant production losses in food-producing species, such as cattle, sheep, and goats.

Antiparasitic animal drugs are used to treat and control parasitic infections and infestations in animals. The parasites that a given drug is effective against are listed in the indication on the drug's label.

Antiparasitic resistance is the genetic ability of parasites to survive the effects of an antiparasitic drug to which they were previously susceptible. Antiparasitic resistance becomes a problem when an increasing percentage of a parasite population carries resistance genes, allowing the parasites to survive treatment with an antiparasitic drug that has been effective in the past.

Australia, New Zealand, South Africa, and South America have struggled with antiparasitic resistance in livestock species for the past few decades. Recent scientific data indicate antiparasitic resistance is now emerging in livestock species in the United States.

Refugia

After an animal is treated with an antiparasitic drug, the susceptible parasites die and the resistant parasites survive to pass on resistance genes to their offspring. If not enough susceptible parasites remain in the environment and in the animal, they cannot dilute the increase in resistant parasites that occurs after treatment. This scenario occurs when there is a lack of *refugia*.

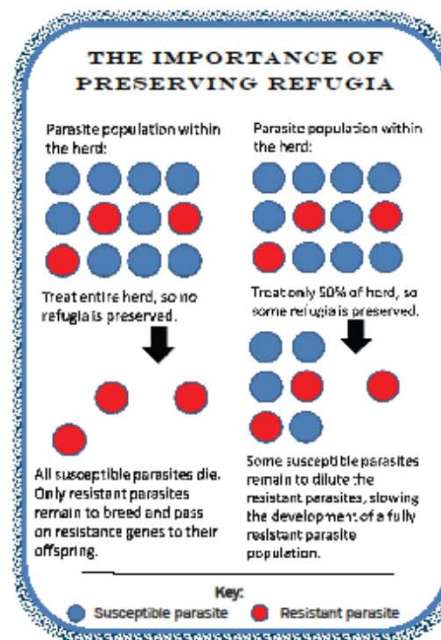
What is refugia?

Refugia is the proportion of the total parasite population that is not selected for antiparasitic drug treatment—essentially, those parasites that are in “refuge” from the drug. Therefore, there's no selection pressure on these parasites to develop resistance. Refugia maintains a proportion of susceptible parasites on the farm and includes:

- Parasites in untreated animals, called host-based refugia.
- Eggs and larvae already on the pasture when the animals are treated, called environmental refugia.
- Life stages of the parasite that are unaffected by drug treatment, such as some larval stages.

Why is preserving refugia important?

Preserving refugia maintains drug-sensitive (susceptible) parasites. The presence of some drug-sensitive parasites decreases (dilutes) the proportion of resistant parasites within the parasite population on a farm.



Progress – More to come



- Collaboration with USDA APHIS allowing for collection of fecal samples during the 2015 Equine National Animal Health Monitoring System (NAHMS) survey
 - ▣ Goal is to estimate prevalence of strongyle resistance in equids on a national and regional basis

Progress – More to Come



- Internet-based survey of US veterinarians and veterinary parasitologists - data collection completed Fall 2015.
- Participants answered questions to assess:
 - ▣ Awareness of antiparasitic resistance
 - ▣ Commonly used strategies for detecting and managing antiparasitic resistance
 - ▣ Opinions on labeling and label statements
- Our goal is to publish the results

Regulatory Roles



- **We are not proposing the removal of any antiparasitics from the market**
- **Recognize that antiparasitic resistance and antimicrobial resistance are separate issues**

Thinking ahead



What we still need



- Practical (evidence-based) guidelines for producers, especially in beef cattle
- Continued research:
 - ▣ Validate methods
 - ▣ U.S. data on cattle refugia
 - ▣ Better diagnostics
 - ▣ Prevalence data for resistance in all grazing species in U.S. (greatest need for data in cattle and horses)

What CVM continues to do



- Work with industry to provide the most up-to-date recommendations on labeling**
- Monitor promotional materials for misleading claims and omission of risk information**

Final thoughts



- Ultimately, we want to ensure that approved antiparasitics remain effective for as long as possible
- This should be a shared goal not only in the US, but throughout the world for the benefit of animal and public health

Resources

- ❑ CVM website: <http://www.fda.gov/animalveterinary/safetyhealth/ucm350360.htm>
- ❑ Docket for public meeting:
<http://www.fda.gov/animalveterinary/resourcesforyou/ucm318015.htm>
- ❑ Public meeting overview:
<http://www.fda.gov/downloads/AnimalVeterinary/ResourcesforYou/UCM344299.pdf>
- ❑ Brochure:
<http://www.fda.gov/downloads/animalveterinary/resourcesforyou/ucm347442.pdf>
- ❑ *Antiparasitic Resistance and Grazing Livestock in the United States*
J Am Vet Med Assoc 2014 May 1;244(9):1020-2.
- ❑ Veterinary Parasitology Special Issue Vol 204, Issues 1-2, Pages 1-80 (30 July 2014)

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