Medically Important Antimicrobials in Animal Agriculture

–

Sheep

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Outline

- Take Home
- Changes to Affected Products
  - Changes to Oral Dosage Form Products
  - Changes to Medicated Feed Products
- Sources of Information
- Take Home

Take Home

All drug sponsors have aligned all affected applications with the GFI # 213 recommendations by the January 2017 target date.

Outline

- Take Home
- Changes to Affected Products
  - Changes to Oral Dosage Form Products
  - Changes to Medicated Feed Products
    - Major & Minor Species
- Sources of Information
- Take Home

Changes to Affected Products

Of the 292 new animal drug applications initially affected by Guidance for Industry #213:

84 were completely withdrawn

Of the remaining 208 applications,

93 applications - oral dosage form - converted from OTC to Rx.

115 applications – medicated feed - converted from OTC to VFD.

Production (e.g., growth promotion) indications were withdrawn from all applications that included such indications for use.

Outline

- Take Home
- Changes to Affected Products

  Changes to Oral Dosage Form Products

  Changes to Medicated Feed products

    - Major & Minor Species
- Sources of Information
- Take Home

Changes to Affected Products

- 21 CFR Part 520

Medically Important Antimicrobials regulated by CVM/FDA as oral dosage form new animal drugs.

93 Applications Transitioned from OTC to Rx Marketing Status.

In reporting year 2015, these applications accounted for ~ 21 % of the sales of all medically important antimicrobials.

21 CFR Part 520
OTC to Rx

- Oral Dosage Form New Animal Drugs
  - (21 CFR Part 520)

- Label – Limitation

- *Federal Law restricts this drug to use by or on the order of a licensed veterinarian.*

Changes to Affected Products

- Rx – Examples
- 21 CFR Part 520.1660d

- Oxytetracycline Hydrochloride
  - N 008-622
  - A 200-026
  - A 200-146
    - Species: Sheep (Domestic)
    - Class: No Use Class Stated or Implied
    - Indication: Control and treatment of bacterial enteritis caused by *E. coli* and bacterial pneumonia (shipping fever complex) caused by *P. multocida* susceptible to oxytetracycline.

Changes to Affected Products

- Rx – Examples
- 21 CFR Part 520.1484

- Neomycin – (Sheep & Goats)
  - A 200-113 A 200-289
  - A 200-130 A 200-378
  - A 200-235 A 200-379
    - Species: Sheep (Domestic)
    - Class: No Use Class Stated or Implied
    - Indication: For the treatment and control of colibacillosis (bacterial enteritis) caused by *Escherichia coli* susceptible to neomycin.

Changes to Affected Products

Affected Oral Dosage Form Antibiotics

Antimicrobial Class	Specific drugs approved for use in water
Aminoglycosides	Apramycin, Gentamicin, Neomycin, Spectinomycin, Streptomycin
Lincosamides	Lincomycin
Macrolides	Carbomycin, Erythromycin, Tylosin
Penicillins	Penicillin
Sulfas	Sulfachloropyrazine, Sulfachlorpyridazine, Sulfadimethoxine, Sulfamerazine, Sulfamethazine, Sulfaquinoxaline
Tetracycline	Chlortetracycline, Oxytetracycline, Tetracycline

Changes to Affected Products

- 21 CFR Part 520
- ELU

- The Animal Medicinal Drug Use Clarification Act (AMDUCA) of 1994 and the regulations published at 21 CFR part 530 describe the requirements for, and restrictions on, extra-label drug use.

Changes to Affected Products

- 21 CFR Part 520
  - Rx – VCPR

- On – label: State VCPR
- Off-label: Federal VCPR (21 CFR Sec.530.3(i))

- See: http://www.ecfr.gov/cgi-bin/text-idx?SID=5ad83a5a41b724e95d9669f83c6475df&mc=true&node=pt21.6.530&rgn=div5

Outline

- Take Home
- Changes to Affected Products

  Changes to Oral Dosage Form Products

  Changes to Medicated Feed Products

  - Major & Minor Species
- Sources of Information
- Take Home

Changes to Affected Products

- 21 CFR Part 558

Medically Important Antimicrobials regulated by CVM/FDA as New Animal Drugs for use in Animal Feed.

115 Applications Transitioned from OTC to VFD Marketing Status.

In reporting year 2015, these applications accounted for ~ 74 % of sales of all medically important antimicrobials.

21 CFR Part 558
OTC to VFD

- VFD Medicated Feed
  - (21 CFR Part 558)

- Label – Special Considerations

- *Federal Law restricts medicated feed containing this veterinary feed directive (VFD) drug to use by or on the order of a licensed veterinarian.*

Voluntary Changes of Affected Products

New Animal Drugs for use in Animal Feed

Antimicrobial Class	Specific drugs approved for use in feed
Aminoglycosides	Apramycin, Hygromycin B, Neomycin, Streptomycin
Diaminopyrimidines	Ormetoprim
Lincosamides	Lincomycin
Macrolides	Erythromycin, Oleandomycin, Tylosin
Penicillins	Penicillin
Streptogramins	Virginiamycin
Sulfas	Sulfadimethoxine, Sulfamerazine, Sulfamethazine, Sulfaquinoxaline
Tetracycline	Chlortetracycline, Oxytetracycline

Extralabel Use

- ELU Prohibited - animal feed

- Limitations of Extralabel use
- …
- (b) Extralabel use of an approved new animal drug or human drug **in or on an animal feed**; 21 CFR Sec. 530.11

Extralabel Use
CPG 615.115

- Policy Statement
- Considerations
  - General
  - Veterinarian
  - Producer
  - Distributor/Manufacturer
  - http://www.fda.gov/ucm/groups/fdagov-public/@fdagov-afda-ice/documents/webcontent/ucm074659.pdf

Changes to Affected Products

21 CFR Part 558

- Major vs Minor Species

The term `major species' means **cattle**, horses, **swine**, **chickens, turkeys**, dogs, and cats, … 21 U.S.C. 321 (nn)

The term `minor species' means animals other than humans that are not major species. 21 U.S.C. 321 (oo)

Extralabel Use
CPG 615.115

- Policy Statement
- Considerations

Extralabel Use
CPG 615.115

- Policy Statement
  - ELU
  - AMDUCA
  - However

Extralabel Use
CPG 615.115

- Policy Statement –
- However, when
- 1. there are no approved treatment options available and
- 2. the health of animals is threatened, and
- 3. suffering or death would result from failure to treat the affected animals,
- extra label use of medicated feed may be **considered** for treatment of **minor species**.

Extralabel Use
CPG 615.115

- Policy Statement –

- … no approved treatment options available …
  - –Goats
  - –Sheep

Goats
OTC - examples

Active Ingredient	Proprietary Name	NADA/ANADA	Label Type	Indications	Marketing Status
Decoquinate (liquid)	DECCOX	N039-417	Type B	For the prevention of coccidiosis in young goats caused by Eimeria christenseni and E. ninakohlyakimovae.	OTC
Decoquinate	DECCOX	N039-417	Type C	For the prevention of coccidiosis in young goats caused by Eimeria christenseni and E. ninakohlyakimovae.	OTC
Decoquinate	DECCOX	N039-417	Type C	For the prevention of coccidiosis in young goats caused by Eimeria christenseni and E. ninakohlyakimovae.	OTC

Goats
OTC - examples

Active Ingredient	Proprietary Name	NADA/ANADA	Label Type	Indications	Marketing Status
Monensin	RUMENSIN	N095-735	Type C	For the prevention of coccidiosis caused by Eimeria crandallis, E. christenseni, and E. ninakohlyakimovae in goats maintained in confinement.	OTC
Morantel tartrate	RUMATEL	N092-444	Type C	For the removal and control of mature gastriointestinal nematode infections of goats including Haemonchus contortus, Ostertagia (Teladorsagia) circumcincta, and Trichostrongylus axei.	OTC

Goats/kids – excluding lactating goats/dairy females 12 months of age or older

VFD - examples

Active Ingredient	Proprietary Name	NADA/ANADA	Label Type	Indications	Marketing Status
Neomycin Sulfate	NEOMIX	N140-976	Type C	For the treatment and control of colibacillosis (bacterial enteritis) caused by *Escherichia coli* susceptible to neomycin.	

Extralabel Use
CPG 615.115

- Policy Statement –

- … no approved treatment options available …
  - –Goats
  - –Sheep

Sheep

- Production Classes

- Breeding Sheep
- Growing Sheep
- Sheep (Multiple classes)

Breeding Sheep VFD - examples

Active Ingredient	Proprietary Name	NADA/ANADA	Label Type	Indications	Marketing Status
Chlortetracyline	CHLORMAX	N046-699	Type C	For reducing the incidence of (vibrionic) abortion caused by Campylobacter fetus infection susceptible to chlortetracycline.	VFD (Effective 1/1/17)
Chlortetracycline	AUREOMYCIN	N048-761	Type C	For reducing the incidence of (vibrionic) abortions caused by Campylobacter fetus infection susceptible to chlortetracycline in breeding sheep.	VFD (Effective 1/1/17)
Chlortetracycline	CLTC	N092-286	Type C	For reducing the incidence of (vibrionic) abortions caused by Campylobacter fetus infection susceptible to chlortetracycline in breeding sheep.	VFD (Effective 1/1/17)
Chlortetracycline	PENNCHLOR	N138-935	Type C	For reducing the incidence of (vibrionic) abortions caused by Campylobacter fetus infection susceptible to chlortetracycline in breeding sheep.	VFD (Effective 1/1/17)
Chlortetracycline	DERACIN	A200-510	Type C	For reduction in the incidence of (vibrionic) abortions caused by *Campylobacter fetus* infection susceptible to chlortetracycline in breeding sheep.	VFD (Effective 1/1/17)

Sheep (Multiple Classes) OTC - examples

Active Ingredient	Proprietary Name	NADA/ANADA	Label Type	Indications	Marketing Status
Decoquinate	DECCOX	N039-417	Type C	For the prevention of coccidiosis in young sheep caused by Eimeria ovinoidalis, E. parva, E. bakuensis, and E. crandallis.	OTC
Decoquinate	DECCOX	N039-417	Type C	For the prevention of coccidiosis in young sheep caused by Eimeria ovinoidalis, E. parva, E. bakuensis, and E. crandallis.	OTC
Decoquinate	DECCOX	N039-417	Type C	For the prevention of coccidiosis in young sheep caused by Eimeria ovinoidalis, E. parva, E. bakuensis, and E. crandallis.	OTC
Decoquinate (liquid)	DECCOX	N039-417	Type B	For the prevention of coccidiosis in young sheep caused by Eimeria ovinoidalis, E. parva, E. bakuensis, and E. crandallis.	OTC

Sheep (Multiple Classes) VFD - examples

Active Ingredient	Proprietary Name	NADA/ANADA	Label Type	Indications	Marketing Status
Neomycin Sulfate	NEOMIX	N140-976	Type C	For the treatment and control of colibacillosis (bacterial enteritis) caused by *Escherichia coli* susceptible to neomycin.	

Sheep (Multiple Classes) VFD - examples

Active Ingredient	Proprietary Name	NADA/ANADA	Label Type	Indications	Marketing Status
Neomycin Sulfate and Oxytetracycline	NEO-TERRAMYCIN	N094-975	Type C	Treatment of bacterial enteritis caused by Escherichia coli and bacterial pneumonia caused by Pasteurella multocida susceptible to oxytetracycline; treatment and control of colibacillosis (bacterial enteritis) caused by E. coli susceptible to neomycin	VFD (Effective 1/1/17)
Neomycin Sulfate and Oxytetracycline	NEO-OXTC	N138-939	Type C	Treatment of bacterial enteritis caused by *Escherichia coli* and bacterial pneumonia caused by *Pasteurella multocida* susceptible to oxytetracycline; treatment and control of colibacillosis (bacterial enteritis) caused by *E. coli* susceptible to neomycin	VFD (Effective 1/1/17)

Sheep (Multiple Classes) VFD - examples

Active Ingredient	Proprietary Name	NADA/ANADA	Label Type	Indications	Marketing Status
Oxytetracycline	TERRAMYCIN	N008-804	Type C	For treatment of bacterial enteritis caused by Escherichia coli and bacterial pneumonia caused by Pasteurella multocida susceptible to oxytetracycline.	VFD (Effective 1/1/17)
Oxytetracycline	OXTC	N095-143	Type C	For sheep for treatment of bacterial enteritis caused by Escherichia coli and bacterial pneumonia caused by Pasteurella multocida susceptible to oxytetracycline.	VFD (Effective 1/1/17)
Oxytetracycline	OTC	N138-938	Type C	For treatment of bacterial enteritis caused by Escherichia coli and bacterial pneumonia caused by Pasteurella multocida susceptible to oxytetracycline.	VFD (Effective 1/1/17)

Extralabel Use
CPG 615.115

- Policy Statement
- Considerations

Extralabel Use
CPG 615.115

- Policy Statement
- Considerations
  - General
  - Veterinarian
  - Producer
  - Distributor/Manufacturer
    - **See Appendix 1 for consideration details**

Extralabel Use
CPG 615.115

- Considerations
  - General - 7
    - Prior written recommendation/VCPR
    - Minor species & indications not on labeling/withdrawal time.
    - Approved Type A medicated article
    - Similar minor species – **mammal = mammal**
    - Not appropriate for unconfined wildlife
    - Animal health/suffering or death
    - Not promoted or advertised

Extralabel Use
CPG 615.115

- Policy Statement
- Considerations
  - General
  - Veterinarian
  - Producer
  - Distributor/Manufacturer
    - **See Appendix 1 for consideration details**

Extralabel Use
CPG 615.115

- Considerations
  - Veterinarian
    - General
    - OTC Medicated Feed
    - VFD Medicated Feed

Extralabel Use
CPG 615.115

- Considerations
  - Veterinarian
    - General
      - All previous General Considerations, plus
      - Indication
      - No therapeutic dosage form that can be used practically under legal ELU
      - Ensure Identity of treated animals
      - Establish a withdrawal period
      - No unsafe drug residues
      - Report adverse drug reactions

Extralabel Use
CPG 615.115

- C. Veterinary Considerations

- General considerations

- Made a determination within the context of a valid veterinarian-client -patient relationship that there is **no approved new animal drug** that
- (i) is labeled for such use, and
- (ii) contains the same active ingredient in the dosage form and concentration necessary for treatment; or, in cases where there is an approved new animal drug, the approved drug is clinically ineffective (see #7) for the use for which the medicated feed is intended;

Extralabel Use
CPG 615.115

- Considerations
  - Veterinarian
    - General
    - OTC Medicated Feed
    - VFD Medicated Feed

Extralabel Use
CPG 615.115

- Considerations
  - Veterinarian
    - OTC Medicated Feed
      - All conditions in General Considerations and in Veterinarian Considerations/General, and
      - Written recommendation including the medical rationale dated within the 6 months prior to use.
      - Provide a copy of recommendation to the client
      - DVM keep a copy of the recommendation to show to FDA on request.

Extralabel Use
CPG 615.115

- Considerations
  - Veterinarian
    - VFD Medicated Feed
      - All conditions in General Considerations and in Veterinarian Considerations/General, and
      - Written recommendation including medical rationale dated within the 6 months prior to use.
      - Provide a copy of recommendation to the client
      - Keep a copy of recommendation for at least 2 years to show to FDA on request.

Extralabel Use
CPG 615.115

- C. Veterinary Considerations
- Veterinary Feed Directive (VFD) Medicated Feed

- Completed the VFD consistent with the approved labeling for the indication. In the "Special Instructions" the veterinarian should note:
  - a. "*This VFD is being issued in accordance with CPG 615.115*";
  - b. The actual species for which the medicated feed is intended (unless that species is already reflected on the VFD because the VFD drug is approved for use in that minor species, but is being used for a different indication); and
  - c. The withdrawal time associated with the extralabel use if different than the labeled withdrawal time as already reflected on the VFD (see section C. Veterinarian Considerations/General).

Extralabel Use
CPG 615.115

- Policy Statement
- Considerations
  - General
  - Veterinarian
  - Producer
  - Distributor/Manufacturer
    - **See Appendix 1 for consideration details**

Extralabel Use
CPG 615.115

- In general, the Agency will not recommend or initiate enforcement action against
  - the veterinarian,
  - animal producer,
  - feed mill, or other distributor
- when extralabel use is **consistent with this document.**

Extralabel Use
CPG 615.115

- E. Regulatory Action Guidance

- Warning Letter(s)

- Domestic Seizure

Outline

- Take Home
- Changes to Affected Products

  Changes to Oral Dosage Form Products

  Changes to Medicated Feed Products

    - Major & Minor Species
- Sources of Information
- Take Home

Sources of Information

Approved Applications: AnimalDrugs@FDA:
https://animaldrugsatfda.fda.gov/adafda/views/#/search

BlueBird labels:
http://www.fda.gov/AnimalVeterinary/Products/AnimalFoodFeeds/MedicatedFeed/BlueBirdLabels/ucm081795.htm

eCFR: http://162.140.57.127/cgi-bin/ECFR?page=browse

VFD Distributors & Licensed Feed Mills:

http://www.fda.gov/downloads/AnimalVeterinary/Products/AnimalFoodFeeds/MedicatedFeed/UCM096059.pdf

http://www.fda.gov/downloads/AnimalVeterinary/Products/AnimalFoodFeeds/MedicatedFeed/UCM089534.pdf

Sources of Information

CPG 615.115:

http://www.fda.gov/ucm/groups/fdagov-public/@fdagov-afda-ice/documents/webcontent/ucm074659.pdf

OMUMS:

http://www.fda.gov/animalveterinary/resourcesforyou/animalhealthliteracy/ucm189540.htm

Questions:

AskCVM@FDA.HHS.GOV

Outline

- Take Home
- Voluntary changes of Affected Products

  Changes to Oral Dosage Form Products

  Changes to Medicated Feed Products

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Take Home

All drug sponsors
have aligned
all affected applications
with the GFI # 213
recommendations
by the January 2017 target date.

Take Home

The applications impacted by these voluntary changes

represent about 95 % of the sales of medically important antimicrobials for reporting year 2015.

Take Home

CVM encourages veterinarians treating sheep and goats to read and follow

1. 21 CFR Part 530 regarding ELU of Rx drugs,

and

2. the considerations in CPG 615.115 regarding ELU of Medicated Feed.


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ADMINISTRATION

Attachment 1

CPG 615.115 Considerations

Extralabel Use
CPG 615.115

- Because of the need to have therapeutic options available for treatment of minor species, and to help ensure animal safe ty and human food safety, FDA is issuing this revised CPG to provide guidance to FDA staff with respect to factors to consider when determining whether to take enforcement action against a veterinarian, animal producer, feed manufacturer, and/or feed distributor for the extralabel use of OTC and VFD medicated feeds in minor species.

Extralabel Use
CPG 615.115

- In general, the Agency **will not recommend** or initiate **enforcement action** against
- the veterinarian,
- animal producer,
- feed mill, or other distributor
- when extralabel use is **consistent with this document.**

Extralabel Use
CPG 615.115

- Policy Statement
- Considerations
  - General
  - Veterinarian
  - Producer
  - Distributor/Manufacturer

Extralabel Use
CPG 615.115

- General considerations

- **All** of the following conditions must be present in order to consider enforcement discretion:

- 1. The medicated feed is used in an extralabel manner only with the express **prior written recommendation** (see section C. Veterinarian Considerations) and oversight of a licensed veterinarian within the context of a valid **veterinarian-client-patient relationship** as defined in 21 CFR 530.3(i),

Extralabel Use
CPG 615.115

- General considerations

- All of the following conditions must be present in order to consider enforcement discretion:

- 2. The medicated feed is used in an extralabel manner only for treatment of minor species … limited to:
- • use in minor **species** not listed in the labeling,
- • use for **indications** (diseases or other conditions) not listed in the labeling, and
- • extension of the labeled **withdrawal time**

- (see section C. Veterinarian Considerations/General).

Extralabel Use
CPG 615.115

- General considerations

- All of the following conditions must be present in order to consider enforcement discretion:

- 3. The **Type A medicated article is approved** for use in or on animal feed and such feed is manufactured and labeled according to the approved labeling as described in 21 CFR part 558;

Extralabel Use
CPG 615.115

- General considerations

- All of the following conditions must be present in order to consider enforcement discretion:

- 4. Extralabel use of medicated feed in a food -producing minor species is limited to use in a minor species similar to the species for which the medicated feed is approved. Extralabel use of medicated feed for:

- • **aquaculture** is limited to medicated feeds approved for use in **aquatic** species;
- • **avian** species is limited to medicated feeds approved for use in **avian** species; and
- • **mammalian** species is limited to medicated feeds approved for use in **mammalian** species.

Extralabel Use
CPG 615.115

- General considerations

- All of the following conditions must be present in order to consider enforcement discretion:

- 5. Extralabel use of medicated feed is limited to a farmed or confined minor species.
-

  Use for the treatment of unconfined wildlife is not appropriate and thus is outside the scope of this CPG;

Extralabel Use
CPG 615.115

- General considerations

- All of the following conditions must be present in order to consider enforcement discretion:

- 6. Extralabel use is limited to therapeutic treatment when the health of an animal is threatened and suffering or death may result from failure to treat. It is unacceptable under any circumstances to use a medicated feed in an extralabel manner for improving rate of weight gain, feed efficiency, or other production purposes.

Extralabel Use
CPG 615.115

- General considerations

- All of the following conditions must be present in order to consider enforcement discretion:

- 7. The person, including veterinarians, animal producers, feed mill distributors, or other distributors, as applicable, has not promoted or advertised the medicated feed for an extralabel use. Such promotional activity is not appropriate because extralabel use of medicated feed is not legally permissible under the FD&C Act.

Extralabel Use
CPG 615.115

- C. Veterinary Considerations

- General considerations
- OTC Medicated Feed
- VFD Medicated Feed

Extralabel Use
CPG 615.115

- C. Veterinary Considerations

- General considerations
- In the course of an inspection or other activity to investigate compliance, in order to consider enforcement discretion in cases where a veterinarian is recommending or authorizing the extralabel use of an approved new animal drug in or on animal feed for use in a minor species, field personnel must also determine that, along with meeting all of the applicable conditions listed above in section B. General Considerations, the veterinarian has done all of the following.

Extralabel Use
CPG 615.115

- C. Veterinary Considerations

- General considerations

- 1. Made a careful diagnosis and evaluation of the therapeutic **indication** for which the drug is to be used;

Extralabel Use
CPG 615.115

- C. Veterinary Considerations

- General considerations

- 2. Made a determination within the context of a valid veterinarian-client -patient relationship that there is **no approved new animal drug** that
- (i) is labeled for such use, and
- (ii) contains the same active ingredient in the dosage form and concentration necessary for treatment; or, in cases where there is an approved new animal drug, the approved drug is clinically ineffective (see #7) for the use for which the medicated feed is intended;

Extralabel Use
CPG 615.115

- C. Veterinary Considerations

- General considerations

3. Ascertained that there is **no therapeutic dosage form that can be practically used under legal extralabel use**;

Extralabel Use
CPG 615.115

- C. Veterinary Considerations

- General considerations

4. Instituted procedures to ensure that the **identity of treated animals** is carefully maintained;

Extralabel Use
CPG 615.115

- C. Veterinary Considerations

- General considerations

- 5. **Establish**ed **a withdrawal period** that is substantially extended beyond that of the approved use (supported by appropriate scientific information) prior to marketing of milk, meat, eggs, or other edible products derived from the treated minor species, if applicable;

Extralabel Use
CPG 615.115

- C. Veterinary Considerations

- General considerations

- 6. Taken appropriate measures to ensure that assigned timeframes for withdrawal are met and **no unsafe drug residues occur** in any food-producing animal subjected to extralabel treatment; and

Extralabel Use
CPG 615.115

- C. Veterinary Considerations

- General considerations

- 7. Has reported any adverse reactions to FDA within 10 days of occurrence by visiting FDA's webpage entitled "How to Report Animal Drug Side Effects and Product Problems" at: http://www.fda.gov/AnimalVeterinary/SafetyHealth/ReportaProblem/ucm055305.htm. The veterinarian also should have reported treatments that were not clinically effective.

Extralabel Use
CPG 615.115

- C. Veterinary Considerations

- General considerations

- 7. Has reported any adverse reactions to FDA within 10 days of occurrence by visiting FDA's webpage entitled "How to Report Animal Drug Side Effects and Product Problems" at: http://www.fda.gov/AnimalVeterinary/SafetyHealth/ReportaProblem/ucm055305.htm. The veterinarian also should have reported treatments that were not clinically effective.

Extralabel Use
CPG 615.115

- C. Veterinary Considerations

- Over-the-counter (OTC) Medicated Feed
- In cases where a veterinarian is recommending the extralabel use of an OTC medicated feed for a minor species, in order to consider enforcement discretion field personnel must determine that, **along with meeting all of the applicable conditions listed above** in sections B. General Considerations and C. Veterinarian Considerations/General, the veterinarian has done **all** of the following:

Extralabel Use
CPG 615.115

- C. Veterinary Considerations

- <u>Over-the-counter (OTC) Medicated Feed</u>
- 1. Made a written recommendation that includes the medical rationale (e.g., diagnosis, drug selection, dose and duration, and the required withdrawal period), dated within 6 months prior to use;

Extralabel Use
CPG 615.115

- C. Veterinary Considerations

- <u>Over-the-counter (OTC) Medicated Feed</u>

- 2. Provided the client with a copy of the written recommendation; and
- 3. Kept copies of the written recommendation and makes them available to the FDA upon request.

Extralabel Use
CPG 615.115

- C. Veterinary Considerations

- Veterinary Feed Directive (VFD) Medicated Feed

Extralabel Use
CPG 615.115

- C. Veterinary Considerations

- Veterinary Feed Directive (VFD) Medicated Feed
- In cases where a veterinarian is authorizing the extralabel use of a VFD medicated feed for a minor species, in order to consider enforcement discretion field personnel must determine that, **along with meeting all of the applicable conditions listed above** in sections B. General Considerations and C. Veterinarian Considerations /General and satisfying the applicable requirements in the regulations relating to VFD drugs under 21 CFR 558.6, the veterinarian has done **all** of the following:

Extralabel Use
CPG 615.115

- C. Veterinary Considerations

- Veterinary Feed Directive (VFD) Medicated Feed
- 1. Completed a separate written recommendation to the client for the extralabel use that includes the medical rationale (e.g., diagnosis, drug selection, dose and duration, and the withdrawal period (see above at section C. Veterinarian Considerations /General), dated within 6 months prior to use;
  - a. Provided the client with a copy of the written recommendation; and
  - b. Kept copies of the written recommendation for 2 years and makes them available to the FDA upon request.

Extralabel Use
CPG 615.115

- C. Veterinary Considerations

- Veterinary Feed Directive (VFD) Medicated Feed

- 2. Completed the VFD consistent with the approved labeling for the indication. In the "Special Instructions" the veterinarian should note:
  - a. "This VFD is being issued in accordance with CPG 615.115";
  - b. The actual species for which the medicated feed is intended (unless that species is already reflected on the VFD because the VFD drug is approved for use in that minor species, but is being used for a different indication); and
  - c. The withdrawal time associated with the extralabel use if different than the labeled withdrawal time as already reflected on the VFD (see section C. Veterinarian Considerations/General).

Extralabel Use
CPG 615.115

- C. Animal Producer (Client) Considerations

Extralabel Use
CPG 615.115

- C. Animal Producer (Client) Considerations
  - General
  - Over the Counter Medicated Feed
  - VFD Medicated Feed

Extralabel Use
CPG 615.115

- C. Animal Producer (Client) Considerations
  - General
- In the course of an inspection or other activity to investigate compliance, in order to consider enforcement discretion with respect to an animal producer using medicated feed in an extralabel manner for a minor species, field personnel must determine that, a long with meeting all of the applicable conditions listed above in section B. General Considerations, the animal producer has done all of the following:

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- C. Animal Producer (Client) Considerations
  - General

- … the animal producer has done all of the following:
-
- 1. Kept complete and accurate records of medicated feeds received, including labels, invoices, and dates fed. These records are kept for at least 2 years from the date of delivery of the medicated feed;

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- C. Animal Producer (Client) Considerations
  - General

- … the animal producer has done all of the following:
-
- 2. Instituted procedures to ensure that the identity of treated animals is carefully maintained;

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- C. Animal Producer (Client) Considerations
  - General

- … the animal producer has done all of the following:
-
- 3. Taken appropriate measures to ensure that assigned timeframes for withdrawal are met and no unsafe drug residues occur in edible products derived from an animal receiving extralabel treatment;

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- C. Animal Producer (Client) Considerations
  - General

- … the animal producer has done all of the following:
-
- 4. Used the medicated feed in accordance with Federal, State, and local environmental and occupational laws and regulations. This is especially important for aquaculture uses;

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- C. Animal Producer (Client) Considerations
  - General

- … the animal producer has done all of the following:
-
- 5. Met the requirements of the Federal Clean Water Act as implemented under the National Pollutant Discharge Elimination System (NPDES), as well as any requirements applicable to ground-water pollution. The producer should contact the offices responsible for issuing NPDES permits, and other similar permits, to be certain there are no objections to the use and release of the drug;

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- C. Animal Producer (Client) Considerations
  - General

- … the animal producer has done all of the following:
-
- 6. Followed user safety provisions as set forth in approved product labeling to protect individuals who may be exposed to the drug.

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- C. Animal Producer (Client) Considerations

- Over-The-Counter(OTC)Medicated Feed
- In cases where a veterinarian is authorizing the extralabel use of an OTC medicated feed for a minor species, in order to consider enforcement discretion, field personnel must determine that the animal producer has kept a copy of the veterinarian's written recommendation for the extralabel use of the medicated feed, the copy is being kept by the animal producer for at least 2 years after feeding the medicated feed, and during that time making it available to FDA upon request.

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- C. Animal Producer (Client) Considerations

- Veterinary Feed Directive (VFD) Medicated Feed
- In cases where a veterinarian is authorizing the extralabel use of a VFD medicated feed for a minor species, in order to consider enforcement discretion, field personnel must determine that the animal producer has complied with the applicable VFD regulations in 21 CFR 558.6, including keeping a copy of the VFD for 2 years and during that time making such records available to FDA upon request.

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- C. Animal Producer (Client) Considerations

- Veterinary Feed Directive (VFD) Medicated Feed
- In cases where a veterinarian is authorizing the extralabel use of a VFD medicated feed for a minor species, in order to consider enforcement discretion, field personnel must determine that the animal producer has complied with the applicable VFD regulations in 21 CFR 558.6, including keeping a copy of the VFD for 2 years and during that time making such records available to FDA upon request.

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- D. Medicated Feed Manufacturer or Distributor Considerations

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- D. Medicated Feed Manufacturer or Distributor Considerations

- In the course of an inspection or other activity to investigate compliance, in order to consider enforcement discretion with respect to an individual or firm who manufactures and/or distributes medicated feed for extralabel use in minor species, field personnel must determine that the medicated feed manufacturer and/or distributor has done all of the following:

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- D. Medicated Feed Manufacturer or Distributor Considerations

- 1. Formulated the medicated feed as approved

- The non-medicated ingredients (nutrients) may be customized to be appropriate for the diet of the minor species as long as the customization is not in conflict with the medicated feed approval. The manufacturer/distributor is expected to engage with the client (animal producer) and/or nutritionist to formulate a medicated feed with appropriate nutrient content for the minor species that is consistent with the terms of the approval.

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- D. Medicated Feed Manufacturer or Distributor Considerations

- 2. Labeled the medicated feed to reflect the approved bluebird label (http://www.fda.gov/AnimalVeterinary/Products/AnimalFoodFeeds/MedicatedFeed/BlueBirdLabels/default.htm)

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- D. Medicated Feed Manufacturer or Distributor Considerations

- 3. Maintained the manufacturing record (including capturing any nutrient modifications) for 1 year as required by 21 CFR part 225. (Note that any records that would also be required under 21 CFR part 507 relating to the manufacturing, processing, packing, or holding of animal food must be kept for at least 2 years); and

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- D. Medicated Feed Manufacturer or Distributor Considerations

- 4. If applicable, met the requirements for the manufacture /distribution of a veterinary feed directive (VFD) medicated feed in 21 CFR 558.6, including maintaining the VFD for 2 years and during that time making such records available to FDA upon request.