Medicated Feeds Overview

Division of Animal Feeds
Medicated Feeds Team

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Rockville, MD
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Agenda

- Definitions and usages
  - Drug Categories
  - Types of Distribution
  - Medicated Products
- Relationship/role in animal drug approval process
- Pre-approval Activities
- Post-approval Activities
  - Current Good Manufacturing Practices (cGMP)
  - Program Monitoring
  - Licensing and Registration

Drug Categories

- Category I
  - no withdrawal period is required at the lowest use level for each species for which they are approved
- Category II
  - a) withdrawal period is required at the lowest use level for at least one species for which they are approved
  - b) regulated on a “no-residue” basis or with a “zero” tolerance level because of a carcinogenic concern, or
  - c) are veterinary feed directive drugs
## Types of Distribution

Medicated Feeds are distributed:

- Over-The-Counter
- Veterinary Feed Directive

## Medicated Products

- Type A medicated article
- Type B medicated feed
- Type C medicated feed

## Medicated Products

- Type A medicated article
  - is a new animal drug
A new animal drug is...

Section 201(v):

- any drug intended for use for animals other than man, including any drug intended for use in animal feed
- does not include animal feed

Medicated Products

• Type A medicated article
  - is a new animal drug
  - with or without inactive ingredients
  - intended for use in animal feed
  - intended solely for further manufacture

Medicated Products

• Type A medicated article is used to make
  – another Type A medicated article
  – a Type B medicated feed
  – a Type C medicated feed
Animal feed is...

- Section 201(w):
  - an article intended for use for food for animals other than man
  - intended for use as a substantial source of nutrients in the diet of the animal
  - is not limited to a mixture intended to be the sole ration of the animal.

Medicated Products

- Type A medicated article - DRUG
- Type B medicated feed - FEED containing DRUG
- Type C medicated feed - FEED containing DRUG

Type B Medicated Feed

- contains a substantial quantity of nutrients
- originates from:  
  a) a Type A medicated article
  b) another Type B medicated feed
  c) an unstandardized drug component (bulk or “drum run”)
### Type B Medicated Feed

- intended solely for the manufacture of:
  - other Type B medicated feed
  - Type C medicated feed

### Type B Medicated Feed

- the maximum concentration of drug(s) is:
  a) if a Category I drug
     - 200 X the highest continuous use level
  b) if a Category II drug
     - 100 X the highest continuous use level
  c) if a drug is not approved for continuous use
     - the highest level used for disease prevention/control

### Components of a Type B Blue Bird Label

- product name
- purpose or indications for use
- active ingredients
- guaranteed analysis
- ingredients
- mixing directions
- warning and caution sections (if any)
- name and address of manufacturer
- net weight statement
Type C Medicated Feed

- Originates from:
  - a) a Type A medicated article
  - b) a Type B medicated feed
  - c) another Type C medicated feed
  - d) an unstandardized drug component (bulk or drum run)

Type C Medicated Feed

- is intended for feeding as:
  - a) the complete feed
  - b) ‘top dressed’
  - c) ‘free choice’

Components of a Type C Blue Bird Label

- product name
- purpose or indications for use
- active ingredients
- guaranteed analysis
- ingredients
- feeding directions
- warning and caution sections (if any)
- name and address of manufacturer
- net weight statement
Major differences between Type B and Type C medicated feed labels

- **Type B**
  - for further mixing
  - cannot be fed

- **Labeling**
  - Mixing directions

- **Type C**
  - for feeding
  - to be fed

- **Labeling**
  - Feeding directions

FDA’s animal drug approval process – already discussed

Where our work fits

Label review

- **Division of Animal Feeds**
  - Office of Surveillance and Compliance (OSC)
  - Center for Veterinary Medicine

- **Office of New Animal Drug Evaluation (ONADE)**
  - Center for Veterinary Medicine

- **Pre-approval**

- **Post-approval**
  - Other units within the OSC
  - Field personnel- FDA
  - State Officials
  - Drug Manufacturers
Labeling of Medicated Products

Medicated Products

- Type A medicated article
- Type B medicated feed
- Type C medicated feed

Label Review

- Types of labels

<table>
<thead>
<tr>
<th>Medicated Product</th>
<th>Pre-approval</th>
<th>Post-approval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type A medicated article</td>
<td>Brand</td>
<td>Brand</td>
</tr>
<tr>
<td>Type B medicated feed</td>
<td>Blue Bird</td>
<td>Brand</td>
</tr>
<tr>
<td>Type C medicated feed</td>
<td>Blue Bird</td>
<td>Brand</td>
</tr>
</tbody>
</table>
Drug X/Drug Y
Growing Turkey Ration
Type B MEDICATED FEED
For the prevention of coccidiosis caused by Eimeria meleagrimitis, E. gallopavonis, and E. adenoeides and for increased rate of weight gain and improved feed efficiency in growing turkeys.

ACTIVE DRUG INGREDIENTS
Drug X ...........................................................................80,000 g/ton
Drug Y…………………………………………….6,000 g/ton

GUARANTEED ANALYSIS
Crude Protein (min)……………………………………………%
Lysine (min)………………………%
Methionine (min)…………………………%
Crude Fat (min)………………………………………………%
Crude Fiber (max)……………………………………………%
Calcium (min)………….%
Calcium (max)………%.%.
Phosphorus (min)…..%.
Salt (min)1……………%
Salt (max)1…………….%
Sodium (min)2…..%.
Sodium (max)2….%
1If added.
2Shall be guaranteed only when total Sodium exceeds that furnished by the maximum salt guarantee.

INGREDIENTS: Ingredients as defined by AAFCO.

MIXING DIRECTIONS: Mix 10 pounds of this Type B medicated feed with 1990 lb non-medicated feed ingredients to manufacture one ton of complete turkey feed containing 400 grams of Drug X and 30 grams of Drug Y.

CAUTION: Do not feed to breeding turkeys.

WARNING: Do not feed five days before slaughter.

MANUFACTURED BY:
BLUE BIRD FEED MILL
Robin, IN 00000

Blue Bird Labels

■ 21 CFR 514.1(b)(3)(v)

– (b) Representative labeling proposed to be used for Type B and Type C medicated feeds containing the new animal drug.

Brand Label – an example
Drug X/Drug Y
Growing Turkey Ration
Type B MEDICATED FEED
For the prevention of coccidiosis caused by Eimeria meleagrimitis, E. gallopavonis, and E. adenoeides and for increased rate of weight gain and improved feed efficiency in growing turkeys.

ACTIVE DRUG INGREDIENTS
Drug X ....................................................................…….…………….……….....80,000 g/ton
Drug Y……………………………………….……………………….........……………6,000 g/ton

GUARANTEED ANALYSIS
Crude Protein (min)………………………………………………............ .............................…..______%
Lysine (min)……………………………………… ……………….............................. .............…. ….….……. .______%
Methionine (min)………………………………………………….................... .......................….….….…….. ______%
Crude Fat (min)…………………………………………………….................. .........................………..…….. ______%
Crude Fiber (max)………………………………………………………......................... ...................………..______%
Calcium (min)…………...……………………… ………………………………………………..……..… .……..______%
Calcium (max)………. .…………………………………………………………………………..… …..….……..______%
Phosphorus (min)…..………………………… ……………………………………………….……… .………..______%
Salt (min)1……………..…………………………………………..................... .......................……………….. ______%
Salt (max)1……………..……………………………………........................... ................….………...………..______%
Sodium (min)2…..……..……………………………………........................ .................…… …….. ......……..______%
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MANUFACTURED BY:
BLUE BIRD FEED MILL
Robin, IN 00000

Net Weight____lbs (______kg)
Bag or Bulk

Comparison between Blue Bird and Brand labels

<table>
<thead>
<tr>
<th>Section</th>
<th>Blue Bird</th>
<th>Brand</th>
</tr>
</thead>
<tbody>
<tr>
<td>Product name</td>
<td>Generic</td>
<td>Brand</td>
</tr>
<tr>
<td>Indications for use</td>
<td>As regulation says</td>
<td>Same</td>
</tr>
<tr>
<td>Active Ingredients</td>
<td>As regulation says</td>
<td>Same</td>
</tr>
<tr>
<td>Guaranteed analysis</td>
<td>Blank levels</td>
<td>Specific levels</td>
</tr>
<tr>
<td>Ingredients</td>
<td>AAFCO statement</td>
<td>List ingredients</td>
</tr>
<tr>
<td>Directions for use</td>
<td>As regulation says</td>
<td>Mostly same</td>
</tr>
<tr>
<td>Warning section</td>
<td>As regulation says</td>
<td>Same</td>
</tr>
<tr>
<td>Caution section</td>
<td>As regulation says</td>
<td>Same</td>
</tr>
<tr>
<td>Manufacturer information</td>
<td>Generic</td>
<td>Exact information</td>
</tr>
<tr>
<td>Net weight statement</td>
<td>Generic</td>
<td>Exact</td>
</tr>
</tbody>
</table>

Where to look for more information?

GFI #181 – Blue Bird Medicated Feed Labels
Where to look for more information?

- **Label format**
  - Official Publication of the Association of American Feed Control Officials
    - Contact Ms. Sharon Krebs at 765-385-1029 or at sharon@aafco.org
    - 21 CFR 501 – Animal Food Labeling

Where to look for more information?

- NADA (BBL)
  - CFR
  - FOI
  - FR
  - Animal Drug List
  - Compendium

Current Good Manufacturing Practices (cGMPs)

- Assures that feed...
  - has the identity and strength, which it purports
  - meets the quality, purity, and safety requirements, which it is represented to possess

- Minimum requirements for manufacture of medicated animal feed
Current Good Manufacturing Practices for Medicated Animal Feed

- 21 CFR 225
  - Feed manufacturer’s required to hold a medicated feed mill license
    - 21 CFR 225.10 – 21 CFR 225.115
  - Feed manufacturer’s NOT required to hold a medicated feed mill license
    - 21 CFR 225.120 – 21 CFR 225.202

Current Good Manufacturing Practices for Licensed Feed Manufacturers

- General Provisions
- Construction and Maintenance of Facilities and Equipment
- Product Quality Control
- Packaging and Labeling
- Records and Reports

Current Good Manufacturing Practices for Non-Licensed Feed Manufacturers

- Facilities and Equipment
  - Buildings and Grounds
  - Equipment
  - Work and Storage Areas
- Product Quality Assurance
  - Components
  - Laboratory Assays
  - Equipment Cleanout Procedures
- Labeling
- Records
  - Formula, production, and distribution records
# Feed Manufacturing Compliance Program

**OBJECTIVES**
- To conduct inspections of registered medicated feed firms and determine whether the firms are in compliance with the Federal Food, Drug, and Cosmetic Act and the implementing regulations.
- To address concerns of drug residue carryover and superpotent and subpotent feeds.
- To verify compliance with VFD requirements as needed.
- To encourage voluntary corrective action by firms when appropriate.
- To initiate administrative and/or regulatory action against violative firms and feed products.

# Medicated Feed Mill Licensing

- 21 CFR 515
- 21 CFR 558
- Form FDA 3448
- Registration of Drug Establishment

## 21 CFR 515

- If licensed:
  - Facilities are allowed to manufacture animal feeds from Category II, Type A medicated articles or certain liquid and free-choice feed, using Category I, Type A medicated articles that must follow proprietary formulas or specifications.
## Significant Regulations for New Animal Drugs For Use in Animal Feeds

- 558.3 - Definitions and general considerations applicable to this part.
- 558.4 - Requirement of a medicated feed mill license.
- 558.5 - Requirements for liquid medicated feed.
- 558.6 - Veterinary feed directive drugs.
- 558.35 – 558.680 - Specific New Drugs For Use in Animal Feeds
- 510.455 - Requirements for free-choice medicated feeds

## Form FDA 3448

A medicated feeds licensee certifies that:

- animal feeds bearing or containing new animal drugs are manufactured and labeled in accordance with the applicable regulations published pursuant to section 512(i) to the Federal Food, Drug and Cosmetic Act (the Act), or in accordance with the index listing published under section 572(e)(2) of the Act;
- are in conformity with current good manufacturing practice (cGMPs); and
- they will establish and maintain all records required and will permit access to, or copying or verification of such records by the FDA

## A medicated feed mill licensee commitments

- possessing current approved or index listed Type B and/or Type C medicated feed labeling prior to receiving the Type A Medicated Article
- Renewing drug establishment registration each year;
- using only non-drug feed components recognized in the Official Publication of the Association of American Feed Control Officials (AAFCO) or sanctions by FDA under 21 CFR 573, 582 and 584 as suitable for use in animal feeds;
- Supplementing license application when changes in ownership or address occur; and
- complying with all other applicable provision of the Act.
Prior to shipment of a new animal drug intended for use in the manufacture of medicated animal feed, the seller must have a written statement from the buyer that the buyer has an approved feed mill license and possesses current approved Type B and/or Type C feed labeling for the drug.

Lists of approved license holders are on the FDA/CVM website.

### Registration of Drug Establishment

Requirements for drug registration are found in

- section 510 of the FFD&C Act
- section 351 of the Public Health Service Act
- part 207 of Title 21 of the Code of Federal Regulations
- The Food and Drug Administration Amendments Act (FDAAA) of 2007 requires that drug establishment registration and drug listing information be submitted electronically.

### Registration of Drug Establishment

- The Drug Registration and Listing System (DRLS) and the new electronic Drug Registration and Listing System (eDRLS).
- FDA no longer accepts drug establishment registration in paper format unless a waiver is granted.
- Licensed feed mill are not required to drug list.
Where to look for more information?

- Approved products and uses
  - 21 Code of Federal Regulations (CFR) section 558
  - Electronic Code of Federal Regulations
    - http://ecfr.gpoaccess.gov/cgi/t/text/text-idx?c=ecfr&tpl=index.tpl
  - The Federal Register
  - Animal Drugs@FDA
    - http://www.accessdata.fda.gov/scripts/animaldrugsatfda/
  - Feed Additive Compendium
    - The Miller Publishing Co., 952-931-0211

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