Understanding the Past and the Present of Medicated Feeds

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Medicated Feeds – Why Them
Medicated feed

2000 lb
Medicated Feed - Parentage

Drug(s) → Medicated feed → Feed
Medicated Products

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

- **API Drug Component**

  - **Type A Medicated Article**
    - Organic carrier (e.g., rice hulls)
    - Non-medicated feed

  - **Type B Medicated Feed**
    - Non-medicated feed

  - **Type C Medicated Feed**

  - Feeding
Approved New Animal Drugs and Their Uses

New Animal Drugs

- Oral
- Implantation or Injectable
- Ophthalmic and Topical
- Intramammary
- Other
- Animal Feeds
Medicated Products

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

- Type A
- Type B
- Type C
Medicated Products

Type A

Type C
Drug flow in 21 CFR 558

**General**
- Type A
  - Type B
    - Type C

**Fixed Type A combinations**
- Type A
  - Type A
    - Type B
      - Type C

**Individual Type A medicated articles**
- Type A
  - Type A
    - Type B
      - Type C
Historical background

- Before and after 1962
  - the Kefauver-Harris Drug Amendments
  - Animal Drug Amendments

- II Generation
  - Proposed, interim, and final rule
  - Medicated Feed Task Force

- ADAA 1996
  - ADAA drug combinations
  - Feed mill license
  - VFD
1962 - The Kefauver-Harris Drug Amendments

- Authorized FDA to monitor the clinical trials of *investigational* drugs
- Introduced the requirement for *effectiveness* of drugs as well as safety before clearing them for marketing
- Imposed a *retroactive* efficacy requirement for drugs previously approved for safety alone
- Introduced the requirement on *prompt reporting* to FDA any adverse reaction or effects and other clinical experience relative to the safety and efficacy of drugs already on the market
- Stipulated that new drugs may not be cleared for marketing if the *labeling* is in any way false or misleading
1968 - Animal Drug Amendments

- The FFDCA was amended in 1968 to include provisions, under a new Section 512, which specifically address animal drugs

  - these amendments were designed to ensure that animal drugs are safe and effective for their intended uses and that they do not result in unsafe residues in foods

  - a major change is the differing requirements for a basic new animal drug and clearance for use of such drug in a medicated feed – the drug had to be approved for use in medicated feed before MFA could be approved
Prior to the enactment of the Amendments, new animal drugs were subject to section 505 of the Act
- If also qualified as:
  - food additives - then they were also subject to the provisions of section 409
  - certifiable antibiotics - then also subject to the provisions of section 507
The FFDCA was amended in 1968 to include provisions, under a new Section 512, which specifically address animal drugs.

- These amendments were designed to ensure that animal drugs are safe and effective for their intended uses and that they do not result in unsafe residues in foods.

- A major change is the differing requirements for a basic new animal drug and clearance for use of such drug in a medicated feed – the drug had to be approved for use in medicated feed before MFA could be approved.

- New sections added defining the terms “new animal drug” (201(w))* and “animal feed” (201(x))**

*now 201(v)  
**now 201(w)
II Generation

- 1/17/1978 – Proposed Rule
- 1/9/1981 – Proposed Rule
- 7/29/1983 – Tentative Final Rule
11 Generation

- 1/17/1978 – Proposed Rule

  - Rectifying terminology
    - “premix” - Type A medicated article
    - “intermediate premix”, - Type B medicated article
    - “supplement” or “concentrate” - Type C medicated article
    - “complete feed” - Type D medicated article
II Generation

- 1/17/1978 – Proposed Rule
- 1/9/1981 – Proposed Rule

Medicated Feed Task Force
1978 - Medicated Feed Task Force

- Consisted of members representing:
  - The Bureau of Veterinary Medicine
  - Executive Director of Regional Operations
  - Associate Commissioner for Regulatory Affairs
  - Office of the Chief Counsel

- Tasked to:
  - Review and examine the existing medicated feed program and to explore and recommend ways to employ resources more efficiently
II Generation

- 1/17/1978 – Proposed Rule
- 1/9/1981 – Proposed Rule

Medicated Feed Task Force Report: “Second Generation of Medicated Feeds”
1/9/1981 – Proposed Rule

- Propose revisions in the current procedures and requirements concerning conditions of approval for medicated feeds containing new animal drugs
- Propose terms defining medicated feed articles
- Respond to comments made on the 1978 proposal
- Respond to comments received from the Task Force
- Explain the implementation process and schedule of the new programs
II Generation

1/9/1981 – Proposed Rule

- **Drug Categories**
  - Category I - require no withdrawal period at the lowest approved use level
  - Category II - require a withdrawal period at the lowest approved use level
  - Category III - “no residue” or a “zero” tolerance

- **Drug Products**
  - Type A medicated article
  - Type B medicated feed
  - Type C medicated feed

- **Labeling**
  - Representative - for the approval of Type B and Type C medicated feed

- **MFA**
  - For any use of any Type A medicated article in the manufacture of Type B or Type C medicated feed
II Generation

7/29/1983 – Tentative Final Rule

- **Drug Categories**
  - Category I - require no withdrawal period at the lowest approved use level
  - Category II - require a withdrawal period at the lowest approved use level

- **Drug Products**
  - Type A medicated article - “would be regulated as new animal drugs”
  - Type B medicated feed - “regulated as animal feeds containing new animal drugs”
  - Type C medicated feed - “regulated as animal feeds containing new animal drugs”

- **Labeling**
  - Representative - generic for the approval of Type B and Type C medicated feeds

- **MFA**
  - For any use of a Type A medicated article, *Category II drug*, in the manufacture of Type B or Type C medicated feed
III Generation


  - New terminology and definitions
    - Type A medicated article - DRUG
    - Type B medicated feed – FEED containing DRUG
    - Type C medicated feed – FEED containing DRUG

  - Drug categories
    - Category I - require no withdrawal period at the lowest approved use level
    - Category II - require a withdrawal period at the lowest approved use level; “no residue” or a “zero” tolerance

  - “Representative labeling”
    - 21 CFR 514.2(b)(11) – “labeling representative of each intended use as stated in the claim” – (the Blue Bird labels)

  - cGMP regulations
    - 21 CFR 225.10–115 – where MFA is required
    - 21 CFR 225.120–202 – where MFA is not required
Producers of medicated feed were required by the act to have an approved MFA for each medicated feed they manufactured.

Drug specific – an MFA was required for each medicated feed manufactured.
Applications

Producers of medicated feed were required by the act to have an approved MFA for each medicated feed they manufactured

- Drug specific – an MFA was required for each medicated feed manufactured

Applications included
- Three copies of form FD-1800 or FD-1900
- Medicated Feed Application
- Labels and promotional material
- Supplements
- Agency evaluations with supporting material
- Notices of approval
- Related correspondence
- Other documentation
FDA-1900 Medicated Feed Application

- Name and address of the applicant
- The registration number
- Original or supplemental application
- Drug name, potency, manufacturer
- The species of animals
- The form of feed (e.g., mash, meal, pellets, liquid...)
- Whether the feed will be shipped in bag or bulk
- Whether the feed is a Type B or Type C

- Whether the feed is for sale, own use, or both
- Generic/brand name of the feed and drug concentration
- Identification of the regulation that the application is based on
- Whether the attached labeling is in draft or final printed form
- A commitment to establish sampling and assaying program
- A statement of minimum and maximum assay variation permitted
- Identification of the authorized agent
- Signature and date
1996 – Animal Drug Availability Act

- The purpose: to facilitate the approval and marketing of new animal drugs and medicated feeds
  - Feed Mill Licensing
  - Veterinary Feed Directive
  - Substantial evidence of effectiveness
  - Combination New Animal Drugs - Feed Use Combinations
1996 – Animal Drug Availability Act

- **Feed mill licensing**
  - **Proposed rule - July 30, 1997**
    - Eliminates the requirement on a feed mill to submit a separate MFA for each medicated feed manufactured at each site
    - Provides for feed mills to be licensed – a licensed facility is allowed to manufacture any approved medicated feed
  - **Final rule - November 19, 1999**
    - Finalizes the approach provided in the proposed rule
    - Maintains the general scheme for categories and types of medicated feeds
    - Provides that those medicated feeds exempted from the MFA requirements would now be exempt from being required to be manufactured in a licensed feed mill
1996 – Animal Drug Availability Act

- Veterinary Feed Directive
  - Proposed rule – July 2, 1999
    - Proposes to amend the animal drug regulations to implement the Veterinary Feed Directive (VFD) drugs section of the ADAA
    - Proposes establishing the requirements relating to the distribution and use of VFD drugs and animal feeds containing VFD drugs
  - Final rule – December 8, 2000
    - Finalizes the approach provided in the proposed rule
    - Specifies the use of drugs permitted only under the professional supervision of a licensed veterinarian in the course of the veterinarian's professional practice
    - This new regulation states the requirements for distribution and use of a VFD drug and animal feed containing a VFD drug
1996 – Animal Drug Availability Act

- Combination New Animal Drugs – Feed Use Animal Drug Combinations
  - Place holder
Where we are today

- **Terminology and definitions**
  - Type A medicated article - DRUG
  - Type B medicated feed – FEED containing DRUG
  - Type C medicated feed – FEED containing DRUG

- **Drug categories**
  - Category I
  - Category II

- **cGMP regulations**
  - 21 CFR 225.10–115 – where license is required
  - 21 CFR 225.120–202 – where license is not required

- “**Representative labeling**”
  - 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.”

- **21 CFR 515**
  - all the medicated feed mill license procedural regulations