Understanding the Past and the Present of Medicated Feeds

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Medicated Feeds – Why Them

Medicated feed

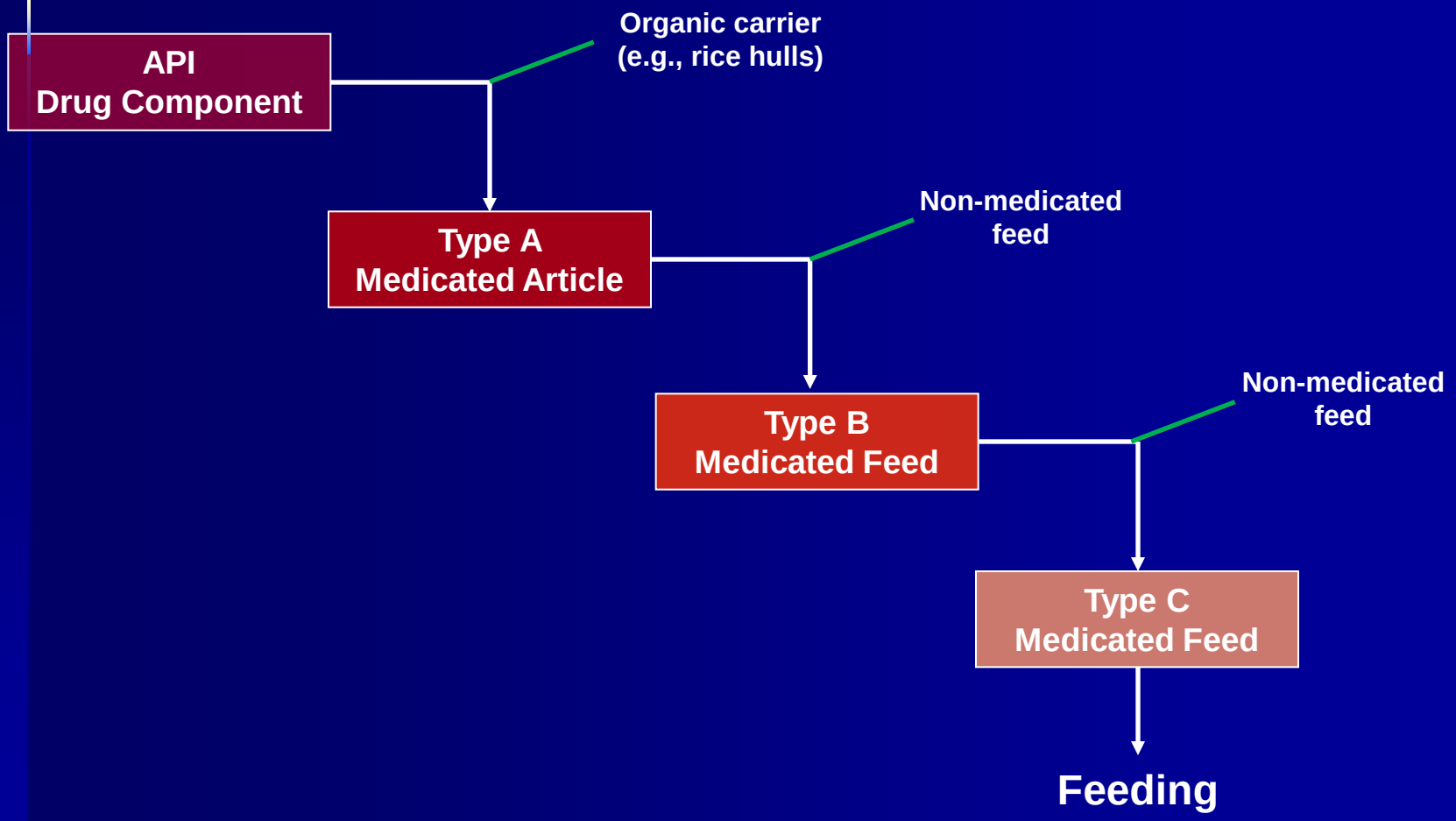
2000 lb

Medicated Feed - Parentage

Medicated Products

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

Medicated Products



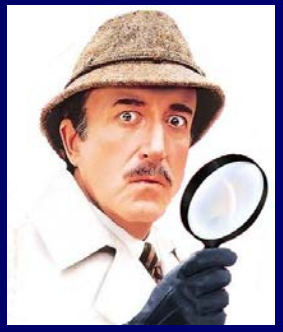
Approved New Animal Drugs and Their Uses

New Animal Drugs

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


OTC
Inspection
Blue Bird
Minor species
Category I
Free-choice
AAFCO
FFDCA
Drum run
Category II
VFD Drug
Continuous use
Index
Feed through pesticide
Complete feed
Liquid
Compendium
Hand feed
VFD Order
Type A
Type B
DAF
Aquaculture
Top dress
AM - PM
Feed mill
21 CFR 558
Assay limits
Type C
21 CFR 226
Records and Reports
21 CFR 225
Medicated feed mill license
Veterinary Feed Directive
More stringent
Labeling
Milk replacer
Extra-label use
Less stringent
Non-lactating
cGMPs
Minor use
Combinations
Intermediate mix

CVM



Blue Bird

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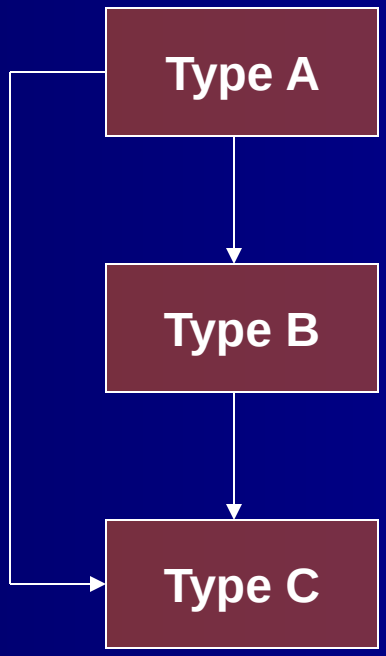

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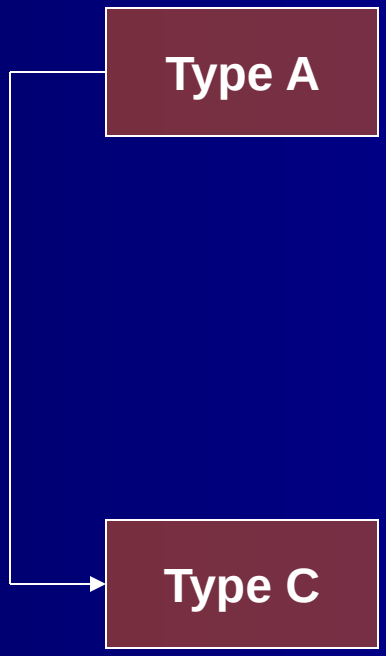
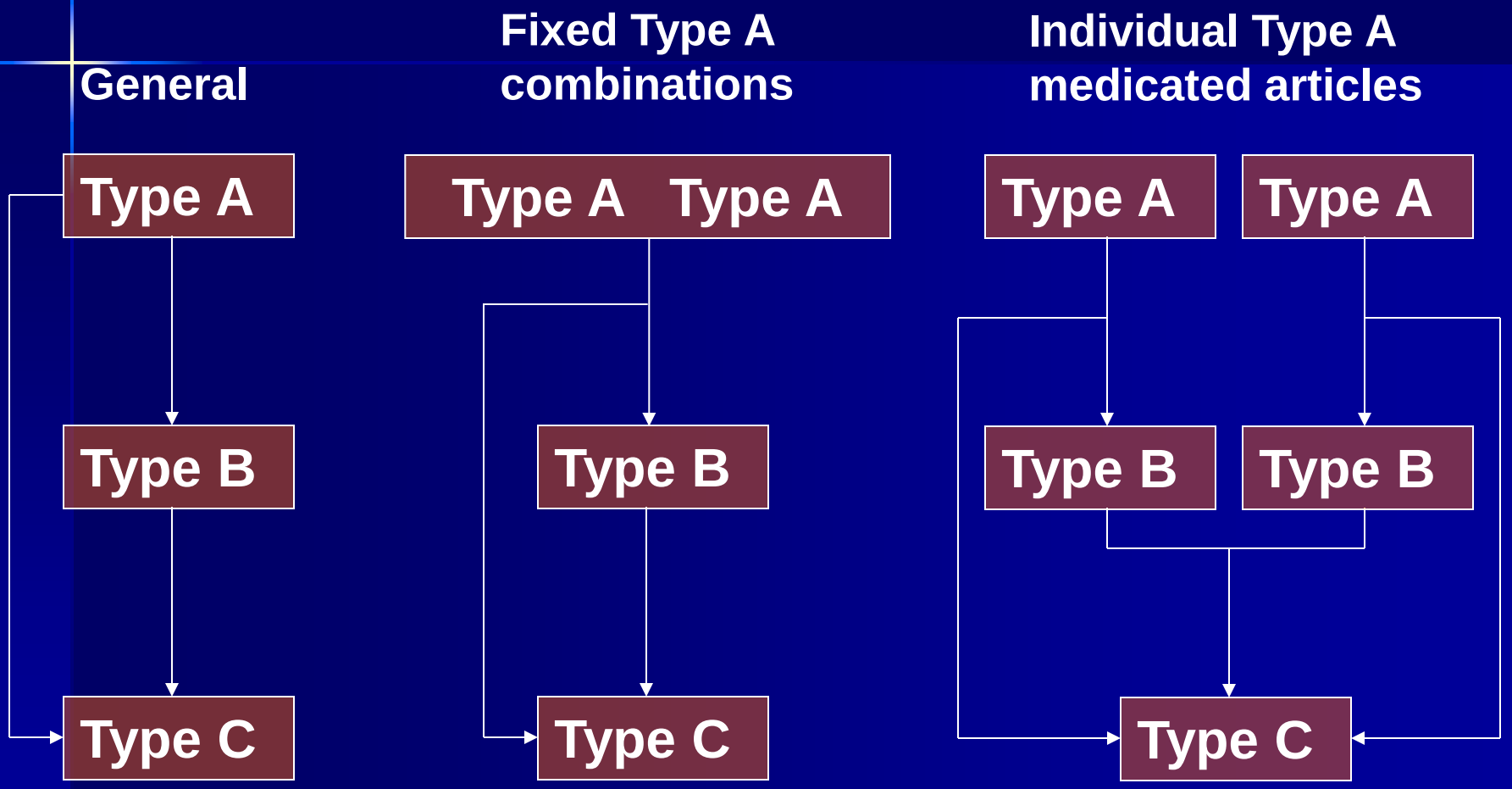


Drug flow in 21 CFR 558



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

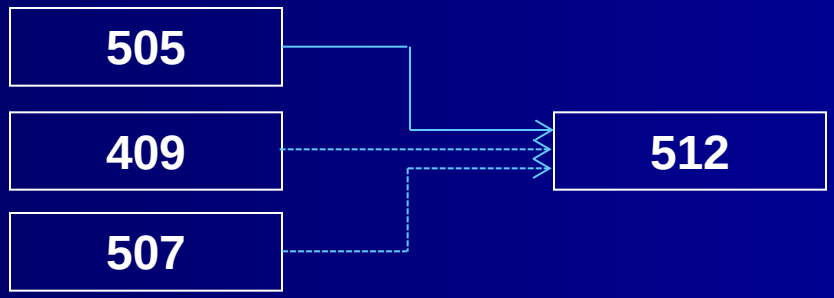
- Authorized FDA to monitor the clinical trials of investigational drugs
- Introduced the requirement for effectiveness of drugs as well as safety before clearing them for marketing
- Imposed a retroactive efficacy requirement for drugs previously approved for safety alone
- Introduced the requirement 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

1968 – Animal Drug Amendments

- 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



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  - 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
- 3/3/1986 – Final Rule

II 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

Medicated Feed Task Force

- 1/9/1981 – Proposed Rule

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"

II Generation

- 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

II Generation

- 3/3/1986 – Final Rule
  - 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

FDA-1900 Medicated Feed Application

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