

# Mitigating Pain in Livestock: What Options are Available

NIAA 2014 Annual Conference

Omaha, Nebraska

April 2, 2014

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U.S. Food and Drug Administration,



# Mitigating Pain in Livestock: What (*Legal*) Options are Available

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# Outline

- Background
- Drugs (approved, unapproved, compounded)
- Extralabel Drug Use
- Pain Mitigation from the Literature (Status)
- Questions
  - Under AMDUCA is extra-label use of analgesics and anesthetics permitted?
  - Is extra-label use of products restricted only to those products that have been approved by FDA and have an NADA or NDA number?

# Pain Mitigation

- Disease pain
  - Cutaneous
  - Visceral – (serosa, distention, swelling)
  - Musculoskeletal – (bone, joint, muscle)
  - (Inflammatory)
- Surgical pain
  - General
  - Localized

# Pain Mitigation (from the literature)

- NSAIDs
  - Aspirin
  - Sodium salicylate
  - Flunixin
  - Ketoprofen
  - Diclofenac
  - Phenylbutazone
  - Meloxicam
  - Carprofen

# Pain Mitigation (from the literature)

- Local anesthetics
  - Lidocaine
  - Mepivacaine
  - Bupivacaine

# Pain Mitigation (from the literature)

- Barbiturates
  - Pentobarbital
  - Thiopental
- Acepromazine
- Benzodiazepines
  - Diazepam
  - Midazolam
- Azaperone
- Xylazine

# Pain Mitigation (from the literature)

- Butorphanol
- Medetomidine
- Ketamine
- Tiletamine-zolazepam (Telazol)
- Guaifenesin
- Tramadol
- Yohimbine



# Pain Mitigation (from the literature)

- Halothane
- Isoflurane
- Propofol
- Guaifenesin
- Tramadol

# Approved Animal Drugs

- To be legally marketed, an animal drug must be the subject of
  - an **approved** new animal drug application (NADA)
  - an **approved** generic application [abbreviated new animal drug] application] (ANADA)
  - a conditional approval
  - an index listing

# Approved Human Drugs

- To be legally marketed, a human drug must be the subject of
  - an **approved** new drug application (NDA)
  - an **approved** generic application [abbreviated new drug application] (ANDA)
  - An OTC Drug Monograph

# Unapproved Animal Drugs

- No pre-approval review
- No post-approval monitoring
- May unfairly compete against approved products
- Reduces the availability of legal, reviewed, tested and monitored drug products

# Unapproved Animal Drugs

- Animal drugs illegally marketed in the United States that have not been approved by the Food and Drug Administration (FDA)
- Unapproved animal drugs have not been reviewed under FDA's legal review processes

# Compounded Animal Drugs

- If compounded from **approved** drugs (as starting ingredients) **MAY** be legal under ELU regulations
- If compounded from bulk ingredients **IS** considered an unapproved animal drug
- Zero tolerance for compounding from bulk ingredients for food-producing animals

# Compounded Animal Drugs

- Unknown quality control/manufacturing standards
- Unknown assurance of purity, potency, or stability
- Potential animal safety and efficacy issues
- **Potential for unknown or unsafe residues**
- Difficult to monitor – No reporting requirements (even less than for other unapproved animal drugs)

# Extralabel Drug Use

- Extralabel is the use of an **approved** drug in a manner that is not in accordance with the approved label directions.
  - e.g. indication, species, dosage level, frequency, route of administration
- Allows veterinarians to prescribe extralabel uses of certain **approved** animal drugs and **approved** human drugs



# Extralabel Drug Use

“Such use is limited to treatment modalities when the health of an animal is threatened or suffering or death may result from failure to treat.”

# Extralabel Drug Use

- **Must** be by or on the order of a veterinarian within the context of a “ valid veterinarian-client-patient relationship”
- **Must** not result in violative residues
- **Must** be in conformance with all other parts of extralabel drug use regulation (21 CFR Part 530)
- **Must** not use drugs prohibited from extralabel use

# Extralabel Drug Use

“Establish a substantially extended withdrawal period prior to marketing of milk, meat, eggs, or other edible products supported by appropriate scientific information.”

# Extralabel Drug Use

“Take appropriate measures to assure that assigned timeframes for withdrawal are met and no illegal drug residues occur in any food-producing animal subjected to extralabel treatment.”

# Extralabel Drug Use

- Approved animal drugs
- Approved human drugs
- Conditionally approved animal drugs
- Indexed animal drugs
- Medicated feeds
- VFD drugs (veterinary feed directive)
- Human OTC monographed drugs
- Unapproved animal drugs
- Drugs compounded from approved drugs
- Drugs compounded from bulk ingredients

# Extralabel Drug Use

- ✓ Approved animal drugs (Rx or OTC)
- Approved human drugs
- Conditionally approved animal drugs
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# Pain Mitigation (from the literature)

- NSAIDs
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  - Sodium salicylate
  - Flunixin
  - Ketoprofen
  - Diclofenac
  - Phenylbutazone
  - Meloxicam
  - Carprofen



# Pain Mitigation (from the literature)

- NSAIDs
  - Aspirin
    - Unapproved animal – cattle, swine, sheep, poultry (marketed)
    - OTC monograph – human (marketed)
  - Sodium salicylate
  - Flunixin
  - Ketoprofen
  - Diclofenac
  - Phenylbutazone
  - Meloxicam
  - Carprofen

# Pain Mitigation (from the literature)

- NSAIDs
  - Aspirin
  - Sodium salicylate
    - Unapproved animal – cattle, swine, poultry (marketed)
  - Flunixin
  - Ketoprofen
  - Diclofenac
  - Phenylbutazone
  - Meloxicam
  - Carprofen

# Pain Mitigation (from the literature)

- NSAIDs
  - Aspirin
  - Sodium salicylate
  - Flunixin
    - Approved animal – horses, cattle, swine (marketed)
  - Ketoprofen
  - Diclofenac
  - Phenylbutazone
  - Meloxicam
  - Carprofen

# Pain Mitigation (from the literature)

- NSAIDs
  - Aspirin
  - Sodium salicylate
  - Flunixin
  - Ketoprofen
    - Approved animal – horses (marketed)
  - Diclofenac
  - Phenylbutazone
  - Meloxicam
  - Carprofen

# Pain Mitigation (from the literature)

- NSAIDs
  - Aspirin
  - Sodium salicylate
  - Flunixin
  - Ketoprofen
  - Diclofenac
  - Phenylbutazone
    - Approved animal – horses (marketed)
  - Meloxicam
  - Carprofen

# Pain Mitigation (from the literature)

- Local anesthetics
  - Lidocaine
  - Mepivacaine
  - Bupivacaine

# Pain Mitigation (from the literature)

- Local anesthetics
  - Lidocaine
    - Unapproved animal, injectable – cattle (marketed)
    - Unapproved animal, topical (marketed)
  - Mepivacaine
  - Bupivacaine

# Pain Mitigation (from the literature)

- Barbiturates
  - Pentobarbital
  - Thiopental
- Acepromazine
- Benzodiazepines
  - Diazepam
  - Midazolam
- Azaperone
- Xylazine



# Pain Mitigation (from the literature)

- Barbiturates
  - Pentobarbital
  - Thiopental
    - Approved animal – dog, cats (not marketed)
- Acepromazine
- Benzodiazepines
  - Diazepam
  - Midazolam
- Azaperone
- Xylazine

# Pain Mitigation (from the literature)

- Barbiturates
  - Pentobarbital
  - Thiopental
- Acepromazine
- Benzodiazepines
  - Diazepam
    - Approved animal – dogs (not marketed)
  - Midazolam
- Azaperone
- Xylazine

# Pain Mitigation (from the literature)

- Barbiturates
  - Pentobarbital
  - Thiopental
- Acepromazine
- Benzodiazepines
  - Diazepam
  - Midazolam
    - No approved/marketed animal products
- Azaperone
- Xylazine

# Pain Mitigation (from the literature)

- Barbiturates
  - Pentobarbital
  - Thiopental
- Acepromazine
- Benzodiazepines
  - Diazepam
  - Midazolam
- Azaperone
  - Approved animal – swine (not marketed)
- Xylazine

# Pain Mitigation (from the literature)

- Barbiturates
  - Pentobarbital
  - Thiopental
- Acepromazine
- Benzodiazepines
  - Diazepam
  - Midazolam
- Azaperone
- Xylazine
  - Approved animal drug – cats, dogs, horses, deer (marketed)

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  - Approved animal – dogs, cats, horses (marketed)
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- Butorphanol
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  - Approved animal – dogs, cats (marketed)
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- Yohimbine



# Pain Mitigation (from the literature)

- Butorphanol
- Medetomidine
- Ketamine
  - Approved animal – cats, primates (marketed)
- Tiletamine-zolazepam (Telazol)
- Guaifenesin
- Tramadol
- Yohimbine

# Pain Mitigation (from the literature)

- Halothane
- Isoflurane
- Propofol
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Yes

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Yes

(for the most part)



