They're not all the same:
Why FDA approval of animal drugs matters

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How do you know the drugs you give your patients are backed up by safety and effectiveness data?
How do you know the bottle you pick up contains the actual amount of drug listed on the label?

How do you know the drug is sterile?

How do you know there are no contaminants in the bottle?

How do you know if you are giving your patient a quality-made product?

Can you rely on the expiration dating and storage information?
How do you know when the edible tissues from animals treated with a drug are safe for humans to consume?
NADA 141-291, Approved by FDA.
See package insert for complete product information.

WARNING: Methimazole has anti-vitamin K activity and may induce bleeding diathesis without evidence of thrombocytopenia. See ADVERSE REACTIONS in package insert.

HUMAN WARNINGS: See package insert for complete product information.

STORAGE INFORMATION: Store at controlled room temperature 25°C (77°F) with excursions between 15°-30°C (59°-86°F) permitted. Keep the container tightly closed to protect from moisture.

DISTRIBUTED BY: Dechra Veterinary Products, 7015 College Boulevard, Suite 525, Overland Park, KS 66211.

NADA 141-292, Approved by FDA.
SUPERIORBUTE® POWDER
(phenylbutazone)
with Sweet Apple Flavor
For Oral Use in Horses Only
NON-STERoidal ANTI-INFLAMMATORY DRUG (NSAID)

CAUTION: Federal law restricts this drug to use by or on the order of a licensed veterinarian. Federal law prohibits the extra-label use of this product in female dairy cattle 20 months of age or older.

Net Contents: 115 grams
ANADA #200-333, Approved by FDA

Manufactured For:
SUPERIOR EQUINE PHARMACEUTICALS, INC.
Pleasant Grove, UT 84062

Made in Canada
"Conditionally approved by FDA pending a full demonstration of effectiveness under application number 141-308."

CA = Conditionally Approved by FDA
PESTICIDES (insecticides, fungicides, rodenticides)

VETERINARY BIOLOGICS (vaccines, bacterins, antisera, diagnostic kits, and other products of biological origin)

REGULATION OF ANIMAL HEALTH PRODUCTS

ANIMAL DRUGS & DEVICES (antimicrobials, physiologic drugs, antiparasiticides, production drugs)

FDA

USDA
EPA

• The Product Registration Number must appear on the label of the product preceded by the phrase EPA Registration No. or EPA Reg. No.

• The registration number may appear on any suitable location on the label or immediate container, however, it must appear on the wrapper or outside container of the package if the number cannot be clearly read through the wrapper or container.
What’s the Difference?

EPA Registered Pesticide

FDA Approved Drug

Foreign Labeled Product
USDA Center for Veterinary Biologics (CVB)

• Look for the U.S. veterinary license number on the product label when buying veterinary biologics. This assures that the product has been manufactured and tested under USDA standards.

• Under Federal law, all information on the labels of USDA-licensed biologics and in accompanying literature must be approved.

The Center for Veterinary Medicine (CVM) regulates the manufacture and distribution of food additives and drugs that will be given to animals.
Center for Veterinary Medicine (CVM)
Center for Veterinary Medicine

Mission Statement

"Protecting Human and Animal Health"
Mission

• Protect Human and Animal Health by ensuring
  • safe and effective new animal drugs reach the market
  • unsafe and ineffective new animal drugs do not reach the market
Animal Health and Animal Food Product Safety

CVM is responsible for regulating animal drugs, devices and food additives

from:

- Animal Drug Manufacturers (300)
- Feed Manufacturers (6,600)
- Livestock and Poultry Producers (over 1 million)
- Specialized Industry/Firms

given to or used on:

- 8.5 billion chickens & turkeys
- 160 million cattle & pigs
- 11 million sheep & goats

consumed by:

- 300 million humans in the U.S.
Companion Animal Medicine and Minor Species

CVM is responsible for regulating drugs, devices and food additives used in companion animals (dogs, cats and horses) and minor animal species...

- 65 million dogs & 75 million cats
- 9.5 million horses
- minor species include all animals other than cattle, swine, chickens, turkeys, horses, dogs and cats
Scientific and Technical Disciplines at CVM

Graph does not display 100% of CVM staffing

Currently 438 employees - July 2009
Office of New Animal Drug Evaluation (ONADE)

Reviews information submitted by drug sponsors who want to obtain approval to manufacture and market animal drugs
Legal Marketing of Animal Drugs

- To be legally marketed [*from section 512 of the Food, Drug, and Cosmetic Act*], 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 or
  - an index listing
What does an approved new animal drug application (NADA) mean?

- The product is safe and effective for its intended use
- The methods, facilities and controls used for the manufacturing, processing and packaging of the drug are adequate to preserve its identity, strength, quality and purity
Technical Sections of an NADA

• Target Animal Safety
• Effectiveness
• Chemistry, Manufacturing, and Controls
• Human Food Safety
• Environmental Impact
• Labeling
• All Other Information
TARGET ANIMAL SAFETY

DEFINITION OF SAFETY

Adequate tests by all methods reasonably applicable to show that the drug is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling.
TARGET ANIMAL SAFETY

- Margin of Safety study (0X, 1X, 3X, 5X)
- Reproductive Safety study
- Animal Class Safety study
- Special cases (specific breeds, injection site irritation)
TARGET ANIMAL SAFETY

- Identify the toxic effects and establish a margin of safety
- Generally conducted in a small number of healthy animals
- An approval may not require all of the types of safety studies
- Safety information is also collected during the effectiveness studies
USER SAFETY

- Potential hazards associated with:
  - manufacturing
    - direct - occupational exposure
    - indirect - manufacturing emissions
  - administration to animals
Substantial evidence consisting of one or more adequate and well controlled investigations, such as
EFFECTIVENESS

- a study in a target species
- a study in laboratory animals
- field investigations
- a bioequivalence study
- an *in vitro* study
EFFECTIVENESS

• Show that the drug is effective compared to a control (usually a placebo control or a positive control) when administered by the intended label instructions

• Field “conditions of use” studies

• Requires adequate and well-controlled studies as are necessary to show the new animal drug will have its intended effect
CHEMISTRY, MANUFACTURING, AND CONTROLS

Determines whether an animal drug will have and maintain the necessary quality, strength, purity, and identity.

- Methods and controls
- Stability data
- Good Manufacturing Practice (GMP) compliance verification - pre-approval inspection
HUMAN FOOD SAFETY

TOXICOLOGY:
- determine the no observable effects level (NOEL), acceptable daily intake (ADI), and safe concentration

RESIDUE CHEMISTRY:
- determine the target tissue, marker residue, slaughter withdrawal, and milk withhold times

MICROBIAL FOOD SAFETY:
- evaluate the safety of antimicrobials with regard to their microbiological effects on bacteria of human health concern

REGULATORY METHOD:
- development and validation of methods to measure drug residues in edible tissues
ENVIRONMENTAL IMPACT

- Categorical Exclusion  or
- Environmental studies
- Environmental assessment
LABELING

- immediate container (vial, syringe, packet) or feed bag labels
- package insert
- packaging (box, carton)
Main Labeling Components

Package Insert
- Written for veterinarians

Client Information Sheet
- Written for owners
- Accompanies certain drug products

Bottle/Vial/Outer Box Labeling
Labels as “Living” Documents

Post-marketing experience, including Adverse Drug Experiences (ADEs)

Sponsor-initiated updates
  - Manufacturing changes
  - New tablet sizes
ALL OTHER INFORMATION

- foreign marketing experience
- reports of pilot studies
- literature reports
The drug can be legally marketed, promoted, and used.
Drug Development Statistics

- The development and FDA approval of a major new animal drug takes 7-10 years

- The cost to develop a major new animal drug can cost up to $100 million

reference: Animal Health Institute (AHI)
http://www.ahi.org/about-animal-medicines/industry-statistics/
How do you know?

Legal Standards
FDA required testing
FDA evaluation
FDA inspections
FDA generated label
Continued monitoring after approval
Enforcement
http://www.fda.gov/AnimalVeterinary/default.htm
CVM – Protecting Human and Animal Health
Thank You!

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