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

Elizabeth Luddy, DVM
Deputy Director, Office of New Animal Drug Evaluation
Center for Veterinary Medicine
US Food and Drug Administration

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?


NuflorGOLD
(florfenicol)
Injectable Solution,
An Antimicrobial
Caution: Federal law restricts this drug to use by or
NADA 141-265, Approved by FDA
Intervet
Schering-Plough Animal Health
100 mL Multiple Dose Vial • 300 mg/mL • Sterile
NuflorGOLD
(florfenicol)
Injectable Solution, An Antimicrobial
NADA 141-265, Approved by FDA
Intervet
Schering-Plough Animal Health


NADA 141-123, Approved by FDA
Contains 7 Syringes
Individually Wrapped
Product 3661101
GastroGard®
(omeprazole)
For Treatment and Prevention of Recurrence of Equine Gastric Ulcers
Dosage Regimen
Directions for Use
Efficacy
Safety
Signs of Ulcer Disease
Package Contents
Storage
Caution
Warning
Customer Assistance
READ PACKAGE INSERT FOR FURTHER INSTRUCTIONS AND IMPORTANT INFORMATION.
1 50604-37041 3
GastroGard®
(omeprazole) Oral Paste for Equine Ulcers
Improves and Heals Gastric Ulcers
Prevents Gastric Ulcer Recurrence
Once-a-Day Dosing
NADA 141-123, Approved by FDA
Contains 7 Syringes
Individually Wrapped
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Once-a-Day Dosing
NADA 141-123, Approved by FDA
Contains 7 Syringes
Individually Wrapped


60
30
VETORYL® CAPSULES
(trilostane)
30 Capsules
CAUTION: Federal law restricts this drug to use by or on the order of a licensed veterinar
NADA 141-291, Approved by FDA
VETORYL® CAPSULES
(trilostane)
30 Capsules
CAUTION: Federal law restricts
NADA 141-291, Approved
VETORYL® CAPSULES
(trilostane)
30 Capsules
CAUTION: Federal law restr
NADA 141-291, Approve

2.5 mg

FELIMAZOLE™

(methimazole) Coated Tablets

100 Tablets

For oral use in cats only.

CAUTION: Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian

NADA 141-292, Approved by FDA.

See package insert for complete product information.

WARNINGS: 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.

Dechra

Code No. : GO/DRUGS/536

Lot:

Mfd.:

Exp.:

DK54A

nmatory conditions
s. In the treatment
ns, specific

Each level scoop
lbutazone.
to 1/2 tablespoon)
dy weight, but not
ms per horse daily.
reduce to a

INSERT UNDERNEATH.

NDC 27053-001-01

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

Sweet Apple Flavor

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

Each level s
Phenylbutaz
One level sc

RESIDU
horses

HUMAN WA
Dispense in

PRECAUTIO
or corticoste

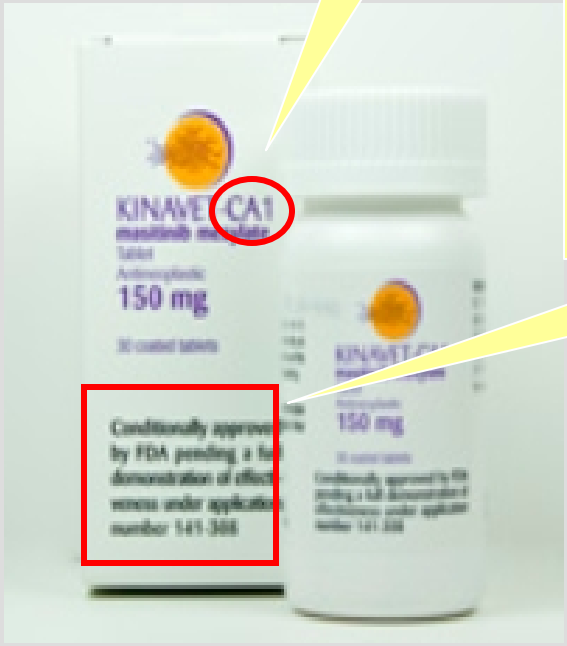
Store at roo
30°C (59-86

SUPERIORB
a registered
Equine Phar

Manufacture
VETOQUINO
Princeville, C

Made in Ca

CA = Conditionally Approved by FDA



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

PESTICIDES
(insecticides, fungicides, rodenticides)

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

REGULATION OF ANIMAL HEALTH PRODUCTS

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

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.

http://yosemite.epa.gov/R10/ECOCOMM.NSF/webpage/Counterfeit%20Pet%20Pesticides

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.

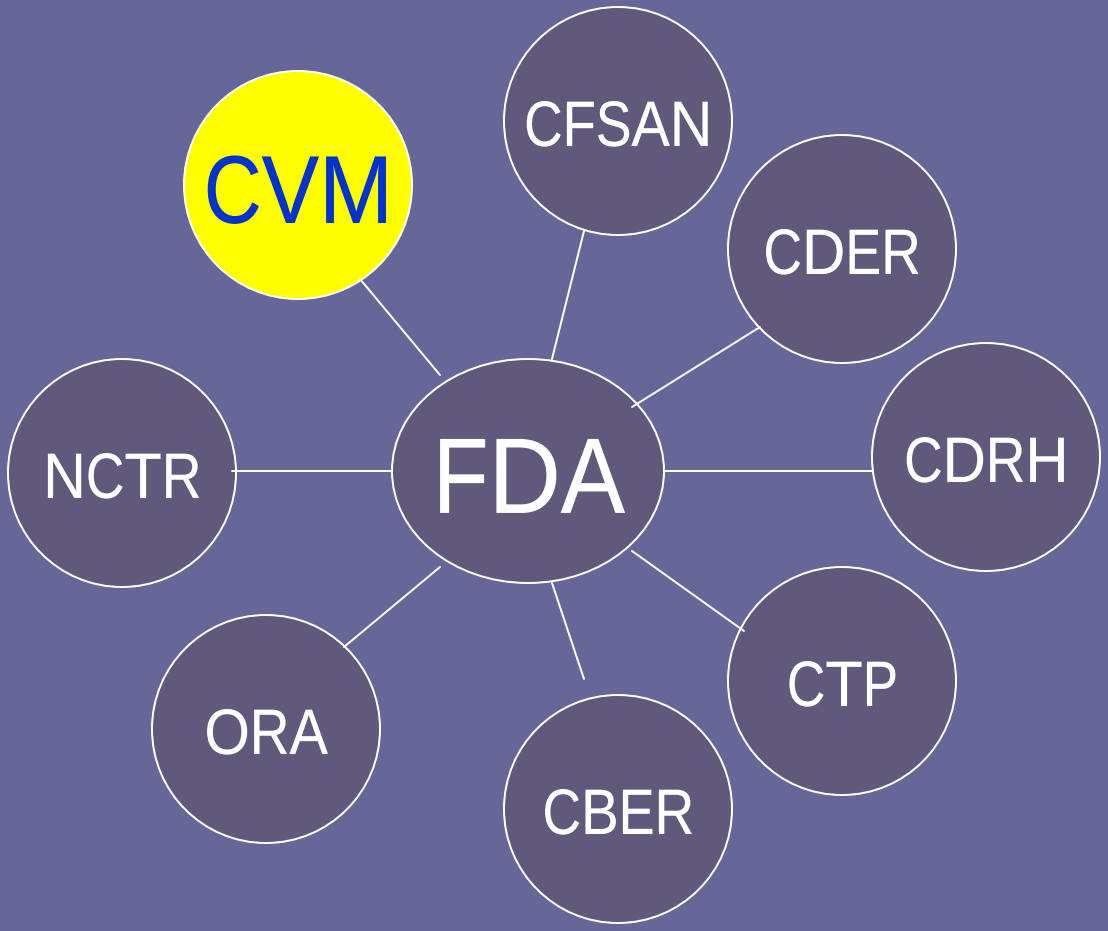
- Under Federal law, all information on the labels of USDA-licensed biologics and in accompanying literature must be approved.

- http://www.aphis.usda.gov/lpa/pubs/vetbiobr.pdf

Center for Veterinary Medicine

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:

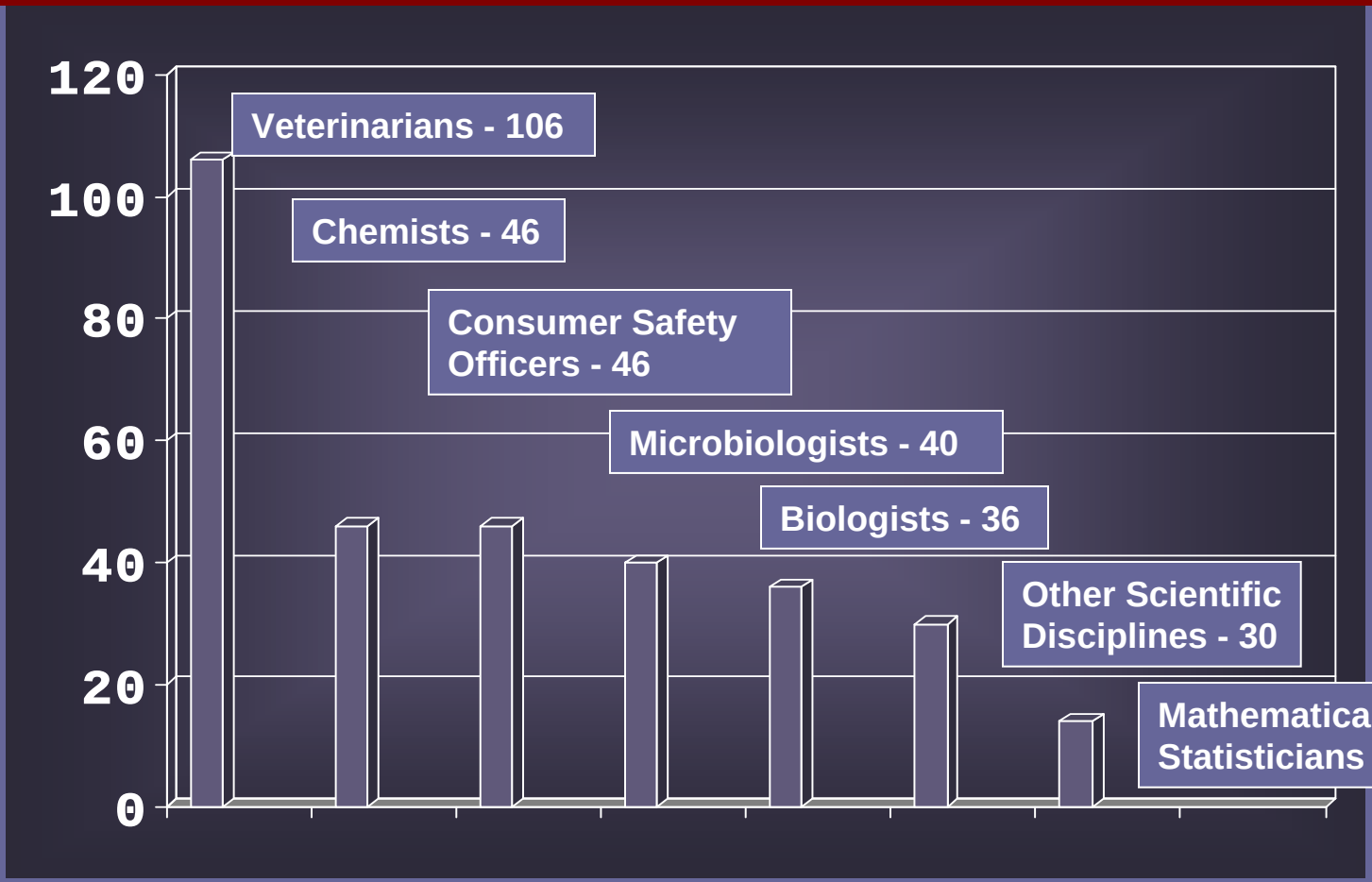
- 300 million humans in the U.S.

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

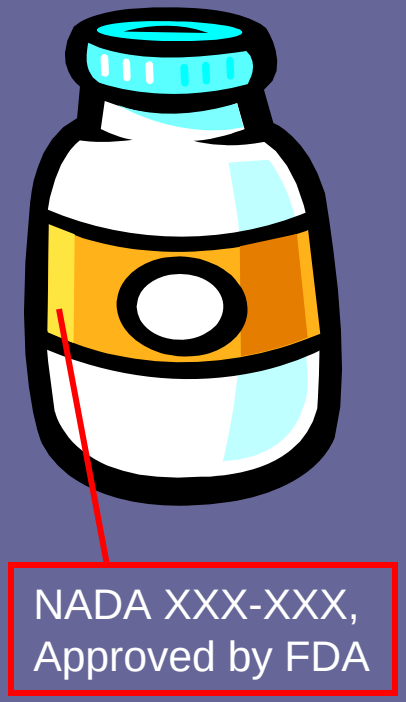
Office of New Animal Drug Evaluation (ONADE)

Reviews information submitted by drug sponsors who want to obtain approval to manufacture and market animal drugs

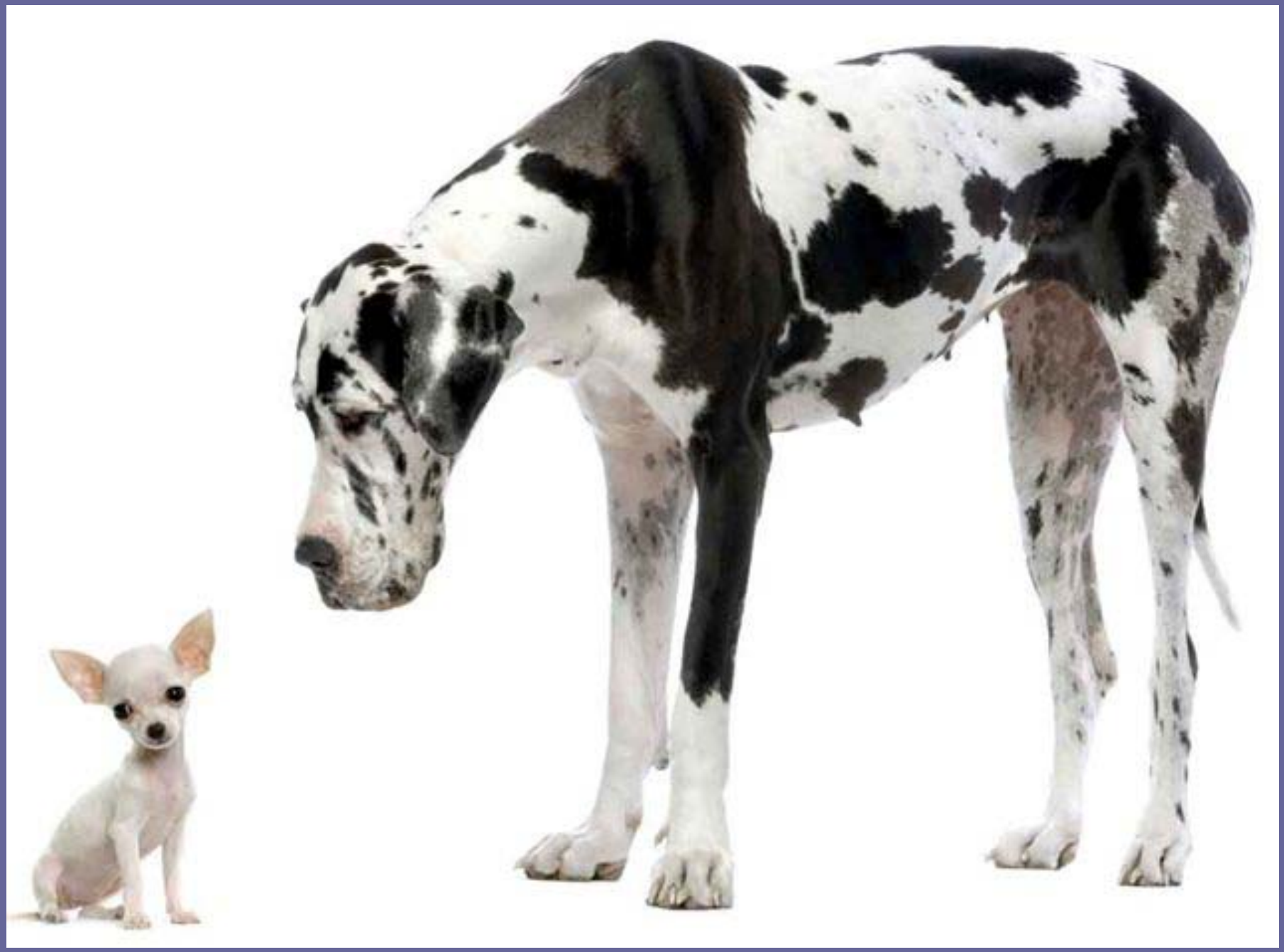
Legal Marketing of Animal Drugs

- 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**

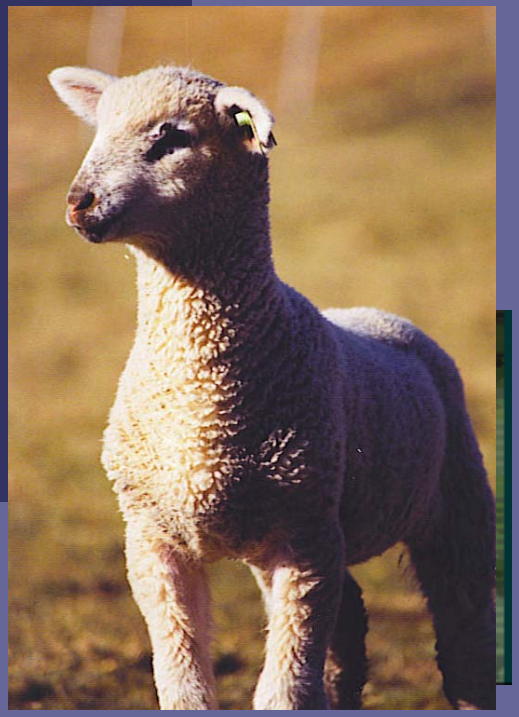
TARGET ANIMAL SAFETY

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

EFFECTIVENESS

DEFINITION OF EFFECTIVENESS

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

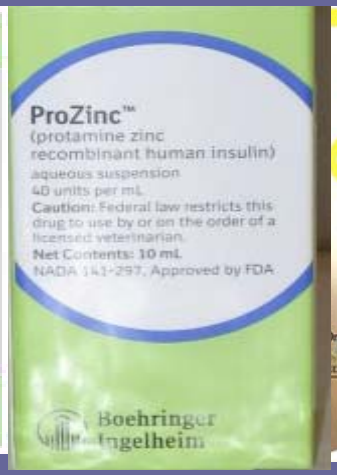
ENVIRONMENTAL IMPACT

- **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

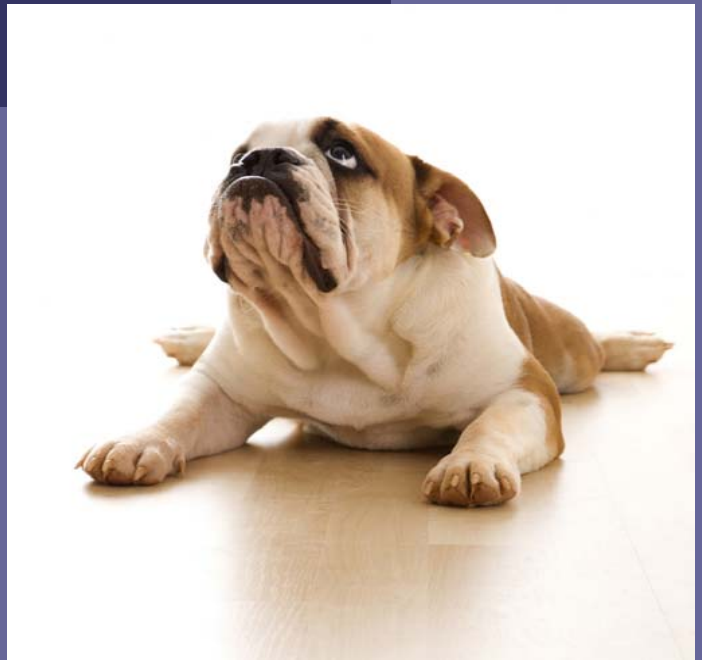
Post-marketing experience, including Adverse Drug Experiences (ADEs)

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

U.S. Department of Health & Human Services www.hhs.gov

FDA U.S. Food and Drug Administration

A-Z Index Search go

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Animal & Veterinary

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Home > Animal & Veterinary

http://www.fda.gov/AnimalVeterinary/default.htm

Unapproved Animal Drugs

FDA has serious concerns about unapproved animal drugs. These drugs are not reviewed by FDA and may not meet FDA's strict standards for safety and effectiveness.

1 2 3

Spotlight

- 3-Nitro (Roxarsone) and Chicken
- About the Center for Medicine (video)
- Feed (video)
- Food Registry for

rts

- Recalls
- Pet Food Recalls
- How to Report a Pet Food Complaint
- Veterinary Adverse Event Voluntary Reporting
- Veterinary Adverse Event Reporting for Manufacturers

Development & Approval Process
New Animal Drug Applications, Electronic Submissions, User Fees, Genetic Engineering, Minor Use/Minor Species, Aquaculture, Food Additive Petitions

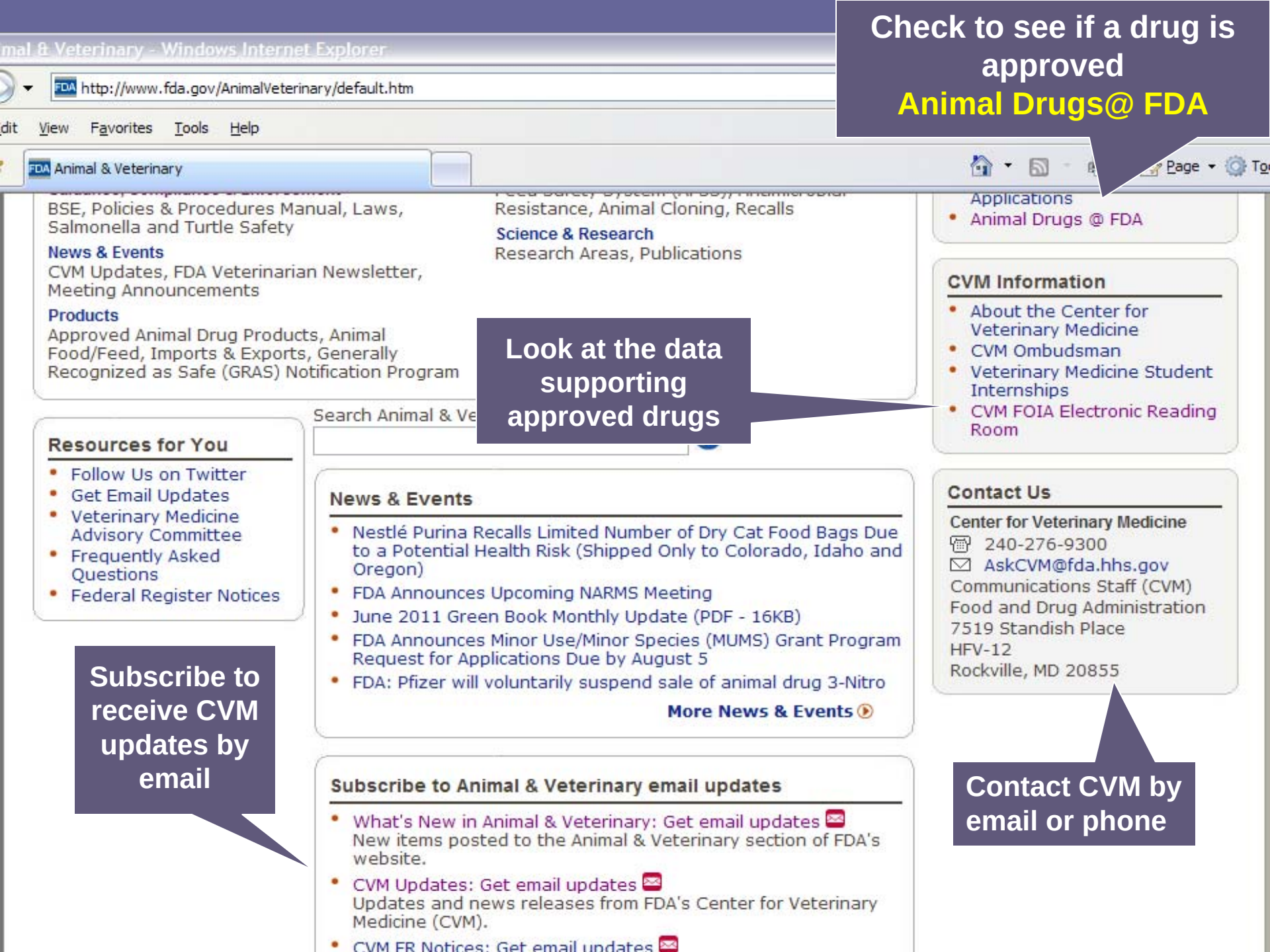
Guidance, Compliance & Enforcement

Resources for You
Animal Health Literacy, Consumer Information, FDA and the Veterinarian

Safety & Health
Adverse Drug Events, Product Safety, Animal Food Safety System (AFSS), Antimicrobial

Approvals & Clearances

- New Animal Drug


Check to see if a drug is approved
Animal Drugs@ FDA
mal & Veterinary - Windows Internet Explorer
http://www.fda.gov/AnimalVeterinary/default.htm
dit View Favorites Tools Help
Animal & Veterinary
Page
BSE, Policies & Procedures Manual, Laws, Salmonella and Turtle Safety
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CVM Updates, FDA Veterinarian Newsletter, Meeting Announcements
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Approved Animal Drug Products, Animal Food/Feed, Imports & Exports, Generally Recognized as Safe (GRAS) Notification Program
Resistance, Animal Cloning, Recalls
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News & Events
Nestlé Purina Recalls Limited Number of Dry Cat Food Bags Due to a Potential Health Risk (Shipped Only to Colorado, Idaho and Oregon)
FDA Announces Upcoming NARMS Meeting
June 2011 Green Book Monthly Update (PDF - 16KB)
FDA Announces Minor Use/Minor Species (MUMS) Grant Program Request for Applications Due by August 5
FDA: Pfizer will voluntarily suspend sale of animal drug 3-Nitro
More News & Events
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Center for Veterinary Medicine
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Communications Staff (CVM)
Food and Drug Administration
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HFV-12
Rockville, MD 20855
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CVM FR Notices: Get email updates

CVM – Protecting Human and Animal Health

Thank You!

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240-276-8312