Embracing Innovation in the Animal Drug Approval Process

Danielle Sholly, Ph.D.
Christina Edwards, Ph.D.

Office of New Animal Drug Evaluation
FDA Center for Veterinary Medicine

Outline

- Organization of FDA and CVM
- Animal drug approval process
- New challenges for the future
- Use of literature in drug approval
- Maximizing collaboration
- New approaches to demonstrate standards

FDA: Human vs. Animal Centers

Human Centers		Animal Center Equivalents
Center for Biologics Evaluation and Research	BIOLOGICS	USDA, Center for Veterinary Biologics
Center for Drug Evaluation and Research	DRUGS	
Center for Devices and Radiological Health	DEVICES	Center for Veterinary Medicine
Center for Food Safety and Nutrition	FOOD	
Tobacco – Center for Tobacco Products	TOBACCO	N/A
National Center for Toxicological Research		
Office of the Commissioner		
Office of Regulatory Affairs		

CVM Organization

CVM Offices	Organization
Office of Director	Communications, International Affairs, and Policy/Regulation
Office of Management	Budget, Human Resources, Training, Daily Operations
Office of Research	Residue Chemistry, Applied Veterinary Research, Animal and Food Microbiology
Office of Surveillance and Compliance	Post-Approval - Surveillance, Compliance, Animal Feeds, and Veterinary Product Safety
Office of Minor Use and Minor Species (MUMS)	Manages programs and incentives helping industry develop drugs for minor species making them legally available.
Office of New Animal Drug Evaluation	Pre-Approval -Therapeutics for Non-Food Animals & Food Animals, Production Drugs, Generic Drugs, Human Food Safety, Environmental, Manufacturing

How the Office of New Animal Drug Evaluation Operates

- Collegial working environment (internal & external)
- ADUFA (Animal Drug User Fee Act)
- AGDUFA (Animal Generic Drug User Fee Act)
- In-person sponsor meetings and teleconferences
- Protocol review process
- Phased review process

Animal Drugs are…

- Regulated under the Federal Food, Drug, and Cosmetic Act (FFDCA)

- Defined as
  - articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals

  - articles (other than food) intended to affect the structure or any function of the body of man or other animals

Therapeutic

Production

Four Critical Standards (21 CFR 514)

- Safety
  - Human Food
  - User
  - Target Animal
- Effectiveness
- Quality Manufactured Product
- Properly Labeled Product

Code of Federal Regulations: http://www.ecfr.gov

Guidances for Industry:
http://www.fda.gov/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/default.htm

Animal Drug Approval Process

Traditional Approval Model

SPONSOR

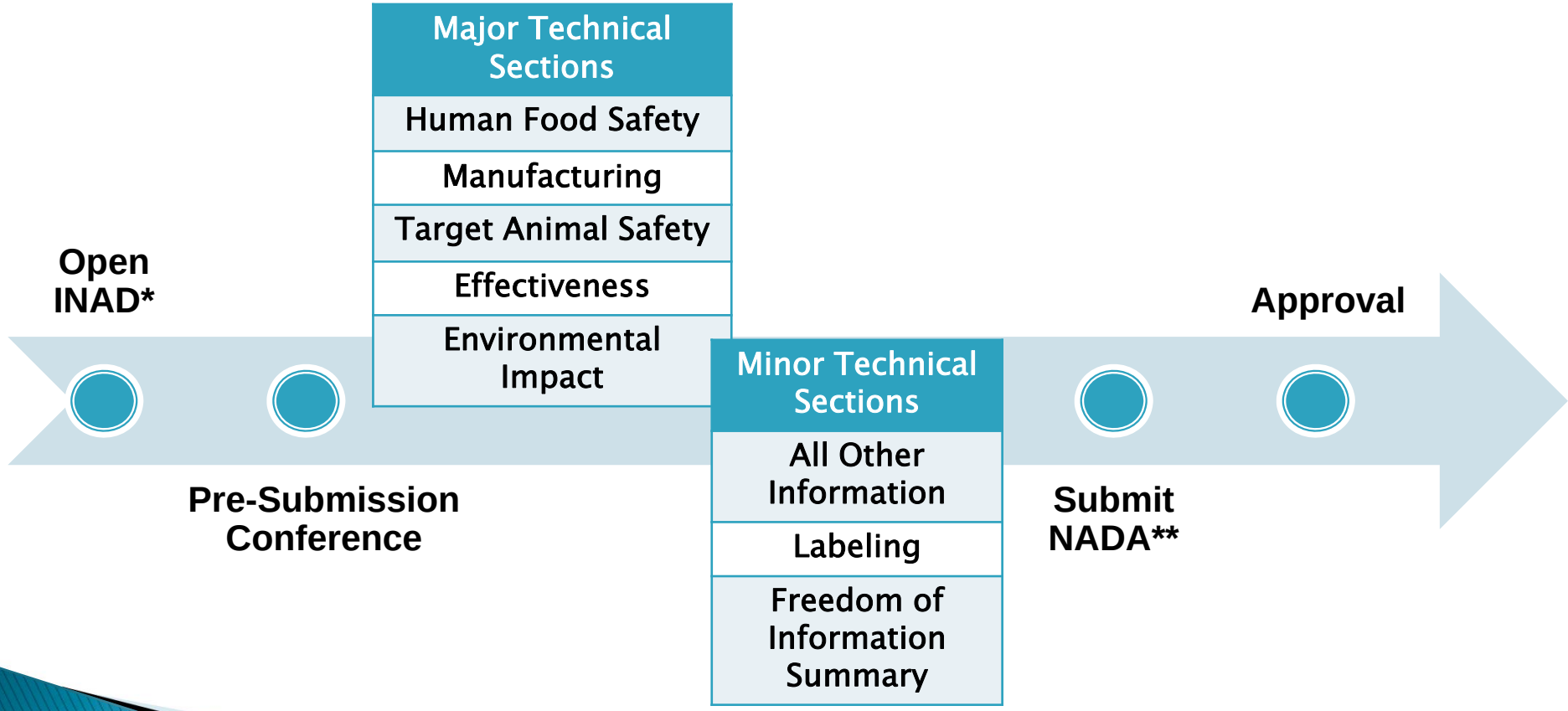
FDA/CVM

Presubmission conference
Agree on development plan

Submissions
Protocols
Studies
Data
Literature
Other Information

Animal Drug Approval Process

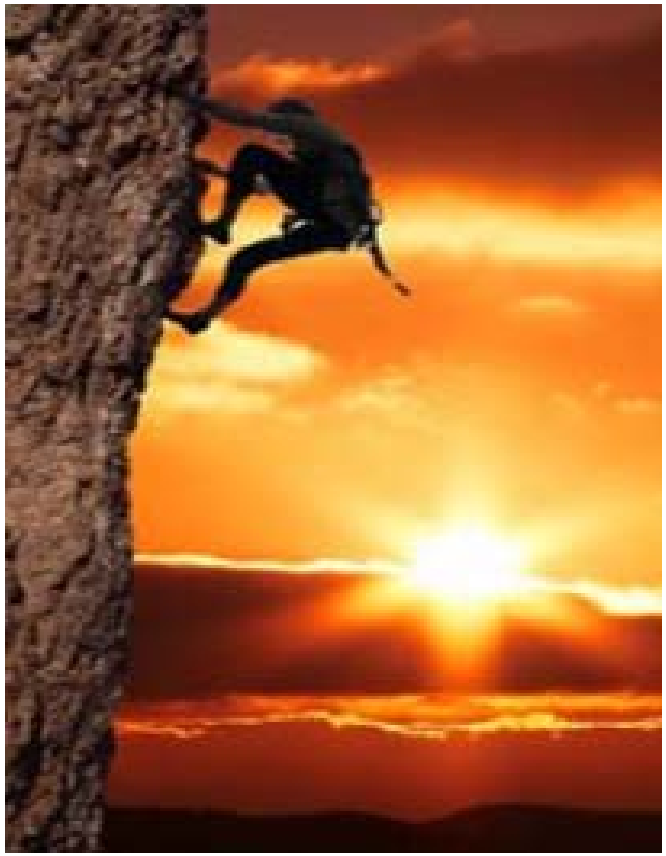
Investigational New Animal Drug Process



*INAD = Investigational New Animal Drug
**NADA = New Animal Drug Application

Our Challenge

- To engage in the development and evaluation of new animal drugs, especially new innovative technologies
  - Non-traditional therapeutic indications
  - Increased safe, affordable and abundant food production
- Engage new collaborators



Meeting the Challenge

Increase predictability of regulatory requirements

- Maximize use of all forms of available information
- Use novel approaches to demonstrate our critical standards

Maximizing information use:
Data collaboration

- Increased use of preliminary data
  - Preliminary data to streamline a clinical study
- Collaborative data sharing within CVM divisions
- Collaborative data sharing across FDA
  - Toxicology (or other) data in a human drug approval package to support an animal approval package?

Maximizing information use:

International collaboration

- European Medicines Agency (EMA) & Veterinary Drug Directorate (VDD)
- Regulatory Cooperation Council (RCC)
- Potential ways to collaborate:
  - Sharing novel evaluation methods
  - Data sharing across regulatory bodies in different countries
  - Single set of studies for EMA and CVM
  - Increasing the consistency of labeling across countries
- How do we better engage researchers from universities and other facilities around the world?

Maximizing information use:
Literature

- Justification

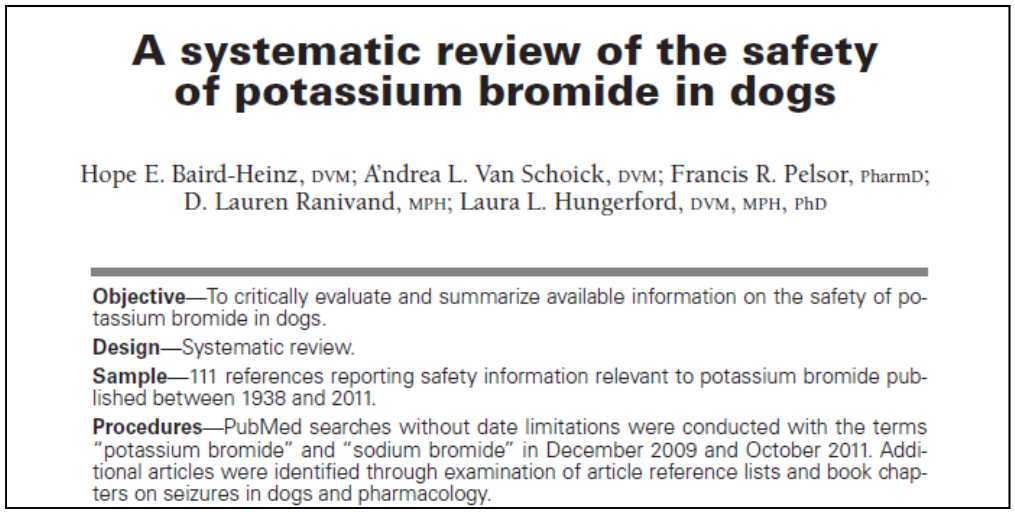
- Data to augment a clinical study to support an approval
  - Support expansion or elements of an indication

- Literature Review

Maximizing information use:

Systematic Reviews & Meta-analyses

- Systematic reviews



A systematic review of the safety of potassium bromide in dogs

Hope E. Baird-Heinz, DVM; A'ndrea L. Van Schoick, DVM; Francis R. Pelsor, PharmD; D. Lauren Ranivand, MPH; Laura L. Hungerford, DVM, MPH, PhD

Objective—To critically evaluate and summarize available information on the safety of potassium bromide in dogs.

Design—Systematic review.

Sample—111 references reporting safety information relevant to potassium bromide published between 1938 and 2011.

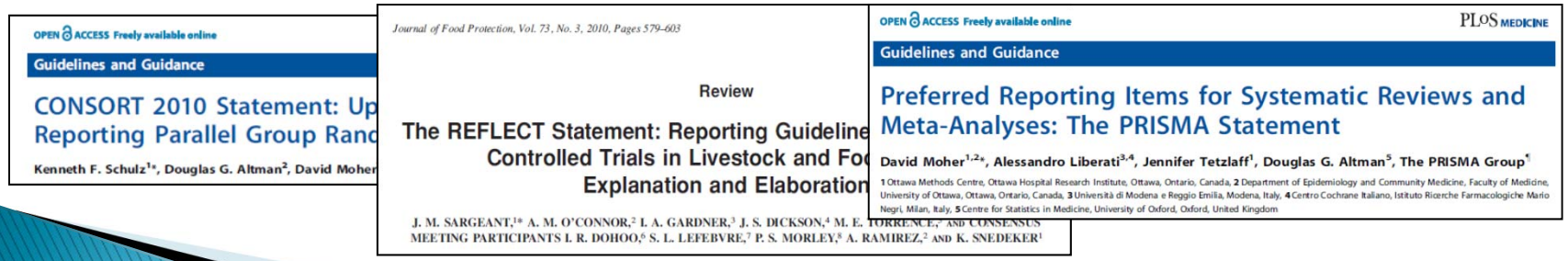
Procedures—PubMed searches without date limitations were conducted with the terms "potassium bromide" and "sodium bromide" in December 2009 and October 2011. Additional articles were identified through examination of article reference lists and book chapters on seizures in dogs and pharmacology.

J Am Vet Med Assoc., 2012; 240:705-715

- Meta-analyses
  - November 25, 2013: [CDER] Public Meeting on Meta-Analyses of Randomized Controlled Clinical Trials for the Evaluation of Risk to Support Regulatory Decisions

Recommendations for the Use of Literature

- Consider published information on formulation, target species, dosage (dose, duration, frequency), route of administration, endpoints, etc.
- Comprehensive search, include published and internal reports
- Present balanced results (both favorable and unfavorable)
- Document search system (database, terms, dates, etc.)
- Consider publication quality and bias
- Consider reporting guidelines



Novel Approaches:

Team Approach

- Innovation Exploration Team (IVET)
  - Think tank for innovation
  - Outreach & cross-fostering best practices of innovation
- Focus Groups
  - "Big Picture" novel technology issues (not specific product)
  - Develop training or advisory documents
  - Example: biomarkers, safety data review
- Technology Teams
  - Cross-center teams
  - Develop scientific expertise for a specific novel technology
  - Pre-development work with sponsors and collaborators (e.g., scientists, other agencies)
  - Assist in development of a regulatory pathway for approval

Novel Approaches:

CVM & Sponsor Interactions

Work outside of traditional INAD/NADA timeframe

- Early (pre-development)
  - Meetings- informal, brainstorming
  - Early Information
  - Tech Team process

- Late
  - Conditional approval
    - MUMS
    - Feasibility for expansion (ADUFA III)
      - http://www.fda.gov/forindustry/userfees/animaldruguserfeeactadufa/default.htm

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Animal Drug Approval Process

New Approach to Traditional Approval Model: Early Information

Short term and narrow scientific focus

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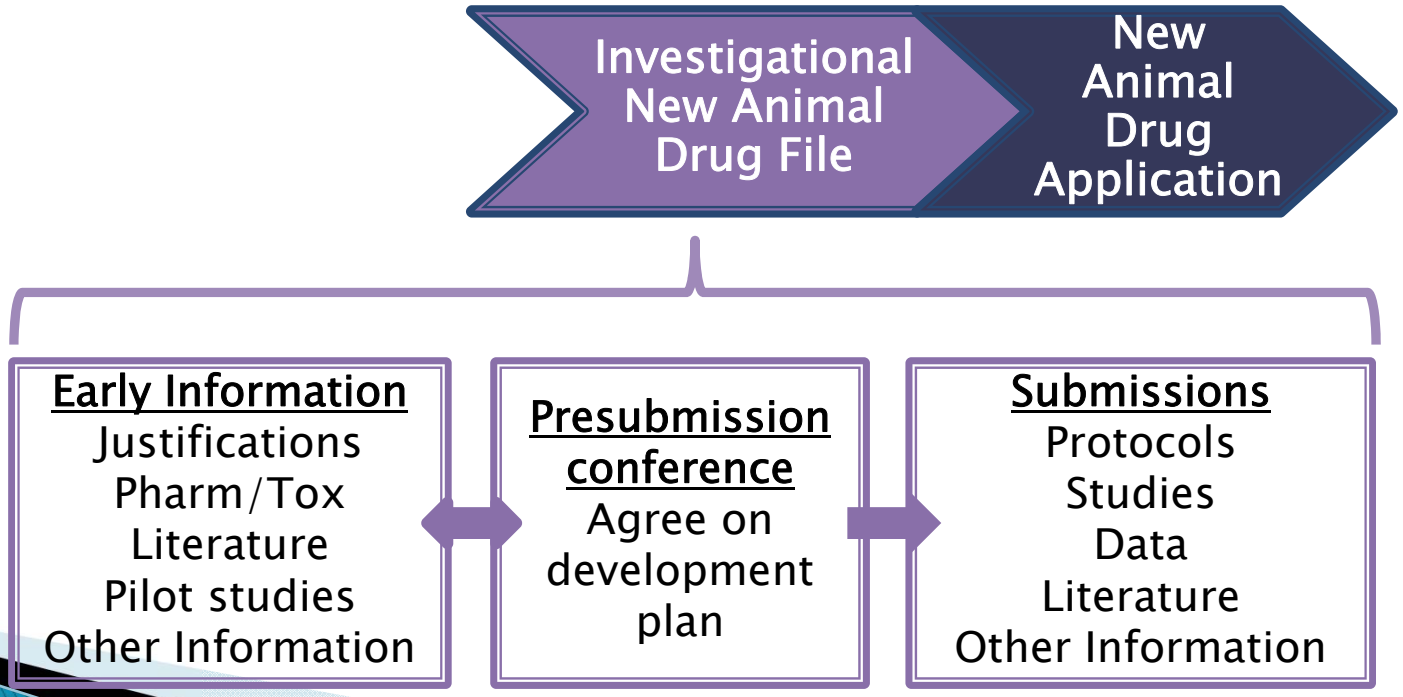

Animal Drug Approval Process

New Approach for Innovative Technologies: Tech Team Process

Long term and broad scientific focus

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Discovery or Acquisition → Development → Full Development → Registration → Support

FDA/CVM

Gather Information
- Collaborative
- Focus on science
- Leverage resources

Identify Issues
- Info needed vs. known
- Gap analysis
- Prioritization

Risk Analysis
- Means-Ends
- Metrics
- Decision modeling

Investigational New Animal Drug File → **New Animal Drug Application**

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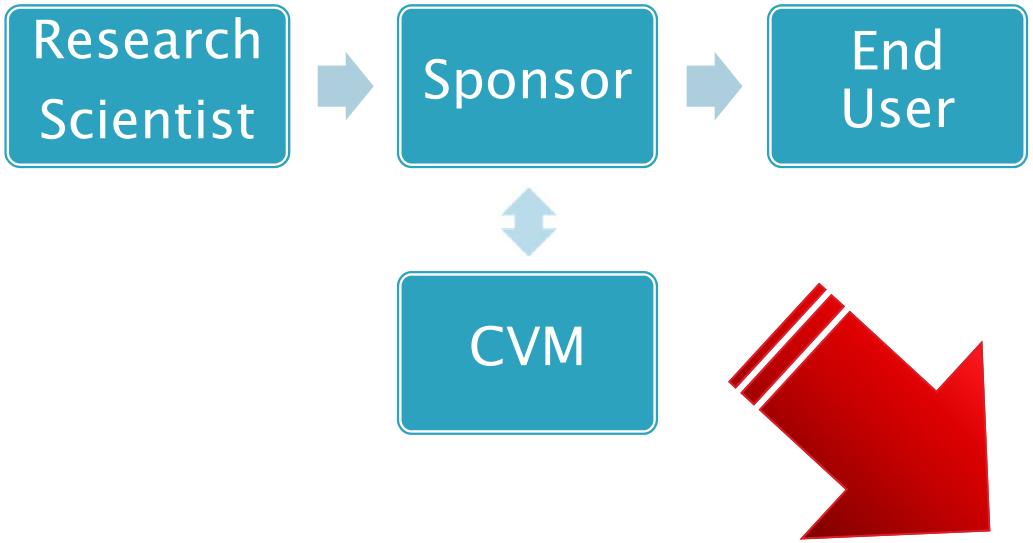
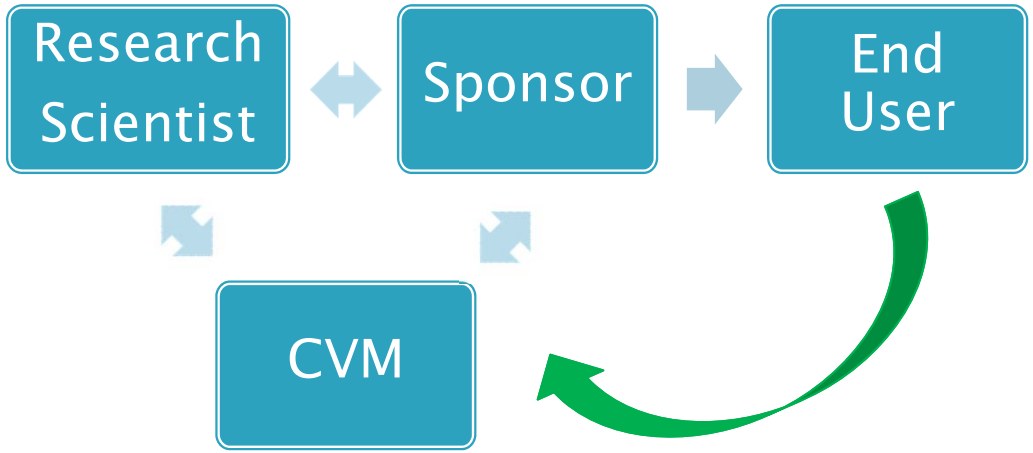
Information flow in **traditional** approval model



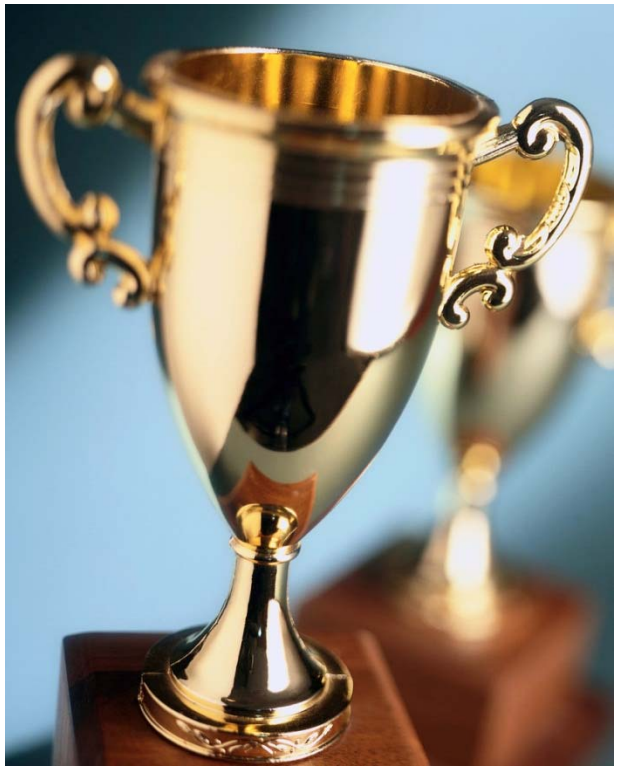
Information flow in **new** approval model



What Do We Need From Our Collaborators?

- Increased collaboration with CVM to work on issues earlier
- New lines of communication and interaction among scientists
- Innovative and creative thinking
- Higher level of scientific engagement
- High quality submissions

What's the Win?



- For drug sponsors
  - Maximize use of all forms of available information
  - Global consistency
  - Early decisions and consultations with CVM
  - Increased predictability
  - Data in an animal drug approval to support a human drug approval and vice versa

What's the Win?



- For end users (bench scientists, animal industry, consumers)
  - Partnerships between animal pharmaceutical industry and university researchers
  - Increased communication for research needs or ideas

Increased availability of safe and effective novel technologies in the marketplace

Questions?


CENTER FOR VETERINARY MEDICINE
Protecting Human and Animal Health

References

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