Manufacturing, Quality and Regulatory Solutions: Center for Veterinary Medicine (CVM)

2015 PDA/FDA Joint Regulatory Conference

Dennis M. Bensley, Ph.D.
Director, Division of Manufacturing and Technologies
Office of New Animal Drug Evaluation

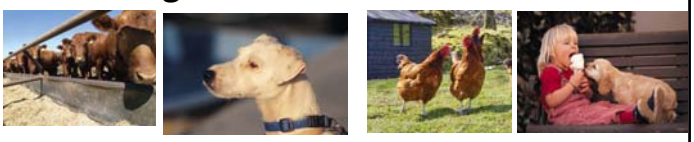
CVM Vision and Mission

Vision

"***Excellence, Innovation, Leadership***"

Mission

"***Protecting Human and Animal Health***"



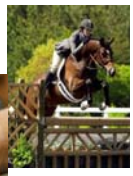
CVM's Core Responsibilities

- New Animal Drug Review
- Animal Generic Drug Review
- Post-approval monitoring of animal drugs and feeds, and marketed animal devices
- Animal Feed – Human Food – Pet Food -- Protection/Safety
- Compliance related actions
- Research to support regulatory decision-making

Companion Animal and Minor Species Medicine

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

- Increase the availability and diversity of safe and effective products that relieve animal pain and suffering, sustain their health, and do not compromise human health.
- Minor Species include all animals other than the following 7 Major Species: cattle, pigs, chickens, turkeys, horses, dogs and cats.



Animal Health and Animal Food Product Safety

CVM is also responsible for regulating animal drugs, devices and food additives used in food producing animals.

From:

- Animal Drug Manufacturers
- Feed Manufacturers
- Livestock and Poultry Producers
- Specialized Industry/Firms

Given to or used on:

- Cattle, pigs, chickens, turkeys, sheep, and goats

Consumed by:

- Millions of humans in the U.S.

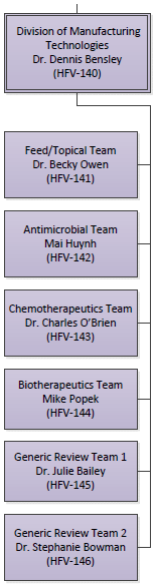
5

CVM's High Priority Public Health Issues

- Implementing the Food Safety Modernization Act of 2010 (FSMA)
- Compounding / Unapproved Animal Drugs
- Antimicrobial Resistance (includes the National Antimicrobial Resistance Monitoring System [NARMS])
- **Animal Drug User Fee Act (ADUFA) and Animal Generic Drug User Fee Act (AGDUFA)**
- Approving Drugs for Minor Use/Minor Species (MUMS)
- Illegal Drug Residues in Animal Derived Foods
- Animal Biotechnology (genetic engineering, biopharm, and cloning)
- International Activities
- Animal Health Literacy – Outreach to Consumers and Stakeholders

6

Division of Manufacturing Technologies



45 FTEs

-CMC pre-approval; technical drug quality resource for CVM

- Manage PAI program

- Manage 2 user fee CMC programs: innovator and generic.

- Pre-approval CMC review of all animal drug products (traditional to biotech); medicated feed; participate in method trials for new medicated feed assays

- External activities (VICH, PDA, USP, stakeholder meetings, CDER collaborations)

CVM User Fee Programs

- Animal Drug User Fee Act (ADUFA)
  - -Currently ADUFA 3 (FY 2014-2018)
  - -99+% on-time for all sentinel submissions (2004-present)
- Animal Generic Drug User Fee Act (AGDUFA)
  - -Currently AGDUFA 2 (FY 2014-2018)
  - -99+% on-time for all sentinel submissions (2009-present)

CMC Review Enhancements

- Shortened review times for certain reactivations and resubmissions.
- CBE-30 reactivations for certain incomplete prior approval supplements.
- Two-phased INAD/JINAD for CMC technical section
- Comparability protocols as INAD/JINAD protocols

CMC Review Enhancements

Shortened review times for certain reactivations and resubmissions (started FY'15), for example:

-INAD **study submissions**: 180 days → 60 days ★
-INAD protocols w/o data: 50 days → 20 days ★
-Original ANADAs: 270 days → 190 days
-JINAD **study submissions**: 270 days → 90 days

★ Only applicable for e-submissions.

CVM Review Enhancements

- CBE-30 reactivations for certain incomplete prior approval supplements (started FY'14).

-Only applicable to for CMC changes reported in prior-approval supplements

-If CVM determines the deficiencies are not substantial, the reactivation to a prior-approval supplement can be submitted as a "Supplement-Changes Being Effected in 30 Days" or CBE30

-Permits sponsors to implement manufacturing changes after 30 days of submitting reported changes in CBE30.

Current CVM User Fee Enhancements

- CBE-30 reactivations for certain incomplete prior approval supplements (started FY'14).

-Our goal is still a one-cycle review , therefore original PA supplement should be complete with appropriate supporting data.

-Does not impact review times, e.g., 120 days for innovator CMC supplemental applications including reactivations.

CMC Review Enhancements

- Two-phased INAD/JINAD for CMC technical section

-Each component should be complete, e.g., appropriate information and supporting data

-Second phase should not be submitted until the first-phase has been completed and any deficiencies are addressed in the second-phase along with the rest of the CMC information.

-The first-phase will never receive a technical section complete letter.

-Both phases have 180 days review times (INADs). 270 days for JINADs.

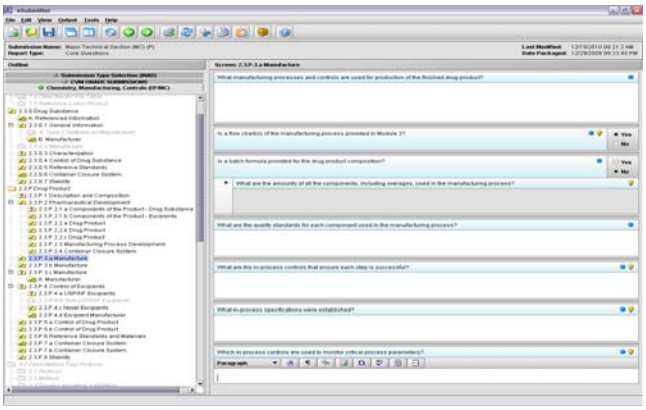
-Shorter review times for resubmissions may also be applied if the second phased component is incomplete.

CMC Review Enhancements

Comparability protocols as INAD/JINAD protocols

- Permit comparability protocols, which currently have a 120 day review as an NADA or 270 days as an ANADA prior approval supplement, to be submitted as protocols without data in a INAD or JINAD file for a review in 50 or 100 days, respectively.
- Sponsors may still submit comparability protocols as prior approval supplements according to 21 CFR 514.8(b)(2)(v), however the supplemental review times will be in effect
- Other appropriate filing strategies may be needed for more complex comparability protocols, e.g., sterile process validation protocols.

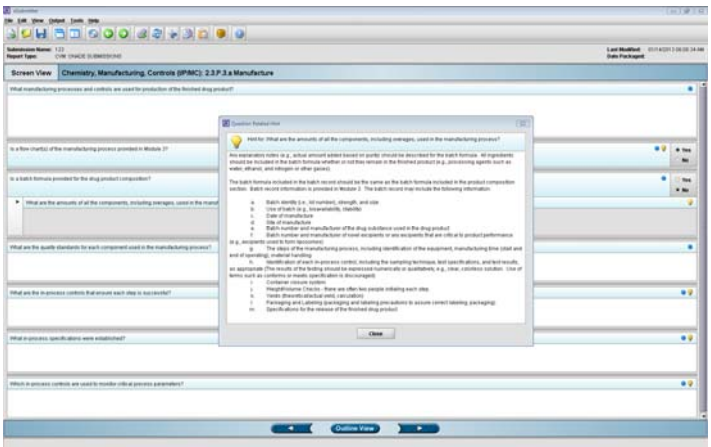
QbR REVIEW PROCESS



All Electronic Review

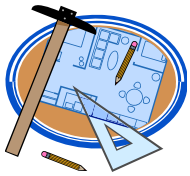
- All electronic submissions submitted via eSubmitter. Paper submissions are scanned.
- Access to DMFs via DARRTS
- Original CMC data submissions utilize extensive Question-based-Review (QbR) process: drug substance, drug product, sterile process validation (3+ years experience)

QbR Review Process



- Focus on approving or "time-to-approval" , non-substantial comments are addressed by other means
- Provide consistency and transparency to stakeholders, i.e. level playing field
- Increase in one-cycle reviews/approvals

OTHER CMC ACTIVITIES



1. Increase collaboration (resource dependent)

   -USP
   -CDER/CBER (e.g., joint CMC guidances, ICH quality initiatives)
   -FDASIA implementation relevant to pre-approval inspections

2. Possible review process/science enhancements (resource dependent)

   -QbR/eSubmitter modifications and possible expansion
   -Establish VMF review team
   -Requiring electronic stability data in xml format (HL7)
   -Monitor and consider CDER new initiatives, e.g., quality metrics, established conditions guidance, for possible adoption

Protecting both Human and Animal Health

THANK YOU!!