FDA’s Role in Regulating Pre-Harvest Interventions for Foodborne Pathogens

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Presentation Overview

• FDA/CVM’s interest and role
• Description of what CVM regulates
• Description of drug approval process
• CVM activities to improve the process
• Considerations for the demonstration of effectiveness
• Challenges
Importance to CVM

• Food safety is a high priority for FDA.

• The production industry lacks sufficient pre-harvest interventions (unmet need).

• Some pre-harvest interventions are regulated by CVM
  • Not vaccines
  • Not slaughter facility interventions
What Does CVM Regulate?

- **Animal Devices**
  - No pre-market approval required

- **Generally-recognized as safe (GRAS) products**
  - No pre-market approval required

- **Animal Food Additives**
  - Pre-market approval required

- **Animal Drugs**
  - Pre-market approval required
  - Includes genetically-engineered (GE) animals

Note: “Water additives” have no regulatory standing within CVM.
Food Additives vs. Drugs

• Food additives
  o Defined as “any substance that directly or indirectly becomes a component of food or that affects a food’s characteristics”
  o Relevant example: “For the maintenance of normal gut health in cattle”

• Drugs
  o Defined as:
    • “articles intended for the use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals”
    • “articles (other than food) intended to alter the structure or any function of the body of man or other animals”
  o Relevant example: “For the reduction in fecal pen prevalence of E. coli O157:H7 prior to shipment to slaughter”
Food Additives vs. Drugs

Take home message:

Any product with an intended effect on *E. coli* O157:H7 [or other pathogenic Shiga-toxin producing *E. coli* (STECs)] would be considered a drug.

Food additives labeled or promoted for the cure, mitigation, treatment, or prevention of disease would be considered a drug and would be considered adulterated or misbranded.
Drug Approval Process

• Requires a sponsor to bring a product to CVM for approval
  • Sponsor generates the needed data and submits to CVM making a case that all required elements have been addressed.
  • CVM will review the information and make an assessment.
  • Routinely an iterative process
  • “Technical sections” frequently submitted separately (phased review)

• The drug approval process does not start with CVM nor does CVM tell a drug sponsor what new animal drugs to research.

WSU E. coli Conference 2012
Greenbelt, MD
Drug Approval Process

Major technical sections

• Effectiveness
• Target Animal Safety
  o Also includes Human User Safety
• Human Food Safety
  o Toxicology
  o Residue Chemistry
  o Microbial Food Safety
• Environmental Impact
• Chemistry, Manufacturing, and Controls
Drug Approval Process

Minor technical sections

• Labeling
• All Other Information (AOI)
What is CVM doing to help the development of interventions?

• Member of the *E. coli* Coalition (now concluded)
  • Joint effort of industry, academia, and government
  • Focused on pre-harvest interventions

• Work with USDA/CVB to coordinate approaches to evaluation

• Work with drug sponsors to streamline the review process
Considerations for the Demonstration of Effectiveness

- Field studies vs. challenge models
  - Inferential value vs. feasibility?

- What’s the best sample for evaluating effectiveness?
  - Feces from rectum
  - Feces from pens
  - Rectoanal Muscosal Swabs (RAMS)
  - Hide swabs
  - Rope-based system

- What’s the best variable to assess?
  - Prevalence
  - Quantity of pathogen
  - Effect on “super-shedders” (using both)
Considerations for the Demonstration of Effectiveness

• Best experimental unit
  • Pen vs. individual

• Magnitude of effect
  • Threshold of reduction vs. significant effect
  • Absolute vs. relative reduction

• Duration of effect
  • Long enough for a fecal effect to be mirrored on hides
  • Long enough to account for normal shipping time
Regulatory Challenges

With the designation of additional pathogenic STECs as adulterants in beef, what is the best way to evaluate and label for these pathogens on a drug product?

- Possible Options:
  - Most difficult – Establish effectiveness for each serotype
  - Less difficult – Establish effectiveness with O157:H7 through field studies, then entertain literature/challenge models for others
  - Least difficult – Establish effectiveness collectively using all pathogenic STEC serotypes (pooled analysis)

- Pros and cons for each
Challenges to Drug Development/Utility

• Regulatory changes
  o Traditional antimicrobials face increased scrutiny due to the potential to engender antimicrobial resistance (GAO report 12-257).

• Market considerations
  o What’s the incentive?
    • Low perceived return on investment?
  o Fewer development-ready products available?

• Concern about cost to producers
  o Who will cover the producers’ cost of using a product?
    • Premium paid to producers who use pre-harvest interventions?
Questions?

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