Genetically Engineered Microorganisms and Animal Food

The Future of Microbial Biotechnology Workshop
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## Animal Food Regulation in the USA

### Drug
- Treats, cures, mitigates, or prevents diseases
- Affects the structure or function of the animal (other than providing nutritive value, taste and aroma)
- Improves animal productivity (i.e.: growth rate, milk production, carcass characteristics)

### Food
- “Articles used for food or drink for man or other animals.”
  - Provides nutritive value, taste, or aroma.
  - Affects the characteristics of food.
  - Directly or indirectly becomes a component of food (processing and packaging).
Animal Food Regulation in the USA

Drug

“Prevents dehydration”

Food

“Source of water, an essential nutrient”
Animal Food

- Amino Acids
- Biomasses
- Alcohols
- Enzymes
- Organic Acids
Regulatory Pathways for Animal Food

• Food Additive
  – Food additive petition process.

• Generally Recognized as Safe (GRAS)
  – Firm’s conclusion that the use of a substance is GRAS.

• Defined Ingredient
  – Association of American Feed Control Officials (AAFCO)
General Considerations

• Microbial Safety
  – Safety of the source organism

• Molecular Biology Description
  – Safety of the host organism
  – Safety of the genetic material used to make the modifications
  – Genetic engineering techniques used to modify the source organism
  – Characterization of the genetic modifications
  – Description and properties of the final source organism
Microbial Safety

• Source organism identity
  – Organism source
    • Purchased from organism culture banks
    • Isolated: from where?
  – Data to substantiate identity and taxonomical classification
    • 16 sRNA and phenotypic tests
    • Third party identity confirmation
Microbial Safety

• Scientific Literature
  – Safety assessment: focus on the genus-species
    • Not strain basis
    • History of use in animal food?
  – Pathogenicity and virulence
  – Animal or human diseases associated with the organism
  – Production of toxins or undesirable substances
  – Absence of safety information in the scientific literature does not mean that there are no safety concerns
Microbial Safety

• Source organism viability in the final market formulation
  – “Dead means dead”
    • Logarithmic reductions are not equivalent to absence
    • Detailed description of kill steps
  – Viable organisms in the market formulation:
    • FAP
    • Can be used by a different firm
Molecular Biology Description

• Plasmid Map

• Detailed description of:
  – Genetic material that was introduced and its source
    • Synthetic or Genomic
      – Information on the gene donor and safety considerations
  – Intentional changes to the nucleotide sequence incorporated into the genome of the source organism
Molecular Biology Description

• Source organism development
  – Description of the technology used
    • Extrachromosomal plasmid, random insertion, homologous recombination, genome editing
    • Techniques used to introduce the plasmid
    • Techniques used to select potential source organism strains
Molecular Biology Description

• Characterization of the source organism
  – Describe the analytical method use and bioinformatics approach to characterize DNA insertions, deletions, and edits
    • Whole genome sequencing, southern blot analysis, sanger sequencing of PCR, biochemical analysis
  – Sequence of nucleotides that were inserted, deleted, or edited
    • Number of copies, location, coding sequence errors or mutations, alterations, resistance genes, unintended proteins, pathway modifications.
Manufacturing Process

• Detail description of the manufacturing process
  – Time, temperature, pH, control points
  – Kill step
  – Specifications
  – Cleaning procedures between batches

• Fermentation Media
  – All substances must be acceptable for use in animal food for their intended use
  – Provide certificate of analysis and regulatory status
Questions

- Bioengineered organisms: case-by-case basis
- Questions: come talk to us!
  - Animalfood-premarket@fda.hhs.gov