How to Effectively use the GRAS Process for Algae-derived Food Ingredients

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Keller and Heckman LLP

- Regulatory, litigation, and business transaction law firm
- Founded in 1962
- Extensive in-house scientific staff
- Biotechnology Practice
  - Support the regulatory work of several algal companies for food, fuel, and other commodity chemicals both domestically and internationally
Determining the Regulatory Status of Algal Food Substance

- Any substance that is intentionally added to food is a “food additive” that is subject to pre-market review and approval unless it is generally recognized as safe (GRAS)

- Types of food and feed regulatory options
  - Food Additive Petition (FAP)
  - New Dietary Ingredient Notification (NDIN)
    - supplements
  - Color Additive Petitions
  - Associations of American Feed Control Officials (AAFCO)
  - GRAS process
    - FDA Center for Food Safety and Applied Nutrition (CFSAN)
    - FDA Center for Veterinary Medicine (CVM)
    - GRAS self-determinations
Three conditions for GRAS Status

(1) General recognition among experts that substance is safe;
(2) Experts must be qualified by scientific training and experience; and
(3) Experts must have based their safety judgment either on scientific procedures or the fact that the substance was commonly used in foods prior to January 1, 1958.
Generally recognized as safe (GRAS)

- Both technical evidence of safety and basis to conclude this technical evidence of safety is known and accepted
- Pivotal studies are published
- Types of product considered
  - Human and animal feed
  - Whole algal cell products
  - Algal extracts
Data Elements of a GRAS position

- General guidelines that should to be evaluated on a case-by-case basis
- Identity of notified substance
  - Chemical identity [e.g., Chemical Abstracts Service (CAS) Registration numbers]
  - Molecular weight and formulas
- Method of manufacture
  - Raw materials with appropriate status (food grade material is commonly used)
  - Process flow diagram
Data Elements of a GRAS Notice

- Product Specifications
  - Dependent on manufacturing process
  - FCC monographs as guidance
  - Mass balance
- Dietary exposure
- Self-limiting levels of use
- Stability
Data Elements of a GRAS position

- **Intended Use**
  - Maximum levels of use
  - Types of food or feed
  - Animal feed: list of target animals
  - Human food: target populations
Data Elements of a GRAS position

- Characterization of the production strain
  - Establishing taxonomy
  - Literature review
    - History of use in food
    - Algal toxins in specific species, genus, or family
    - Allergenicity
    - Development and publication of data may be needed
  - Traditional strain improvements
  - Antibiotic activity
Data Elements of a GRAS Notice

- Applicable genetic modifications to algal strain
  - Detailed description of genetic modifications
  - Donor microorganism(s) assessment
  - Toxin and allergen analysis of introduced coding regions
  - Metabolic “spill over” effects
Data Elements of a GRAS Notice

- Toxicological Studies (case-by-case basis)
  - Short-term (14-28 days) rodent feeding study
  - Subchronic (90 days) rodent feeding study
  - Short-term (1 year)
  - Lifetime (2 year) rodent with in-utero exposure
  - Multigenerational reproduction feeding (2 generations minimum)
  - Mutagenicity
GRAS position update and resources

- Based recommendations on experience and review of successful filings for similar products and intended uses
- Changes such as additional modifications to the algal strain, manufacturing process, product specifications, etc. may require an update to GRAS position

Useful Resources:
- Toxin analysis: http://mvirdb.llnl.gov/
- Allergen analysis: http://www.allergenonline.org/
- FDA GRAS: http://www.fda.gov/Food/IngredientsPackagingLabeling/GRAS/
- FDA guidance for industry #221
Regulatory Updates

- White House Office of Science and Technology Policy (OSTP) issued a memo on July 2, 2015 to initiate an update of the regulatory system for biotechnology products
  - Public engagement workshop tentatively scheduled for Fall 2015

- FDA Food Safety Modernization Act (FSMA)
  - Regulatory pathways (FAPs, NDINs, GRASNs) remain the same, however it is possible that more FDA inspections will occur in the future
THANK YOU

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