Proteins: Dietary Supplements (and/or Foods)

Kit Goldman, Ph.D.
Proteins can be classified and labeled as either a food or a dietary supplement (or both)

Depends on claims and marketing/positioning (CFR 21 Chapter 1 Subchapter B Part 101)

- Food
  - If intended as a meal replacement or as part of the diet
  - May have health claims
  - Structure function claims tend to focus on effects derived from nutritive value

- Dietary Supplement
  - Structure/function claims may focus on non-nutritive as well as nutritive effects
  - May contain additional DS ingredients
  - All DS must have appropriate disclaimer on label for non-nutritive Structure/function claims
  - DS are not intended to "diagnose, treat, cure or prevent any disease"
### Nutrition Facts

**Serving size:** 2 scoops (70g)

<table>
<thead>
<tr>
<th>Amount Per Serving</th>
<th>Calories 280</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% Daily Value*</td>
</tr>
<tr>
<td><strong>Total Fat</strong></td>
<td>9g</td>
</tr>
<tr>
<td>Saturated Fat</td>
<td>3.5g</td>
</tr>
<tr>
<td>Trans Fat</td>
<td>0g</td>
</tr>
<tr>
<td>Polyunsaturated Fat</td>
<td>0.5g</td>
</tr>
<tr>
<td>Monounsaturated Fat</td>
<td>4g</td>
</tr>
<tr>
<td><strong>Cholesterol</strong></td>
<td>40mg</td>
</tr>
<tr>
<td><strong>Sodium</strong></td>
<td>135mg</td>
</tr>
<tr>
<td><strong>Total Carbohydrate</strong></td>
<td>20g</td>
</tr>
<tr>
<td>Dietary Fiber</td>
<td>2g</td>
</tr>
<tr>
<td>Total Sugars</td>
<td>3g</td>
</tr>
<tr>
<td>Includes 1g Added Sugars</td>
<td>2%</td>
</tr>
<tr>
<td><strong>Protein</strong></td>
<td>32g</td>
</tr>
</tbody>
</table>

*The % Daily Value (DV) tells you how much a nutrient in a serving of food contributes to a daily diet. 2,000 calories a day is used for general nutrition advice.

**Vitamin D** 7mcg  35%
**Calcium** 585mg  45%
**Iron** 1mg  6%
**Potassium** 470mg  10%
**Vitamin A** 315mcg  35%
**Vitamin C** 32mg  35%
**Phosphorus** 438mg  35%
**Magnesium** 210mg  50%
### Supplement Facts

- **Serving Size:** 40g (2 Scoops)  
- **Servings Per Container:** 30  

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Amount (g)</th>
<th>% DV*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calories</td>
<td>170</td>
<td></td>
</tr>
<tr>
<td>Calories from Fat</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>Total Fat</td>
<td>6</td>
<td>9%</td>
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<tr>
<td>Saturated Fat</td>
<td>4</td>
<td>20%</td>
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<tr>
<td>Trans Fat</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>Total Carbohydrates</td>
<td>7</td>
<td>2%</td>
</tr>
<tr>
<td>Dietary Fiber</td>
<td>3</td>
<td>4%</td>
</tr>
<tr>
<td>Sugars</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Protein</td>
<td>20</td>
<td>40%</td>
</tr>
</tbody>
</table>

- **Vitamin A:** 2500 IU  
- **Vitamin C:** 30 mg  
- **Vitamin D:** 200 IU  
- **Vitamin E:** 15 IU  
- **Vitamin K:** 3.2 mcg  
- **Thiamin:** 0.75 mg  
- **Riboflavin:** 0.03 mg  
- **Niacin:** 0.4 mg  
- **Vitamin B6:** 1 mg  
- **Folate:** 8 mcg  
- **Vitamin B12:** 0.24 mcg  
- **Calcium:** 70 mg  
- **Iron:** 6.3 mg  
- **Phosphorus:** 120 mg  
- **Iodine:** 3 mcg  
- **Magnesium:** 20 mg  
- **Zinc:** 0.6 mg  
- **Selenium:** 42 mcg  
- **Copper:** 0.2 mg  
- **Manganese:** 0.26 mg  
- **Chromium:** 12 mcg  
- **Molybdenum:** 33.75 mcg  
- **Chloride:** 1.36 mg  
- **Sodium:** 460 mg  
- **Potassium:** 190 mg  

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Proteins of Interest to the Dietary Supplement Team

- **Whey Protein**
  - Isolate
  - Concentrate
  - Whey protein

- **Vegetable Proteins**
  - Pea
  - Soy
  - Rice

- **Hydrolyzed collagen**

- **Undenatured collagen**
Protein Attributes

Discussion at USP Protein Roundtable February 2017

- Identification Tests for Proteins from various sources
- Quantitative Determination of Proteins
- Determination of Purity
- Limits for Contaminants
Challenges to Developing Specifications for Proteins

- Methods specific to a particular protein may not be available
- Specific methods may require significant development time and equipment e.g.
  - Amino Acid profiling
  - Mass spectroscopy
  - SDS page gel electrophoresis
- Protein conformation may be important (undenatured collagen)
- Natural crop variability may affect composition
- Processing method may affect composition
- Non-protein components (such as lactose, fat content etc.) may require quantification
- Non-protein specific methods (Kjeldahl or Dumas) used for protein quantification
Composition/Contamination/Purity

- **Composition Tests**
  - Non-protein nitrogen
  - LOD
  - Fat
  - Ash
  - Lactose (for dairy products)

- **Contaminants**
  - Heavy metals (arsenic is a concern for rice protein)
  - Mycotoxins (Aflatoxin) and pesticides for vegetable proteins
  - Nitrogen containing compounds (e.g. Nitrile, Nitrate, Melamine, Cyanuric acid, Urea, Amidinoureia, Ammelide, Ammeline, Biuret, Cyromazin, Dicyandiamide)
  - Microbial contamination
USP dietary supplement group collaborating with the Foods Group on protein specification development – Expert Panel and monograph development
USP’s Food Program

A global resource for **food integrity and safety solutions** including science-based standards, tools, and services to improve confidence in the global food supply chain.
### FCC Scope

<table>
<thead>
<tr>
<th>Category</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Food-grade chemicals</td>
<td>Emulsifiers, minerals, Amino acids</td>
</tr>
<tr>
<td>Processing aids</td>
<td>Enzymes, solvents, Filter media, boiler water additives</td>
</tr>
<tr>
<td>Foods</td>
<td>Fructose, dextrose, sucrose, Whey, amino acids</td>
</tr>
<tr>
<td>Flavoring agents</td>
<td>Natural and synthetic flavors, Essential oils</td>
</tr>
<tr>
<td>Functional food ingredients</td>
<td>Olestra, salatrim, high-oleic canola oil, Diacylglycerol oil, lycopene, scFOS</td>
</tr>
</tbody>
</table>

**1966 (512 monographs)**

**2018 (~1200 monographs)**
Dietary Proteins of Interest

• Dairy Proteins – Whey & Casein
• Pea Protein/Soy Protein
• Rice Protein
• Potato Protein
• Other Specialty Proteins
• EMA threatens the integrity of the food supply and thereby introduces public health and other risks.

• Dietary protein ingredients usually merit premium prices, and are traded at high volume rendering them particularly susceptible to adulterations, which are not necessarily recognized utilizing current specifications and analytical methods/standards in FCC.

• The adulteration of protein ingredients has had enormous impacts on economic costs, public health, as well as public confidence on safety of food supply and government regulatory systems.
Whey Protein Concentrate

Published in: FCC 10.2S, FCC 10.3S
First Published: Prior to FCC 6
Last Revised: FCC 8, First Supplement

DESCRIPTION

Whey Protein Concentrate occurs as either a liquid or a dry product. It is the substance obtained by the removal of sufficient nonprotein constituents from whey so that the finished dry product contains NLT 25.0% protein. Whey Protein Concentrate is produced by physical separation techniques such as precipitation, filtration, or dialysis. The acidity of the Whey Protein Concentrate may be adjusted by the addition of safe and suitable pH-adjusting ingredients. The final product is pasteurized.

Function: Texturizer; nutrient; emulsifier; water-binding aid; gelling agent

Packaging and Storage: Store in tight containers, protected from humidity.

IDENTIFICATION

Procedure

Acceptance criteria: A sample exhibits the compositional profile specified below with respect to Ash (Total), Fat, Lactose, Loss on Drying, and Protein.

- **Protein, Nitrogen Determination, Appendix IIIC**
  - **Analysis:** Calculate the percentage of protein:
    \[
    \text{% Protein} = \frac{N}{6.38}
    \]
  - **N** = percent nitrogen
  - 6.38 = nitrogen-to-protein conversion factor
  - **Acceptance criteria:** NLT 90.0% on the dried basis
Dietary Protein EP

• **Duration proposed:** Dec 2017-June 2020

• **Purpose:** Develop, validate, and recommend new specifications, analytical tests and related scientific documents relevant to USP for dietary proteins.

• **Outcomes:** Support the creation of new and modernization of current *FCC* monograph(s), *FCC* Identity Standard(s), or general test(s) and assay(s), as well as USP reference materials.
1) Develop recommendations on analytical methods and reference materials based on the needs of industry, regulators and other stakeholders;

2) Carry out or manage development and validation (potentially external) of the test methods;

3) Develop FCC standards (including monograph standards, identity standards, general tests and assays, etc.) with tests, specifications, and potentially reference materials for proposal to the Food Ingredients Expert Committee.

4) Manage implementation of potential FCC standards, academic publications and outreach to support the use of the proposed standards.

5) Coordinate with Dietary Supplement Expert Committees
Dietary Protein EP-Priority

Matrices: Whey Protein Concentrate & Whey Protein Isolate

Methodology:

1. Amino Acid Profiling
2. LC/MS (peptide mapping and whole protein LC/MS)
3. Gel Electrophoresis
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<tr>
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<th>Name</th>
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<tbody>
<tr>
<td>1.</td>
<td>Sneh Bhandari, Ph.D.</td>
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<tr>
<td>2.</td>
<td>Spencer Carter, Ph.D.</td>
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<td>3.</td>
<td>Jonathan Willard DeVries, Ph.D.</td>
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<td>5.</td>
<td>Jaap Evers</td>
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<td>Christophe Fuerer, Ph.D.</td>
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<td>Boyan Gao, Ph.D.</td>
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<td>19.</td>
<td>Wei Zhu, Ph.D.</td>
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Dietary Protein EP-Meeting Plans

1) Kick-off Teleconference: March 19th 2018
2) F2F meeting: May 31st 2018
3) Future meetings in plan.