Premarket Notification for New Dietary Ingredients

FDA / CFSAN
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AHPA’s Presentation

- Herbal dietary ingredients defined
- NDI Notification requirements
- Review of NDIs to date
- AHPA’s HOC is a presumptive list of ‘old’ herbal dietary ingredients in 321(ff)(1)(C)
- ‘Old’ herbal dietary ingredients in 321(ff)(1)(F)
- Suggestions and recommendations
The term dietary supplement—

(1) means a product (other than tobacco) intended to supplement the diet that bears or contains one or more of the following dietary ingredients:

(A) a vitamin;
(B) a mineral;
(C) an herb or other botanical;
(D) an amino acid;
(E) a dietary substance for use by man to supplement the diet by increasing the total dietary intake; or
(F) a concentrate, metabolite, constituent, extract, or combination of any ingredient described in clause (A), (B), (C), (D), or (E)
Types of Herbal DIs 21 U.S.C. 321

★ (C) an herb
★ (C) an other botanical

★ (F) a concentrate of an herb or botanical
★ (F) a metabolite of an herb or botanical
★ (F) a constituent of an herb or botanical
★ (F) a extract of an herb or botanical
★ (F) a combination of herbs or botanicals
NDI Notification 21 CFR 190.6

- the name and address of the distributor or manufacturer (either of the DI or the DS)
- the name of the ingredient, which must include the Latin binomial (including author) if the ingredient is a botanical
- a description of the supplement containing the ingredient, including the level of use and conditions of use
- the evidence on which a reasonable expectation of safety is based, including copies and, as necessary, English translations of references
- a signature
NDIs to date

★ 249 as of November 9, 2004

- 15 notifications for dietary *supplements*
- 194 unique DI notifications
- 245 specific ingredients identified

★ 194 unique notifications

- 83 non-herbal DIs
- 111 herbal DIs
  - ★ 33 unprocessed herbs
  - ★ 26 herb constituents
  - ★ 52 herbal extracts (or concentrates, etc.)
NDIs to date November 2004

- Herbal Constituents: 13%
- Herbal Extracts: 27%
- Unprocessed Herbs: 17%
- Non-herbal DIs: 43%
### NDIs to date November 2004

<table>
<thead>
<tr>
<th>Category</th>
<th># Notifications</th>
<th># Filed by FDA</th>
<th>% Filed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-herbal DIs</td>
<td>83</td>
<td>52</td>
<td>63%</td>
</tr>
<tr>
<td>Unprocessed herbs</td>
<td>33</td>
<td>7</td>
<td>21%</td>
</tr>
<tr>
<td>Herb extracts, etc.</td>
<td>52</td>
<td>19</td>
<td>37%</td>
</tr>
<tr>
<td>Herbal constituents</td>
<td>26</td>
<td>17</td>
<td>65%</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>194</strong></td>
<td><strong>95</strong></td>
<td><strong>49%</strong></td>
</tr>
</tbody>
</table>
Missing data  (per 21 CFR 190.6)

★ Plant part not named
   ▶ No. 238: *Hoodia gordonii*
   ▶ No. 247: *Phellinus linteus*

★ Confused nomenclature
   ▶ No. 248: kakadu plum fruit extract - *Terminalia ferdinandiana* or *Terminalia lapides*?

★ Botanical name not given
   ▶ No. 216: freeze-dried kimchi
Missing data (per 21 CFR 190.6)

★ “it is unclear... whether the test substances used in the referenced studies are qualitatively or quantitatively similar to” the NDI

★ “…inadequate information presented in the notification to characterize and identify your specific ‘new dietary ingredient.’”
<table>
<thead>
<tr>
<th><strong>Identity (NDI)</strong></th>
<th>Latin name + part</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DS Description</strong></td>
<td>Dose of DI + Conditions of use (inc. labeling); other DIs not needed</td>
</tr>
<tr>
<td><strong>Evidence</strong></td>
<td>History of use; other evidence</td>
</tr>
</tbody>
</table>
# Needed data for herbs

<table>
<thead>
<tr>
<th>Identity (NDI)</th>
<th>(321(\text{ff})(1)(F))</th>
</tr>
</thead>
<tbody>
<tr>
<td>... + solvent + ratios + all ingredients + process description + form ([ + % \text{ ‘markers’ } + \text{characterization} + \text{purity}])</td>
<td>(321(\text{ff})(1)(F))</td>
</tr>
<tr>
<td><strong>DS Description</strong></td>
<td>Dose of DI + Conditions of use (inc. labeling); other DIs not needed</td>
</tr>
<tr>
<td><strong>Evidence</strong></td>
<td>History of use of similar DI; other evidence</td>
</tr>
</tbody>
</table>
Old' Herbs - 201(ff)(1)(C)

★ 1995: Call for ‘old’ herbal DI's

★ 1996: List of 1656 herbs “believed to have been marketed in the United States as a dietary supplement or dietary ingredient before October 15, 1994” sent to FDA


△ 2048 species (inc +/- 550 in 1st edition (1992))

△ Over 500 Chinese herbs

△ Over 300 Ayurvedic herbs

△ 25 fungi; 23 seaweeds
‘Old’ Herbs - 201(ff)(1)(C)

★ Disclaimers:

✈ The listing of a particular species of plant in this work is not, therefore, in and of itself, evidence that such species was marketed in the United States prior to October 15, 1994.

✈ Similarly, the exclusion of a particular plant should not be seen as proof of or an indication that such plant was not marketed in the United States prior to October 15, 1994.
‘Old’ Herb Extracts - 201(ff)(1)(F)

★ Standard extract forms
  - Decoctions; Extracts (liquid and powdered); Tinctures; Syrups; etc.

★ Standard extract solvents (food grade)
  - Alcohols; Glycerin; Oils; Vinegar; Water or Steam; etc.

★ Standard extraction processes
  - Maceration; Percolation; Spray-drying; etc.
Suggestions

★ Modify 190.6:
  ✔️ For herbal NDIs the part of the plant must be stated
  ✔️ Clarify that identity of the NDI is required

★ Assume HOC herbs are ‘old’ (+ many extracts)

★ Refuse filings for new dietary supplements

★ Refuse filings for old dietary ingredients (black pepper; cinnamon; clove; ginger; ginseng; etc.)

★ Prioritize enforcement based on safety concerns

★ Assume int’l use as “present in the food supply”
Suggestions

★ Refrain from overly broad interpretations:
   ▲ 239: Notice “does not provide specifications of purity… or a compositional analysis” of this herb
   ▲ Also: “…no information [on] other components” in DS

★ Clarify when a new dose (of an NDI) is an NDI

★ Establish minimum criteria for NDI review, e.g.:
   ▲ ‘Administrative’ parts of 190.6
   ▲ Identity of NDI

★ More timely access at FDA docket
   ▲ AHPA / NPI will create searchable database