Specifications: How Industry can Interpret the USP’s Standards in Monograph and Regulatory Requirements: Purity is NOT microbiology

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“Verification of what is in the bottle and nothing else”
111.70 – (Written) Specification

For what?
- raw material
- in-process
- labels
- finished product

Specifications must Including:
- Identity
- Purity
- Strength
- Composition
- Limits of contaminants or adulterants
- Any point, step, or stage in MFG
- Packaging

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<table>
<thead>
<tr>
<th>Ranking Yr./Yr.</th>
<th>Description</th>
<th>Citation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,1,1,1</td>
<td>Finished Product (FP) Specification</td>
<td>111.70 (e)</td>
</tr>
<tr>
<td>2, &gt;10, 2, 2</td>
<td>Written Procedures: QC Ops</td>
<td>111.103</td>
</tr>
<tr>
<td>10, 4, 3, &gt;5</td>
<td>Written Procedure: Complaint</td>
<td>111.553</td>
</tr>
<tr>
<td>9, 0, 4, 3</td>
<td>Verifying FP Specification</td>
<td>111.75 (c)</td>
</tr>
<tr>
<td>4, 7, 5, 0</td>
<td>Master Manufacturing Records (established AND for each size)</td>
<td>111.205 (a)</td>
</tr>
</tbody>
</table>

*Top “observations” from the FDA Form 483-Inspectional Observations issued after dietary supplement investigations by FDA investigators.
Product Review

Preamble

Purity:
Sec. 111.70 Specifications

**Table 1**

<table>
<thead>
<tr>
<th>FDA Term</th>
<th>Interpretation of quality attributes in the Preamble as pertaining to dietary supplements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identity</td>
<td>The “identity” of a dietary supplement refers to the dietary supplement’s consistency with the master manufacturing record and/or that it is the same as described in the master manufacturing record.</td>
</tr>
<tr>
<td>Purity</td>
<td>The “purity” of a dietary supplement refers to that portion or percentage of a dietary supplement that represents the intended product.</td>
</tr>
<tr>
<td>Strength</td>
<td>The “strength” of a dietary supplement relates to its concentration. By concentration, we mean the quantitative amount per serving (for example, weight/weight, weight/volume, or volume/volume). Therefore, for purposes of this final rule, strength does not refer simply to the quantity of an ingredient, rather it refers to the amount of a stated ingredient per a specified unit of measure.</td>
</tr>
<tr>
<td>Composition</td>
<td>A dietary supplement’s “composition” refers to the specified mix of product and product-related substances in a dietary supplement.</td>
</tr>
</tbody>
</table>

http://www.nutraceuticalsworld.com/issues/2017-03/view_features/establishing-specifications-as-required-by-dietary-supplement-cgmps/990
Product Review
Preamble

Purity:

• “purity” is used 185 times in Preamble
• “b. Purity. The “purity” of a dietary supplement refers to that portion or percentage of a dietary supplement that represents the intended product.” ~Page 199
Product Review
Purity: Astaxanthin
Astaxanthin (pronounced “asta - zan - thin”) is a red carotenoid and exceptionally powerful antioxidant found in certain species of plants, animals and microalgae. Grown on the pristine Kailua-Kona Coast of Hawaii, Cyanotech sources astaxanthin from natural microalgae Haematococcus pluvialis, nature’s richest and most concentrated source of astaxanthin.
Purity:

• Example: Amount/mg of the substance
• Think of the element or molecule among the other “stuff”
• “…if measuring a standard at 90% purity, there is 90% of the targeted compound”
• By some definitions, the other 10% is impurities; however, not to be confused with the FDA term “contaminants”.
• The area under the main peak when using HPLC
Chemical Purity: Astaxanthin

Astaxanthin Esters

Identification:
- A. Thin-Layer Chromatography
- B. HPLC

Assay:
- Content of Total Astaxanthin
Take Aways:

✓ A purity specification does NOT refer to microbiology.
✓ Understand Good Manufacturing Practices for Dietary Supplements or
✓ Hire someone that does (consultant, chemist, or trade association)
✓ Utilize the industry references available including USP-DS
Thank you!

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